2013 Report on the Management of Overweight and Obesity in Adults:

Full Panel Report Supplement

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PREAMBLE AND TRANSITION TO ACC/AHA GUIDELINES TO REDUCE CARDIOVASCULAR RISK

The goals of the American College of Cardiology (ACC) and the American Heart Association (AHA) are to prevent cardiovascular (CV) diseases, improve the management of people who have these diseases through professional education and research, and develop guidelines, standards and policies that promote optimal patient care and cardiovascular health. Toward these objectives, the ACC and AHA have collaborated with the National Heart, Lung, and Blood Institute (NHLBI) and stakeholder and professional organizations to develop clinical practice guidelines for assessment of CV risk, lifestyle modifications to reduce CV risk, and management of blood cholesterol, overweight and obesity in adults.

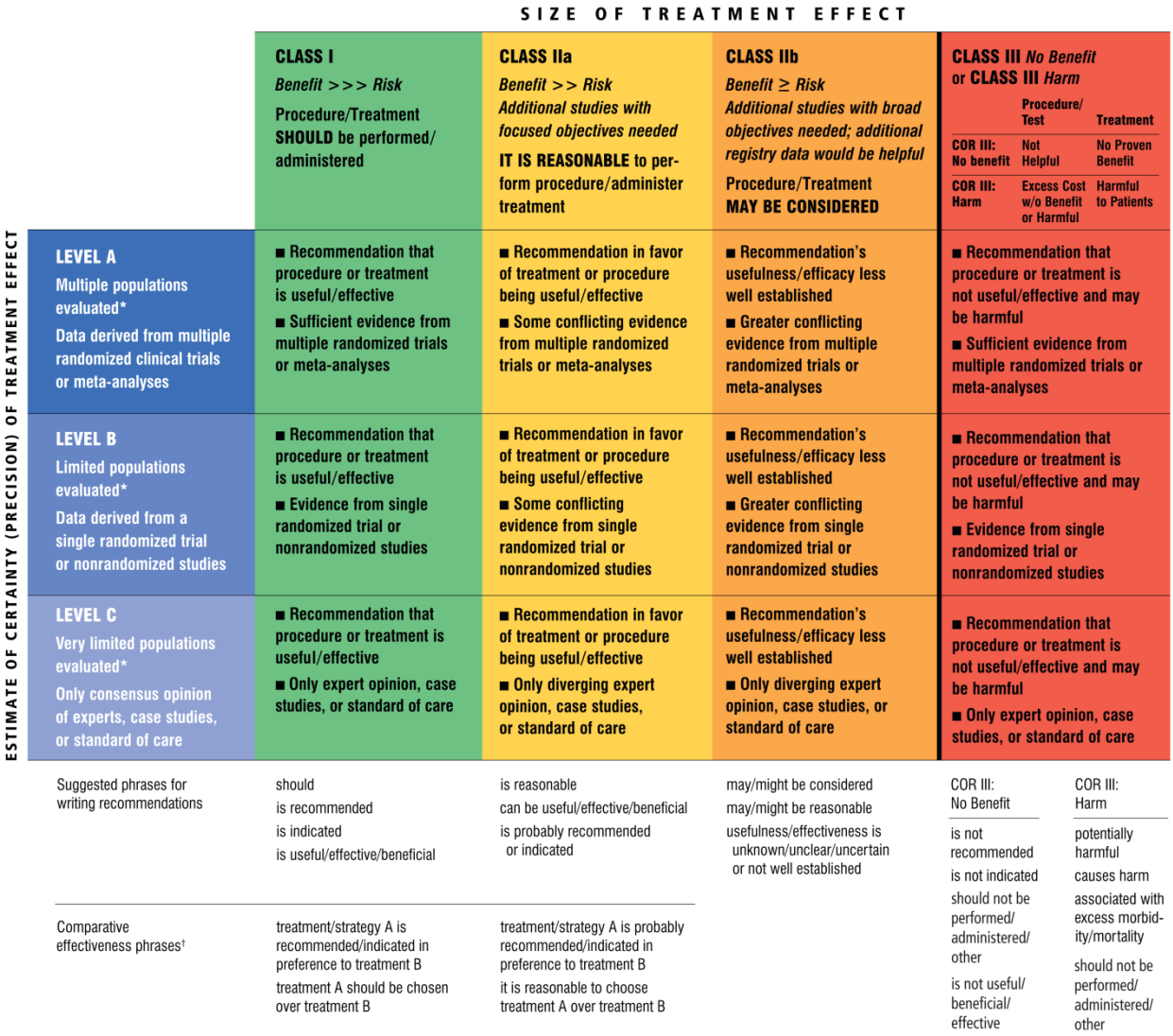
In 2008, the NHLBI initiated these guidelines by sponsoring rigorous systematic evidence reviews for each topic by expert panels convened to develop critical questions, interpret the evidence and craft recommendations. In response to the 2011 report of the Institute of Medicine on the development of trustworthy clinical guidelines (1), the NHLBI Advisory Council (NHLBAC) recommended that the NHLBI focus specifically on reviewing the highest quality evidence and partner with other organizations to develop recommendations (2,3). Accordingly, in June 2013 the NHLBI initiated collaboration with the ACC and AHA to work with other organizations to complete and publish the 4 guidelines noted above and make them available to the widest possible constituency. Recognizing that the expert panels did not consider evidence beyond 2011 (except as specified in the methodology), the ACC, AHA and collaborating societies plan to begin updating these guidelines starting in 2014.

The joint ACC/AHA Task Force on Practice Guidelines (Task Force) appointed a subcommittee to shepherd this transition, communicate the rationale and expectations to the writing panels and partnering organizations and expeditiously publish the documents. The ACC/AHA and partner organizations recruited a limited number of expert reviewers for fiduciary examination of content, recognizing that each document had undergone extensive peer review by representatives of the NHLBAC, key Federal agencies and scientific experts. Each writing panel responded to comments from these reviewers. Clarifications were incorporated where appropriate, but there were no substantive changes as the bulk of the content was undisputed.

Although the Task Force led the final development of these prevention guidelines, they differ from other ACC/AHA guidelines. First, as opposed to an extensive compendium of clinical

information, these documents are significantly more limited in scope and focus on selected critical questions in each topic, based on the highest quality evidence available. Recommendations were derived from randomized trials, meta-analyses, and observational studies evaluated for quality, and were not formulated when sufficient evidence was not available. Second, the text accompanying each recommendation is succinct, summarizing the evidence for each question. The Full Panel Reports include more detailed information about the evidence statements that serves as the basis for recommendations. Third, the format of the recommendations differs from other ACC/AHA guidelines. Each recommendation has been mapped from the NHLBI grading format to the ACC/AHA Class of Recommendation/Level of Evidence (COR/LOE) construct (Table 1) and is expressed in both formats. Because of the inherent differences in grading systems and the clinical questions driving the recommendations, alignment between the NHLBI and ACC/AHA formats is in some cases imperfect. Explanations of these variations are noted in the recommendation tables, where applicable.

Table 1. Applying Classification of Recommendation and Level of Evidence



A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even when randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

In consultation with NHLBI, the policies adopted by the writing panels to manage relationships of authors with industry and other entities (RWI) are outlined in the methods section of each panel report. These policies were in effect when this effort began in 2008 and throughout the writing process and voting on recommendations, until the process was transferred to

ACC/AHA in 2013. In the interest of transparency, the ACC/AHA requested that panel authors resubmit RWI disclosures as of July 2013. Relationships relevant to this guideline are disclosed in Appendix 1.

Systematic evidence reports and accompanying summary tables were developed by the expert panels and NHLBI. The guideline was reviewed by the ACC/AHA Task Force and approved by the ACC Board of Trustees, the AHA Science Advisory and Coordinating Committee, and the governing bodies of partnering organizations. In addition, ACC/AHA sought endorsement by other stakeholders, including professional organizations. It is the hope of the writing panels, stakeholders, professional organizations, NHLBI, and the Task Force that the guidelines will garner the widest possible readership for the benefit of patients, providers and the public health.

Guidelines attempt to define practices that meet the needs of patients in most circumstances and are not a replacement for clinical judgment. The ultimate decision about care of a particular patient must be made by the healthcare provider and patient in light of the circumstances presented by that patient. As a result, situations might arise in which deviations from these guidelines may be appropriate. These considerations notwithstanding, in caring for most patients, clinicians can employ the recommendations confidently to reduce the risks of atherosclerotic cardiovascular disease events.

See Tables 2 and 3 for an explanation of the NHLBI recommendation grading methodology.

Table 2. NHLBI Grading the Strength of Recommendations

Grade	Strength of Recommendation*
A	**Strong recommendation** There is high certainty based on evidence that the net benefit† is substantial.
B	**Moderate recommendation** There is moderate certainty based on evidence that the net benefit is moderate to substantial, or there is high certainty that the net benefit is moderate.
C	**Weak recommendation** There is at least moderate certainty based on evidence that there is a small net benefit.
D	**Recommendation against** There is at least moderate certainty based on evidence that it has no net benefit or that risks/harms outweigh benefits.
E	**Expert opinion ("There is insufficient evidence or evidence is unclear or conflicting, but this is what the Panel recommends.")** Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, but the Panel thought it was important to provide clinical guidance and make a recommendation. Further research is recommended in this area.
N	**No recommendation for or against ("There is insufficient evidence or evidence is unclear or conflicting.")** Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, and the Panel thought no recommendation should be made. Further research is recommended in this area.

*In most cases, the strength of the recommendation should be closely aligned with the quality of the evidence; however, under some circumstances, there may be valid reasons for making recommendations that are not closely aligned with the quality of the evidence (e.g., strong recommendation when the evidence quality is moderate, like smoking cessation to reduce CVD risk or ordering an ECG as part of the initial diagnostic work-up for a patient presenting with possible MI). Those situations should be limited and the rationale explained clearly by the Panel.
†Net benefit is defined as benefits minus risks/harms of the service/intervention.
CVD indicates cardiovascular risk; ECG, electrocardiography; MI, myocardial infarction; and NHLBI, National Heart, Lung, and Blood Institute.

Table 3. Quality Rating the Strength of Evidence

Type of Evidence	Quality Rating*
• Well-designed, well-executed† RCTs that adequately represent populations to which the results are applied and directly assess effects on health outcomes. • MAs of such studies. Highly certain about the estimate of effect. Further research is unlikely to change our confidence in the estimate of effect.	High
• RCTs with minor limitations‡ affecting confidence in, or applicability of, the results. • Well-designed, well-executed nonrandomized controlled studies§ and well-designed, well-executed observational studies‖. • MAs of such studies.	Moderate

Moderately certain about the estimate of effect. Further research may have an impact on our confidence in the estimate of effect and may change the estimate.	
• RCTs with major limitations. • Nonrandomized controlled studies and observational studies with major limitations affecting confidence in, or applicability of, the results. • Uncontrolled clinical observations without an appropriate comparison group (e.g., case series, case reports). • Physiological studies in humans. • MAs of such studies. Low certainty about the estimate of effect. Further research is likely to have an impact on our confidence in the estimate of effect and is likely to change the estimate.	Low

*In some cases, other evidence, such as large all-or-none case series (e.g., jumping from airplanes or tall structures), can represent high or moderate quality evidence. In such cases, the rationale for the evidence rating exception should be explained by the Panel and clearly justified.
†Well-designed, well-executed refers to studies that directly address the question, use adequate randomization, blinding, allocation concealment, are adequately powered, use ITT analyses, and have high follow-up rates.
‡Limitations include concerns with the design and execution of a study that result in decreased confidence in the true estimate of the effect. Examples of such limitations include, but are not limited to: inadequate randomization, lack of blinding of study participants or outcome assessors, inadequate power, outcomes of interest are not prespecified or the primary outcomes, low follow-up rates, or findings based on subgroup analyses. Whether the limitations are considered minor or major is based on the number and severity of flaws in design or execution. Rules for determining whether the limitations are considered minor or major and how they will affect rating of the individual studies will be developed collaboratively with the methodology team.
§Nonrandomized controlled studies refer to intervention studies where assignment to intervention and comparison groups is not random (e.g., quasi-experimental study design)
‖Observational studies include prospective and retrospective cohort, case-control, and cross sectional studies.

ITT indicates intention-to-treat, MA, meta-analysis; and RCT, randomized controlled trial.

1. ABOUT THE GUIDELINE

1.1 Introduction

1.1.1 Overview

Managing Overweight and Obesity in Adults: Guidelines from the Expert Panel represents the state-of-the-art in critical appraisal of the scientific evidence in five critical areas: risks of obesity

and overweight, benefits of weight loss, and three treatment modalities for achieving weight loss—diet, comprehensive lifestyle change, and bariatric surgery. This report was developed by an expert panel appointed by the NHLBI to update the 1998 *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. The panel chose the five areas based on their importance and relevance to PCPs and the availability of quality research in each area.

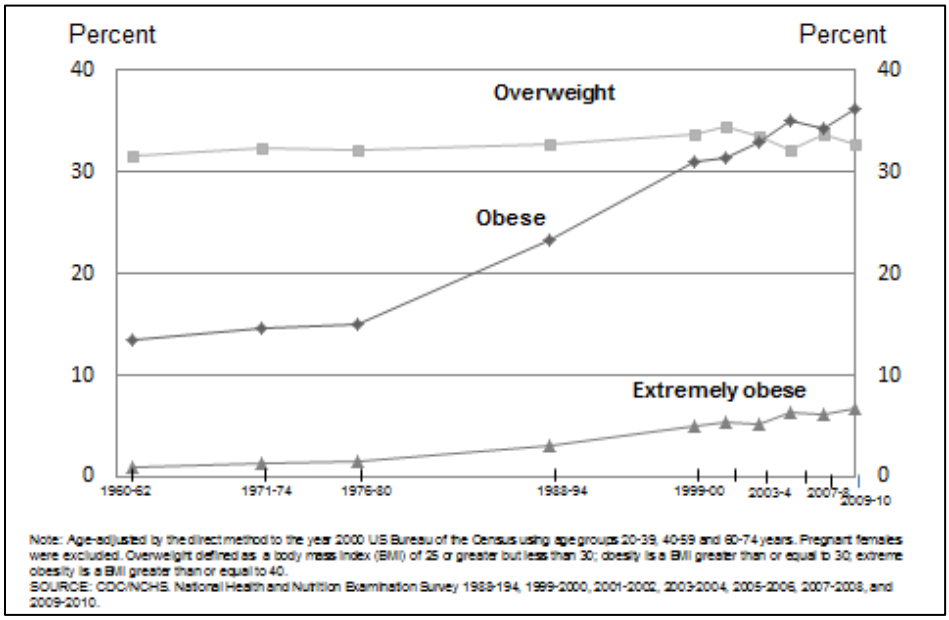
Using a strict, evidence-based methodology to assure rigor and minimize bias, the panel formulated five critical questions (CQs) from a broad and comprehensive list of 23 questions. The panel followed a prespecified methodological development process also used to update the other three ACC/AHA Prevention Guidelines. The first step included a systematic review of the literature for a specific period of time and obtaining a quality rating for each of the papers meeting inclusion criteria. Generally, the panel used papers rated at least good or fair to develop evidence tables and summary tables for all five CQs. When the papers rated good or fair were not available to address a specific component of a CQ, the panel used the papers rated as poor quality to draw conclusions from the evidence. Due to resource constraints, CQ1 and CQ2 used only SRs/MAs rather than individual studies. For each of the CQ's the panel members reviewed the final list of included and excluded articles along with the quality ratings and had the opportunity to raise questions on citations that were missing from the literature search as well as appeal the quality ratings to the methodology team. The team then reexamined these papers and presented their rationale for either keeping or changing the quality rating of the papers. The panel members also played a key role in examining the evidence tables and summary tables to be certain that the data from each paper was accurately displayed. For CQ1 and CQ2, the panel created spreadsheets of the data from the SRs and MAs included in their evidence review.

In the next step, the panel reviewed summary tables of the evidence to formulate evidence statements, rating them as high, moderate, or low, according to the strength of evidence. To grade the body of the evidence and the strength of the recommendations, the NHLBI adapted a system developed by the United States Preventive Services Task Force. Using the graded evidence statements, the panel wrote recommendations and graded them using this system. Along the way, there were strict measures to manage conflict of interest. This process produced guidelines backed by stringent measures to prevent bias and ones that clinicians can trust.

1.1.2 Scope of the Problem

Since the publication of the 1998 Clinical Guidelines (4), the rates of overweight (BMI 25 to 29.9 kg/m^2) and obesity (BMI 30 kg/m^2 or greater) among U.S. adults have not diminished, although there may be a slowing in the trajectory of increase. There are continuing adverse shifts in the distribution of body mass index (BMI) among the U.S. population. From 1998 to 2008, overweight rates were stable and obesity prevalence showed no significant increasing trend among women (adjusted odds ratio (OR) for 2007–2008 vs. 1999–2000) while the rates of obesity in men have significantly increased (5). Figure 2, below, shows the changes in prevalence of overweight, obesity, and extreme obesity (BMI 40 kg/m^2 or greater) from 1960 through 2008, using measured body weight and height from the National Health and Nutrition Examination Survey (NHANES) surveys (6). Furthermore, the latest available rates (7) indicate no decline in obesity rates in the United States; the age-adjusted rates for U.S. adults for 2010 indicate that 35.7 percent are obese, with women aged 60 and older having the highest rates (42.3 percent). Perhaps of greatest concern is the shift in the obese BMI distribution to a higher prevalence of BMI$\geq$40 kg/m^2, which was 6.6 percent in years 2009–2010 (6) and appears to be stabilizing over the last five years.

Figure 2. Trends in adult overweight, obesity, and extreme obesity among adults ages 20 to 74 years: United States, 1960–62 through 2009–10



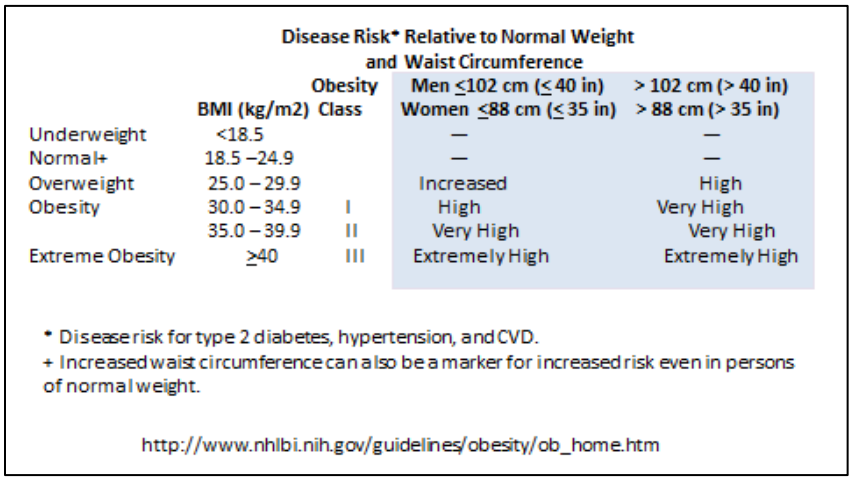
2.2 Background

The 1998 guidelines on overweight and obesity addressed the identification of and risks associated with overweight and obesity and the health effects of weight loss. They also presented various treatment strategies for weight loss, including diet, physical activity, behavior therapy, pharmacotherapy, and surgery. Unlike the previous obesity guidelines, the 2013 guidelines are not intended to be comprehensive; instead, they focus on five CQs based on current knowledge. Notably, the 1998 guidelines accomplished a number of major objectives and presented valuable recommendations on assessment and classification of continued value. First, the guidelines classified overweight and obesity according to BMI, which is calculated by dividing the weight in kilograms by the square of the height in meters (kg/m^2). Overweight is classified as a BMI of 25 to 29.9 kg/m^2, and obesity is classified as Class 1 (BMI 30–34.9 kg/m^2), Class II (BMI 35–39.9 kg/m^2), and Class III or extreme obesity (BMI $\geq$40 kg/m^2). This terminology replaces the term

"morbid obesity," because this term has derogatory connotations, the panel recommends that health care practitioners avoid using it.

Second, the 1998 guidelines linked body fat location to health risks. BMI correlates fairly well with total body fat on a population basis; however, it has limitations in predicting excess body fat associated with health risk on an individual basis. The panel identified excess abdominal fat as associated with greater health risks (abnormal lipid, pro-thrombotic and pro-inflammatory risk factors as well as organ infiltration by fat) than that in peripheral regions. Waist circumference is the most practical measure of abdominal fat. The panel identified waist circumference cutpoints of 40 inches for men and 35 inches for women to aid in individual risk assessment. These guidelines on assessment and classification enabled physicians to identify and treat high-risk patients in their practice. Figure 3 summarizes the 1998 guidelines. This 2013 report reevaluates the association of BMI and waist circumference cutpoints with the risk of CVD, its risk factors, and overall mortality. What are the CVD-related and overall mortality risks associated with overweight and obesity.

Figure 3. The 1998 Clinical Guidelines: Classification of Overweight and Obesity by BMI, Waist Circumference, and Associated Disease Risk



			Disease Risk* Relative to Normal Weight and Waist Circumference	
	BMI (kg/m2)	Obesity Class	Men ≤102 cm (≤ 40 in) Women ≤88 cm (≤ 35 in)	> 102 cm (> 40 in) > 88 cm (> 35 in)
Underweight	<18.5		—	—
Normal+	18.5 –24.9		—	—
Overweight	25.0 – 29.9		Increased	High
Obesity	30.0 – 34.9	I	High	Very High
	35.0 – 39.9	II	Very High	Very High
Extreme Obesity	≥40	III	Extremely High	Extremely High

* Disease risk for type 2 diabetes, hypertension, and CVD.
+ Increased waist circumference can also be a marker for increased risk even in persons of normal weight.

http://www.nhlbi.nih.gov/guidelines/obesity/ob_home.htm

2.2.1 Critical Questions on Overweight and Obesity

The first two CQs address weight-related CVD health risks and benefits of weight loss associated with detectable improvements in CVD risk factors/events, while the other three address treatments for overweight and obesity. The five CQs are as follows:

CQ1: Among overweight and obese adults, does weight loss produce CVD health benefits and what health benefits can be expected with different degrees of weight loss?

CQ2: What are the CVD-related health risks of overweight and obesity and are the current cutpoints for overweight (BMI 25–29.9kg/m^2), obesity (BMI $\geq$30kg/m^2), and waist circumference (>102 cm (M) and >88 cm (F)) appropriate for population subgroups?

CQ3: Which dietary strategies are effective for weight loss?

CQ4: What is the efficacy/effectiveness of a comprehensive lifestyle intervention program (i.e., diet, physical activity, and behavior therapy) in facilitating weight loss or maintaining weight loss?

CQ5: What is the efficacy and safety of bariatric surgery? What is the profile (BMI and comorbidity type) of patients who might benefit from surgery for obesity and related conditions?

2.2.2 Critical Questions on Weight-Related Health Risks And Benefits of Weight Loss

The panel chose CQ1 and CQ2 to help health care practitioners determine when to recommend weight loss. CQ1 asks if weight loss affects CVD risk factors, events, and what cardiovascular health benefits can be expected with different degrees of weight loss. The association of weight loss with increased mortality in many epidemiologic studies challenges explanation. Many

scientists think this may be due to measurement of unintentional weight loss in those studies. Still, this association mandates caution in prescribing weight loss, unless patients are at significant risk for comorbidity, and there is evidence that patients will benefit from weight loss.

CQ2 addresses the CVD-related health risks of overweight and obesity. This question asks if the current, widely-accepted cutpoints for overweight (BMI 25 to 29.9 kg/m^2) and obesity (BMI $\geq$30 kg/m2) and waist circumference (>102 cm (M) and >88 cm (F)) are appropriate for identifying elevated risk of cardiovascular disease, diabetes, hypertension, dyslipidemia, and all-cause mortality in the overall population and key subgroups. This is an important topic because PCPs need to know when to recommend weight loss. All recommended weight loss interventions should be based on an assessment of benefits and risks.

2.2.3 Critical Questions on Treatments for Overweight and Obesity

Patients are interested in popular weight loss diets and often see the health care practitioner as an authoritative source on such diets. CQ3 asks which dietary strategies are effective for weight loss.

The 1998 Clinical Guidelines approach to obesity treatment begins with lifestyle modification—changes in dietary intake and physical activity—and can be facilitated by key behavioral strategies. Typically, comprehensive weight loss programs employ all three components but may vary in modes of delivery, settings, and implementation strategies. CQ4 seeks to determine the efficacy and effectiveness of a comprehensive approach. This question asks how much weight loss can be achieved and how long can it be sustained when these

state-of-the-art approaches are used, and what is the relative impact of varying some key characteristics of how comprehensive programs are delivered to patients.

Surgery for obesity is an increasingly accepted and accessible option. In fact, Medicare and many insurers now reimburse for this type of surgery. The most frequently used surgical procedures are the laparoscopic gastric band, laparoscopic or open Roux-en-Y (RYGB), sleeve gastrectomy, and biliopancreatic diversion (BPD). CQ5 asks about the efficacy and safety of these procedures by evaluating long-and short-term benefits (risk factors, morbidity, and mortality) and safety. CQ5 also asks about the profile of patients (BMI and comorbidity type) who might benefit from this surgery. Answers to these questions will guide primary care physicians on appropriate recommendations for obese patients who may be surgical candidates.

The panel decided *not* to address pharmacotherapy for chronic obesity management with a specific CQ. When the panel selected CQs, only two medications were available and approved for chronic use (orlistat and sibutramine). In addition, neither was prescribed widely in primary care, and sibutramine was removed from the market in 2010. The panel did, however, address the effect of orlistat on weight loss and risk factors in CQ1, since the question dealt with the effect of weight loss on risk via a variety of methods and several meta-analyses covered this topic. Other medications were in later stages of development, but there were insufficient published data to conduct a systematic review. In the interim, two recently approved medications for weight loss—the combination phentermine and topiramate (8-10) and lorcaserin (11-13)—have a growing evidence base. There are also several SRs of pharmacotherapy (14-17).

2.2.4 Challenges of Achieving Weight Loss in Primary Care Practice

Patients face many challenges in achieving weight loss, including learning a certain set of skills and behaviors. Part of PCPs' role is to help patients learn and practice these skills. CQ4 presents evidence that a comprehensive approach to lifestyle change for weight loss is achievable, and CQ3 underscores the efficacy of many alternative dietary interventions for healthy weight loss when implemented by qualified nutrition professionals. PCPs may also prescribe weight loss medications as an adjunct or refer appropriately selected patients for different kinds of bariatric surgery, which CQ5 examines.

PCPs also must be knowledgeable about the underlying biology that fights weight loss and promotes weight regain. Since the 1998 guidelines, research has shown that for a given environment, body size is predicted largely by genetic factors. In fact, there are strong physiologic mechanisms that resist weight loss and promote regain after weight loss: changes in fat, gut, and neural signals that regulate appetite and metabolism. Dynamic physiological adaptations occur with decreased body weight, which may alter the time course of individual weight change in response to behavioral interventions (17).

Understanding obesity as a complex, chronic disease is essential for providing effective health care for overweight and obese patients. The pathway to effective weight loss and weight loss maintenance is through long-term changes to eating and physical activity behaviors. Respect for patients and their autonomy and practitioner skills in coaching and motivating patients are all qualities that promote successful obesity management. Increasingly, these skills are being addressed in postgraduate training programs. An important role for PCPs is to assist patients in developing these skills, including referral to trained interventionists where appropriate.

A final note on the challenges of weight loss must address the potential harms of weight loss, itself. In addition to the risks of pharmacological or surgical treatments for obesity, there are other weight loss risks such as cholelithiasis. Improvements in fertility with weight loss may result in unplanned pregnancy. In addition, dietary restriction and weight loss may lead to hypoglycemia or hypotension in those on medication, requiring careful monitoring and dose adjustment as needed. Finally, for older people, weight loss is advised with caution and is not advisable for those over 80 years; reduced muscle mass and frailty may occur.

2.2.5 Challenges to Adapting Guidelines' Recommendations for Primary Care Practitioners

One major challenge to developing recommendations from evidence reviews is that the evidence was invariably based upon populations, either large ones from epidemiologic studies or smaller ones in randomized clinical trials. Because the data are aggregated, they do not consider the individual. Thus, the challenge was to make recommendations appropriate to the needs of the individual patient being seen in a real practice.

The Obesity Panel members believe that the recommendations in these guidelines can inform health care practitioners and help guide their assessment and treatment recommendations. Their intention is to guide practitioners in achieving best practices in the real world.

2 PROCESS AND METHODS OVERVIEW

2.1 Background and Description of the Project

To address its mission to accelerate the application of health research to strategies and programs for the prevention, detection, and treatment of cardiovascular, lung, and blood diseases, and to narrow the discovery-delivery gap, the NHLBI has sponsored the development of clinical practice guidelines since the 1970s. In 2005, recognizing the need to update the most recent cardiovascular guideline reports, the NHLBI convened stakeholder groups to provide input on the next-generation guidelines development process. As a result, these groups recommended five integral and complementary steps:

- Maintain risk-factor-specific cardiovascular clinical practice guidelines.
- Take a standardized and coordinated approach to the risk factor guidelines updates.
- Take a more evidence-based approach to development and implementation.
- Give more attention to implementation issues and work closely with stakeholders in health care and community systems for translation and dissemination of the evidence base.
- Develop an integrated cardiovascular disease (CVD) risk reduction guideline that addresses the realities of clinical practice where individuals often have multiple risk factors that interact in various ways to accelerate the development of CVD.

In 2008, the NHLBI established expert panels to develop updates of the guidelines for high blood cholesterol, high blood pressure, and overweight/obesity. In addition, three work groups were convened to examine crosscutting issues: risk assessment, lifestyle intervention, and guidelines

implementation. These work groups were formed to develop their own recommendations and to provide input to the expert panels. A Guidelines Executive Committee, composed of panel and work group co-chairs and NHLBI staff, coordinated the work of the panels and work groups.

In October 2011, the National Program to Reduce Cardiovascular Risk (NPRCR) was established to help implement the clinical guidelines through the many stakeholder organizations, which comprise the Coordinating Committee. The NPRCR includes thought leaders representing cardiovascular health, primary care, health services research, health informatics, and Federal agencies working on cardiovascular risk reduction activities.

2.2 Overview of Evidence-Based Methodology

To continually improve the quality and impact of NHLBI guidelines, the guideline development process was updated to assure rigor and minimize bias. Part of this process included using a rigorous evidence-based methodology, and developing evidence statements and recommendations based on SRs of the biomedical literature for specific periods of time.

The development process followed most of the standards from the Institute of Medicine report, "Clinical Practice Guidelines We Can Trust," which states that trustworthy guidelines should:

- Be based on a systematic review of the existing evidence.
- Be developed by a knowledgeable, multidisciplinary panel of experts and representative of key affected groups.
- Consider important patient subgroups and patient preference, as appropriate.

- Be based on an explicit and transparent process that minimizes distortion, biases, and conflicts of interest.

- Provide a clear explanation of logical relationships between alternative care options and health outcomes, and provide ratings of both the quality of evidence and the strength of the recommendations.

- Be reconsidered and revised as appropriate when important new evidence warrants modifications of recommendations

The NHLBI convened expert panels and workgroups consisting of clinical and non-clinical experts to develop the guidelines. The Obesity Guidelines Panel included individuals with specific expertise in a range of areas: psychology, nutrition, physical activity, bariatric surgery, epidemiology, internal medicine, and other clinical specialties. In creating the guidelines, all panels and work groups followed the same methods, with variations as needed to reflect the evidence in the field as well as time and resource constraints. The methodology included numerous components and followed a prespecified development process. Directed by NHLBI, with support from a methodology contractor and a systematic review and general support contractor, the expert panels and work groups:

- Developed an evidence model.

- Constructed critical questions (CQs) most relevant to clinical practice. CQs followed the "PICOTS" (patient population, intervention/exposure, comparison group, outcome, timing, and setting) format.

- Identified (a priori) I/E criteria for each CQ

Directed by the NHLBI, with input from the panels and work groups, the contractor staff:

- Developed a search strategy based on I/E criteria for each CQ.

- Executed a systematic electronic search of the published literature from relevant bibliographic databases for each CQ. The date for the overall literature search was from January 1998 to December 2009. Since CQ1 and CQ2 used SRs and meta-analyses, the literature search included those published from January 2000 to October 2011. CQ3 and CQ4 added major RCTs published after 2009 with greater than 100 people per treatment arm; and CQ5 added some major studies published after 2009 that met the I/E criteria.

- Screened, by two independent reviewers, thousands of abstracts and full text articles to identify relevant original articles, SRs, and/or MAs. They applied rigorous validation procedures to ensure that the selected articles met the pre-established I/E criteria before they were included in the final review results.

- Determined, by two independent raters, the quality of each included study. The methodology staff, with NHLBI input, adapted study-rating instruments and trained study raters on the use of these instruments. Six quality assessment tools were designed to assist reviewers in the critical appraisal of a study's internal validity.

- Reviewers used the study ratings to judge each study to be of "good," "fair," or "poor" quality. The reviewers used the ratings to assess the risk of bias in the study due to flaws in study design or implementation.

- Abstracted relevant information from the included studies into an electronic central repository database. Templates with lists of data elements pertinent to the established I/E criteria were constructed and used to support abstraction.

- Constructed detailed evidence tables to organize the data from the abstraction database.

- Analyzed the evidence tables and constructed summary tables, which display the evidence in a manageable format to answer specific parts of the CQ.

The Expert Panels and Work Groups:

- Used summary tables to develop evidence statements for each CQ. The quality of evidence for each evidence statement was graded as high, moderate, or low based on scientific methodology, scientific strength, and consistency of results. (See discussion below.) For CQ1 and CQ2, spreadsheets with relevant data from SRs/MAs rather than summary tables were developed.

- Used the graded evidence statements to write clinical recommendations and grade the strength of each recommendation.

- Performed Guideline Implementability Appraisals, planned and coordinated by the NHLBI Implementation Work Group, to identify and address barriers to guideline implementation.

- Drafted a report that underwent a formal peer review process initially completed under the auspices of the NHLBI that included 10 scientific experts and representatives of selected Federal agencies.

See Appendix 2 for more details on the evidence-based process and Appendix 3 for literature search strategies used for CQs.

3.2.1 System for Grading Body of Evidence and Strength of Recommendations

The NHLBI adapted a system developed by the U.S. Preventive Services Task Force to grade the body of the evidence and strength of the recommendations. The panels graded the evidence statements for quality as high, moderate, or low (see Table 1 below). They then graded the recommendations as Strong Recommendation (Grade A), Moderate Recommendation (Grade B), Weak Recommendation (Grade C), Recommendation Against (Grade D), Expert Opinion (Grade E), or No Recommendation for or Against (Grade N) (see Table 2 below). The grades provide guidance to PCPs and other practitioners on how well the evidence supports the evidence statements and recommendations. The strength of the body of evidence represents the degree of certainty, based on the overall body of evidence, that an effect or association is correct. Appendix 2-6 describes how four domains of the body of evidence—risk of bias, consistency, directness, and precision—were used to grade the strength of evidence.

Table 1.0 Quality Rating the Strength of Evidence

Type of Evidence	Quality Rating*
• Well-designed, well-executed[§] RCTs that adequately represent populations to which the results are applied and directly assess effects on health outcomes. • MAs of such studies. Highly certain about the estimate of effect. Further research is unlikely to change our confidence in the estimate of effect.	High
• RCTs with minor limitations[†] affecting confidence in, or applicability of, the results. • Well-designed, well-executed nonrandomized controlled studies[$] and well-designed, well-executed observational studies[+]. • MAs of such studies.	Moderate

Moderately certain about the estimate of effect. Further research may have an impact on our confidence in the estimate of effect and may change the estimate.	
• RCTs with major limitations. • Nonrandomized controlled studies and observational studies with major limitations affecting confidence in, or applicability of, the results. • Uncontrolled clinical observations without an appropriate comparison group (e.g., case series, case reports). • Physiological studies in humans. • MAs of such studies. Low certainty about the estimate of effect. Further research is likely to have an impact on our confidence in the estimate of effect and is likely to change the estimate.	Low

*In some cases, other evidence, such as large all-or-none case series (e.g., jumping from airplanes or tall structures), can represent high or moderate quality evidence. In such cases, the rationale for the evidence rating exception should be explained by the panel and clearly justified.

§ Well-designed, well-executed refers to studies that directly address the question, use adequate randomization, blinding, allocation concealment, are adequately powered, use ITT analyses, and have high follow-up rates.

† Limitations include concerns with the design and execution of a study that result in decreased confidence in the true estimate of the effect. Examples of such limitations include, but are not limited to: inadequate randomization, lack of blinding of study participants or outcome assessors, inadequate power, outcomes of interest are not pre-specified or the primary outcomes, low follow-up rates, or findings based on subgroup analyses. Whether the limitations are considered minor or major is based on the number and severity of flaws in design or execution. Rules for determining whether the limitations are considered minor or major and how they will affect rating of the individual studies will be developed collaboratively with the methodology team.

$ Nonrandomized controlled studies refer to intervention studies where assignment to intervention and comparison groups is not random (e.g., quasi-experimental study design)

+ Observational studies include prospective and retrospective cohort, case-control, and cross sectional studies.

Table 2.0 Grading the Strength of Recommendations

Grade	Strength of Recommendation*
A	**Strong recommendation** There is high certainty based on evidence that the net benefit+ is substantial.
B	**Moderate recommendation** There is moderate certainty based on evidence that the net benefit is moderate to substantial, or there is high certainty that the net benefit is moderate.
C	**Weak recommendation** There is at least moderate certainty based on evidence that there is a small net benefit.
D	**Recommendation against** There is at least moderate certainty based on evidence that it has no net benefit or that risks/harms outweigh benefits.
E	**Expert opinion ("There is insufficient evidence or evidence is unclear or conflicting, but this is what the panel recommends.")** Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, but the panel thought it was important to provide clinical guidance and make a recommendation. Further research is recommended in this area.
N	**No recommendation for or against ("There is insufficient evidence or evidence is unclear or conflicting.")** Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, and the panel thought no recommendation should be made. Further research is recommended in this area.

*In most cases, the strength of the recommendation should be closely aligned with the quality of the evidence; however, under some circumstances, there may be valid reasons for making recommendations that are not closely aligned with the quality of the evidence (e.g., strong recommendation when the evidence quality is moderate, like smoking cessation to reduce CVD risk or ordering an ECG as part of the initial diagnostic workup for a patient presenting with possible MI). Those situations should be limited and the rationale explained clearly by the panel

+ Net benefit is defined as benefits minus risks/harms of the service/intervention

3.3 Critical Question-Based Approach

The body of this report is organized by CQ. For each CQ:

- The rationale for its selection is provided and methods described.
- The body of evidence is summarized, and evidence statements, which include a rating for quality, are presented. A narrative summary also supports each evidence statement.

- Recommendations and recommendation strength are accompanied by a summary of how the recommendation derives from the evidence and a discussion of issues the expert panel considered in formulating the recommendation.

A detailed description of the evidence based approach and methods is provided in Appendix 2. The appendix presents all tools used in the development of the present SRs, as well as documentation for search strategies and results from the search of the published literature. See Appendix 3 for information on the literature search strategies used for each of the critical questions considered in the evidence review, their PRISMA diagrams, and their list of studies rated as poor with the rationale behind the rating. PRISMA stands for Preferred Reporting Items for Systematic Reviews and Meta-Analyses and is an evidence-based minimum set of items for reporting in SRs and MAs.

3.3.1 Rationale for Choosing the Critical Questions for the Obesity Guidelines

Overweight and obesity affect more than two in three U.S. adults. Data from the National Health and Nutrition Examination Survey, 2009–2010 suggests that obesity estimates for men and women did not differ significantly from those for 2003–2008. Increases in population obesity prevalence rates appear to be slowing or leveling off (18), although of concern is the prevalence of obesity, now at more than 35 percent of U.S. adults and severe obesity (BMI $\geq$40 kg/m^2), now at approximately 6.6 percent of U.S. adults. The epidemic of obesity is associated with a "twin epidemic" of type 2 diabetes, which threatens to reverse the gains in CVD mortality reduction observed over the last half-century. Obesity is also associated with other biological and psychological comorbidities. All these findings severely, affect public health and health care delivery costs. Consequently, the Obesity Guidelines Panel created up-to-date guidelines on the

evaluation and management of obesity to help PCPs identify patients at risk for weight-related comorbidities and inform them about the benefits and risks of weight loss achieved with various approaches.

3.3.2 Critical Questions on Overweight and Obesity

The Obesity Guidelines Panel began the process of selecting CQs by collecting proposed questions and topic areas, prioritizing questions based on resource constraints, and ranking the questions through discussion and voting. From the 23 identified questions, the panel chose five CQs to address. The topics considered but not selected included the following: genetics, binge eating disorders, physical activity, pharmacotherapy, and cost effectiveness of interventions to treat and manage obesity.

The first two CQs address weight-related health risks of obesity and benefits of weight loss, while the other three address treatments and for overweight and obesity. The five CQs are as follows:

CQ1: Among overweight and obese adults, does weight loss produce CVD-related health benefits and what health benefits can be expected with different degrees of weight loss?

CQ2: What are the CVD-related health risks of overweight and obesity and are the current cutpoints for overweight (BMI 25–29.9kg/m^2) and obesity (BMI $\geq$30kg/m^2) and waist circumference (>102 cm (M) and >88 cm (F)) appropriate for population subgroups?

CQ3: Which dietary intervention strategies are effective for weight loss?

CQ4: What is the efficacy/effectiveness of a comprehensive lifestyle intervention program (i.e., diet, physical activity, and behavior therapy) in facilitating weight loss or maintaining weight loss?

CQ5: What is the efficacy and safety of bariatric surgery? What is the profile (BMI and comorbidity type) of patients who might benefit from surgery for obesity and related conditions?

The panel chose CQ1 and CQ2 to help health care practitioners determine when to recommend weight loss. CQ1 asks if weight loss affects CVD risk factors and events, and what CVD-related health benefits can be expected with different degrees of weight loss. The association of weight loss with increased mortality in many epidemiologic studies challenges explanation. Many scientists believe this may be due to measuring *unintentional* weight loss in those studies. Still, this association suggests that practitioners should be cautious in prescribing weight loss, unless patients are at high risk for comorbidity or there is evidence that patient will benefit from weight loss.

CQ2 addresses the CVD-related health risks of overweight and obesity. This question asks if the widely accepted cutpoints defining individuals as overweight (BMI 25–29.9 kg/m^2) and obese (BMI $\geq$30kg/m^2) and the current waist circumference cutpoints (>102 cm (M) and >88 cm (F)) are appropriate for identifying elevated risk of cardiovascular disease, diabetes, hypertension, dyslipidemia, and all-cause mortality in population subgroups. This is an important topic on which to comment, because PCPs need to know when to recommend weight gain prevention or weight loss.

CQ3 asks which dietary strategies are effective in achieving weight loss. Patients are interested in the popular weight-loss diets and view the primary care practitioner as an authoritative source on such diets. To achieve weight loss, most practitioners recommend a comprehensive approach: diet, physical activity, and behavior therapy. CQ4 seeks to determine the efficacy and effectiveness of a comprehensive approach. Specifically, this CQ asks how much weight loss can

be achieved and how long it can be sustained when these state-of-the-art approaches are used and what is the impact of each of the components of the comprehensive programs.

Since the 1998 Obesity Clinical Guidelines Report, bariatric surgery has evolved and is now being used more frequently. Surgical procedures most often used include the laparoscopic gastric band, laparoscopic or open RYGB, sleeve gastrectomy, and BPD. CQ5 explores the efficacy and safety of these procedures, including the long-and short-term benefits (risk factors, morbidity and mortality) and safety. In addition, CQ5 asks what profile (BMI and comorbidity type) of patients might benefit from bariatric surgery. Answers to these questions will help guide PCPs in advising and referring obese patients for this surgery.

The five CQs on overweight and obesity will help practitioners identify patients who need intervention and determine which weight loss techniques to recommended. Importantly, the questions target areas in which recent research has yielded discoveries. They also highlight important topics in which informed practitioners can impact public health.

3 CRITICAL QUESTION 1

3.1 Statement of the Question

1. Among overweight and obese adults, does achievement of reduction in body weight with lifestyle and pharmacological interventions affect CVD risk factors, CVD events, morbidity, and mortality?

    a. Does this effect vary across population subgroups defined by the following demographic and clinical characteristics:

1. Age
2. Sex
3. Race/ethnicity
4. Baseline BMI
5. Baseline waist circumference?
6. Presence or absence of comorbid conditions?
7. Presence or absence of CVD risk factors?

b. What amount (shown as percent lost, pounds lost, etc.) of weight loss is necessary to achieve benefit with respect to CVD risk factors, morbidity, and mortality?

1. Are there benefits on CVD risk factors, CVD events morbidity, and mortality from weight loss?
2. What are the benefits of more significant weight loss?

c. What is the effect of sustained weight loss for 2 or more years in individuals who are overweight or obese, on CVD risk factors, CVD events and health and psychological outcomes?

1. What percent of weight loss needs to be maintained at 2 or more years to be associated with health benefits?

3.1.1. By Population Subgroups

- Age

- Sex
- SES - no evidence anticipated
- Race/ethnicity
- Baseline BMI (Overweight (BMI 25.0–29.9) vs. obese (BMI ≥30.0)
- Baseline Waist Circumference
- Presence or Absence of Comorbid conditions
  - Diabetes
  - Metabolic syndrome
  - Depression
  - Quality of life issues
- Presence or Absence of CVD risk factors
  - Smoking
  - More than one risk factor
  - Baseline (not necessarily pre-treatment) LDL-C >100 mg/dL
  - Triglycerides ≥200 mg/dL
  - HDL-C<40 mg/dL

- Hypertension
- Diminished cardio-respiratory fitness
- Previous CVD event
- Elevated CRP

3.1.2. By Amount of Weight Loss

- Different cutpoints
- Significant weight loss ·

3.1.3. By Weight Loss Maintenance

- Different cutpoints

3.2 Selection of the Inclusion/Exclusion Criteria

Panel members developed eligibility criteria, based on a PICOTS approach, for screening potential studies for inclusion in the evidence review. The criteria included the PICOTS criteria as the first six and then also several others related to study design, language, publication type, and publication time frame. Table 3.0 presents the details of the PICOTS approach for CQ1.

Table 3.0 Criteria for Selection of Publications for CQ1

	Inclusion criteria	Exclusion criteria
Population	Adults	• Children • Animals studies
Intervention	Single or multi lifestyle or pharmacologic interventions	• Any pharmacological agents that are not FDA approved for long-term treatment of

	Inclusion criteria	Exclusion criteria
		obesity. • Bariatric surgical interventions (laparoscopic adjustable gastric banding; laparascopic RYGB; open RYGB; bilio-pancreatic bypass/duodenal switch; GS)
Comparator	• No intervention (except for in pharmacological interventions where the comparator can be lifestyle) • Usual care, control, or minimal treatment	
Outcomes	Reduction in body weight as measured by: • Weight (kg, lbs., %) • Body fat measures: (BMI and BMI change) • Waist circumference • Waist-hip ratio • Percent body fat (includes body composition changes) • Weight loss maintenance • Percent reduction of excess weight **Must have one a body weight measure plus one or more of the following outcomes** <u>CVD Events (allows for self-reported weight)</u> • Myocardial infarction • Heart failure • Hospitalization for heart failure or stroke <u>CVD Risk Factors</u> • Systolic blood pressure or diastolic blood pressure • Total cholesterol, HDL-C, LDL-C, Non-HDL-C, Triglycerides • Fasting insulin, fasting glucose, HbA1c, diagnosis of diabetes • Smoking Status • C-reactive protein (CRP) Morbidity • CHD/CVD • Chronic renal failure • Nonalcoholic steatohepatitis • Depression Mortality • CVD-related • All-cause Body Composition Changes • Quality of Life – Function	Self-reported weight (only allowed in studies reporting CVD events; for risk factors, the studies have to report measured weight) Studies that combine weight loss and weight maintenance after successful weight loss results in a manner that does not allow the two study designs to be independently assessed.

	Inclusion criteria	Exclusion criteria
	– Disability	
Time	• Intervention period: no limits • Follow-up period is 6 months or more, with breakdowns where possible by: ≥6 months to 12 months; greater than one year.	Follow-up of less than 6 months
Setting	• U.S. • European Union • Australia • New Zealand • Israel • Any clinical or research setting	Countries not applicable to western weight goals and diets
Study Design	• SRs of RCTs or controlled clinical trials	• All other studies
Language	• Full-text must be available in English	• Studies where the abstract only, and not the full text, is available in English
Publication Type	• Published SR/MA studies	• Unpublished literature – Unpublished industry-sponsored trials – Other unpublished data • FDA Medical and Statistical reviews • Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Publication Time Frame	• Search for SRs/MAs between 2000-10/2011	• Studies published before 2000

3.3 Introduction and Rationale for Question and Inclusion/Exclusion Criteria

CQ1 addresses the health benefits of weight loss in overweight and obese adults in terms of reduction in terms of cardiovascular risk factors, events, morbidity and mortality. Our goal was to determine whether risk reduction varied as a function of pre-weight loss risk factors, degree of overweight, age, sex, ethnicity and waist circumference. We also sought to assess what degree of weight loss is associated with detectable improvements in CVD risk factors/events, whether there is evidence for greater improvements with greater weight loss, and the benefits of prolonged (≥2

years) weight loss. This is an important topic because health care providers should be able to judge the relative benefits of reducing weight and be able to explain these benefits to patients considering a weight loss program.

3.4 Methods for Critical Question1

The Obesity Panel formed subcommittees for each of its five CQs. For CQ1 the subcommittee was chaired by a physician and was composed of physicians and investigators representing academic institutions across the U.S.

Question 1 addresses the relationship between weight loss and reductions in CVD risk factors and events as a function of the pre-existing status of the patients being treated. The methodology team assisted by applying the PICOTS criteria. The methodology team also worked with the CQ1 panel members to develop and refine the detailed I/E criteria. CQ1 was initially intended to be a de novo systematic review of original studies plus SRs/MAs). In 2011, the CQ was de-scoped and restricted to SRs/MAs only. In order to accomplish our goal within the allocated resources the NHLBI staff and panel members decided that CQ1 and CQ2 would focus primarily on evidence available from SRs, MAs and a limited number of individual articles that represent studies with impact equal to SRs and MAs. This approach allowed the CQ1 members to address some, but not all elements of CQ1.

The literature search for CQ1 included an electronic search of the Central Repository for SR/MAs published in the literature from January 2000 - October 2011. The Central Repository contains citations pulled from seven literature databases (PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts). The search produced 1633

citations, with 3 additional citations identified from non-search sources (i.e., by the panel members) (19-21).

Figure 5 below of the PRISMA diagram outlines the flow of information from the literature search through the various steps used in the systematic review process.

The titles and abstracts of 1630 publications were screened against the I/E criteria independently by two reviewers which resulted in 669 publications being excluded and 697 publications being retrieved for full text review to further assess eligibility. Six hundred and ninety-seven full-text publications were independently screened by two reviewers who assessed eligibility by applying the I/E criteria; 669 of these publications were excluded based on one or more of the I/E criteria (see specified rationale as noted in the PRISMA).

Forty-two of the 697 full-text publications met the criteria and were included. The quality (internal validity) of these 42 publications was assessed using the quality assessment tool developed to assess SRs/MAs or RCTs (see Appendix 2). Of these, 14 publications were rated as poor quality (22-35). The rationales for all of the poor quality studies are included in Appendix 3. The remaining 28 publications were rated good or fair quality (19,20,36-61) and included in the evidence base that was used to formulate the evidence statements and recommendations. The panel members reviewed the final articles on the include list along with their quality ratings and had the opportunity to raise questions. The review of evidence for CQ1 was based largely upon SRs and MAs of randomized clinical trials and observational cohort studies that were published between the years of 2001 and 2011. Results from selected individual RCTs that included approximately the same number of participants/observations as were available in the SRs and MAs within topic areas (diabetes/glucose, lipids and blood pressure) were also used.

Approval was received from NHLBI to use relevant data from an RCT study (i.e., Look AHEAD). The following is the rationale. Look AHEAD (Action for Health in Diabetes) is a prospective, multicenter, randomized clinical trial that examined the effects of intervention vs. usual diabetes care, referred to as diabetes support and education (DSE), on cardiovascular morbidity and mortality in 5,145 overweight or obese participants with type 2 diabetes. This single trial provides data on more patients than the two MAs by Norris (50) and Norris (47) (N=4659), almost as many as the Norris (49) (N=5956) and Orozco (62) (N=5956). The investigators provided 4-year comparison outcome data (20). The investigators provided 4-year comparison outcome data (Look AHEAD, (Wing 2010) and, more importantly, 1≥year dose-response data that relates the amount of weight loss to pre-defined CVD risk factors (19).

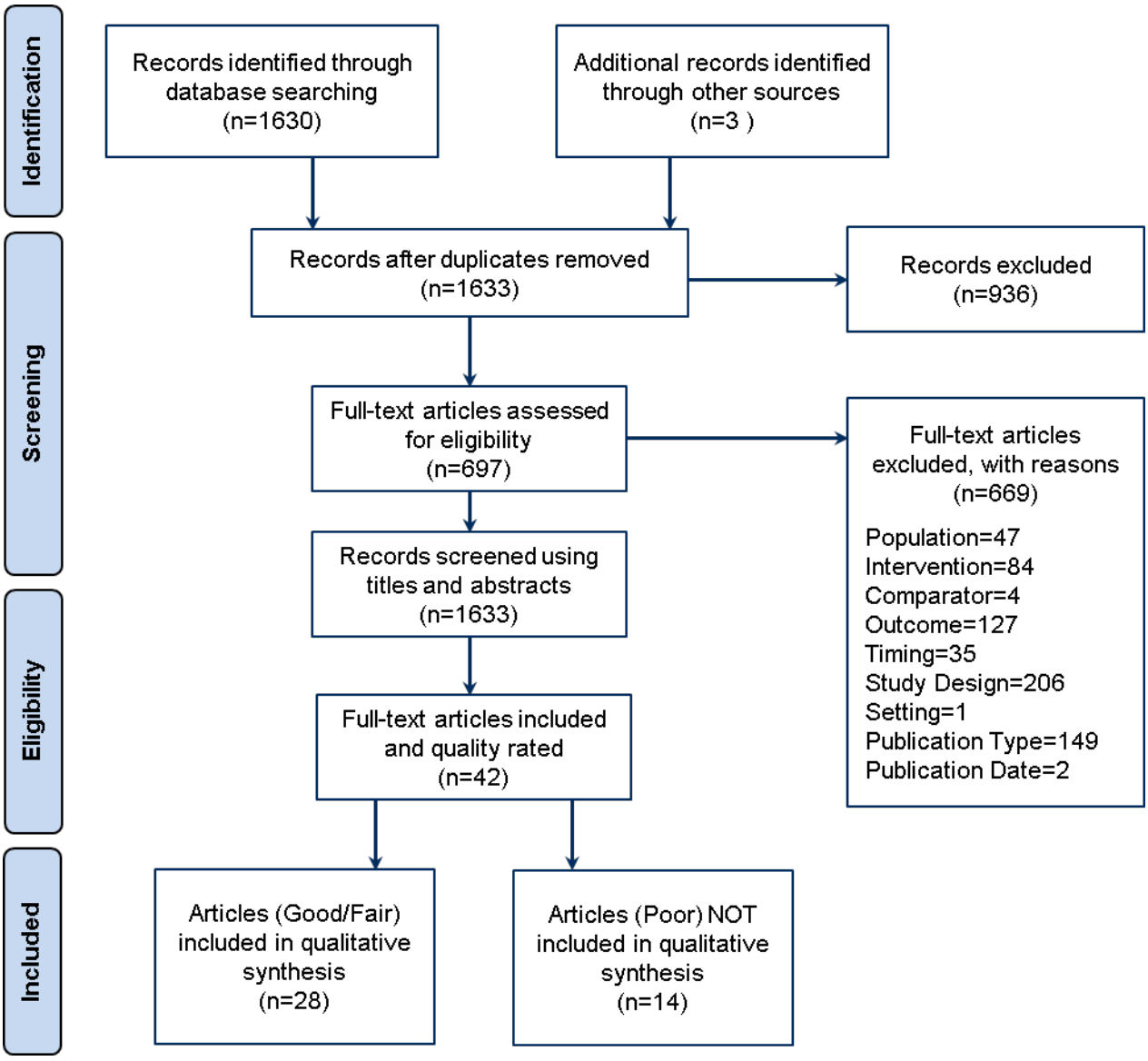
Subsequent to receiving approval to include relevant data from Look AHEAD, an additional search was made (of the de novo citations include during the early screening stages) for RCTs of similar size to the Look AHEAD (≥5,000); through this process; no additional relevant studies were found.

For this CQ1, spreadsheets (containing key information from the SRs/MAs and the Look AHEAD studies) were created by the panel members; these spreadsheets (cross-checked by the methodology and systematic review teams for accuracy) formed the basis for panel deliberations.

To examine the possible effects of weight loss on mortality, longitudinal, prospected cohort studies were used in order to assure enough events were recorded that would assure a reasonably accurate estimate of effect. These types of studies are, by necessity, different from prospective randomized clinical trials, in which for ethical reasons the control group must receive the standard

of care for cardiovascular risk factors. In observational cohort studies the participants may or may not receive community standard care for risk factors.

Figure 5. PRISMA Diagram Showing Selection of Articles for Obesity Question 1



3.5 Evidence Statements and Summaries

3.5.1. Weight Loss and Risk of Diabetes–Spreadsheets 1.1–1.4b

Diabetes outcomes were derived from nine SRs/MAs and two primary publications from the Look AHEAD study. The literature available to us did not specifically address whether age, sex, ethnicity or waist circumference influence the response to weight loss in terms of CVD risk reduction.

Evidence Statement 1—In overweight and obese adults at risk for type 2 diabetes, average weight losses of 2.5-5.5 kg at 2 or more years, achieved with lifestyle treatment (with or without orlistat) reduces the risk of developing type 2 diabetes by 30-60 percent.

Strength of Evidence: High

Rationale: MAs and SRs (36,38,48), largely using the same database, consistently find that intentional weight loss reduces the risk of developing type 2 diabetes in at risk populations. Typically, at risk populations are overweight/obese, have glucose intolerance, a family history of type 2 diabetes, and often other co-morbidities such as hypertension and dyslipidemia. The estimates of risk reduction are quite consistent between studies.

Evidence Statement 2—In overweight and obese adults with type 2 diabetes, 2–5 percent weight loss achieved with 1–4 years of lifestyle treatment (with or without orlistat) results in modest reductions in fasting plasma glucose concentrations and lowering of HbA1c by 0.2 - 0.3 percent.

Strength of Evidence: High

Rationale: Some of the meta-analysis included in the evidence base used pooled results from studies dating from the late 1970s through the early 2000's (38,39,50). As a result, theses authors included non-comprehensive weight loss approaches and studies with widely varying degrees of success in terms of weight loss. Modest average weight loss was reported in many older studies, which was associated with insignificant reductions in fasting blood glucose. Furthermore, some meta-analysis combined glucose and HbA1C data from persons with and without type 2 diabetes (39). Our concern was that this analytical approach would not truly reflect the impact of interventions on improvements in HbA1C in type 2 diabetes, because persons normal glucose and HbA1C values do not become "more normal" with weight loss. Thus, some of the pooled data from SRs/MAs was difficult to interpret with regards to the question of whether and how much weight loss is needed to affect diabetes-related outcomes. One advantage of examining outcomes from older studies, however, is that the control groups generally received weak interventions, both in terms of supportive and pharmacotherapy. The evolving evidence that pharmacotherapy for hyperglycemia, hyperlipidemia and hypertension had clear medical benefits required changes in subsequent study designs - ethically, the control groups for lifestyle treatment must be provided with aggressive pharmacotherapy for these CVD risk factors. As a result, improvements in CVD risk factors in lifestyle treatment relative to control groups in more recent studies is less impressive than in older studies. Unfortunately, in the literature base for this critical question, only the Look AHEAD papers provided data as to the confounding effects of greater use of medications in control groups. The between-group differences in medication use were not addressed in SRs/MAs in a manner that we could assess.

Evidence Statement 3—In overweight and obese adults with type 2 diabetes, those who achieve greater weight loss at one year with lifestyle therapy (with or without orlistat) have greater

improvements in HbA1C. Weight loss of 5–10 percent is associated with HbA1C reductions of 0.6–1.0 percent and reduced need for diabetes medications.

Strength of Evidence: High

Rationale: This pattern is seen both in a meta-analysis examining different studies with different amounts of weight loss (47,49), as well as within a large, prospective randomized clinical trial (19). As noted, the probability of achieving a clinically meaningful reduction in HbA1C is increased with weight loss of 2–5 percent, and the probability increases further as the amount of weight loss increases. The relationship between the amount of weight loss and the improvement in HbA1C between different studies was commented upon by Norris (47,49). The reports of Wing (19,20) Korhonen, Heller, Uusitupa and Zapotoczky [cited, all referenced in Norris et al. (47,50)] and the Norris 2004 and Norris 2005 MAs, included data on the average weight loss and average change in HbA1C. Those studies with the greatest weight loss had the greatest decline in HbA1C. The Look AHEAD trial (46) provided data regarding the relationship between weight loss and improvement in glycemic control, blood pressure and blood lipids. They found a strong relationship between the amount of weight loss and the improvement in these risk factors irrespective of the group to which the participants were assigned (intensive lifestyle or diabetes support and education). In the Look AHEAD trial (19) there was dose-response relationship between weight loss and the likelihood of achieving a clinically meaningful improvement in HbA1C (a reduction of at least 0.5 percent). A 2–5 percent weight loss results in a statistically significant increase in the likelihood of achieving a reduced HbA1C compared with the weight stable (gained ≤2 percent or lost <2 percent) group. However, on average the improvements in glucose and HbA1C with 2–5 percent weight loss are modest. The Look AHEAD group (19) found that the dose-response relationships between weight loss and the average reduction in

fasting glucose and HbA1C was such that those losing ≥15 percent of body weight over 1 year had an average reduction in fasting glucose of ~ 35 mg/dL and an average decrease of ~ 0.9 percent in HbA1C. These improvements in fasting glucose and HbA1C were seen despite a significantly reduced need for anti-diabetic medications in the group treated with intensive lifestyle intervention (ILI) compared with the control group (20).

Evidence Statement 4—In overweight and obese adults with type 2 diabetes treated for 1 year with lifestyle therapy (with or without orlistat), those who lose more weight achieve greater reductions in fasting plasma glucose concentrations. Those who achieve weight losses of 2–5 percent are more likely to have clinically meaningful (>20 mg/dl lowering) reductions in fasting glucose than those who remain weight stable (defined as gaining ≤2 percent, or losing <2 percent).

Strength of Evidence: High

Rationale: The Look AHEAD group and Avenell et al (38) examined the dose-response relationship between weight loss and lowering of fasting plasma glucose concentrations. Both found a dose-response relationship, such that greater degrees of weight loss were associated with greater reductions in fasting glucose. The Look AHEAD investigators examined the relationship between weight loss and weight loss categories and the likelihood of achieving a clinically meaningful improvement in fasting blood glucose (a priori defined as >20 mg/dL decrease). This group reported that a 2-5 percent weight loss results in a ~70 percent increase in the likelihood of achieving a 20 mg/dL reduction in fasting glucose compared to being weight stable (gained ≤2 percent or lost <2 percent). In addition, those who lost 2–5 percent of body weight were less likely to require anti-diabetic medications than those who remained weight stable. However, the odds of achieving this ≥20 mg/dL glucose reduction goal in the weight stable group was not reported in a manner that allowed us to determine the absolute likelihood of significant glucose

lowering with 2–5 percent weight loss. It appears there were no significant differences in average fasting plasma glucose between the weight stable and 2–5 percent weight loss groups in the Look AHEAD participants at 1 year. The reductions in HbA1C with weight loss may be more apparent than reductions in fasting plasma glucose because HbA1C reflects the integrated glycemic response. Lifestyle intervention (with or without orlistat) may be effective in improving insulin action/secretion, such that postprandial blood glucose levels may be more improved than fasting blood glucose. In addition, the day-to-day variability in fasting blood glucose in type 2 diabetes will make it more difficult to detect improvements in glycemia using this outcome than if HbA1C is used.

Evidence Statement 5—As comprehensive lifestyle treatment of overweight and obese adults with type 2 diabetes continues over 4 years, some weight regain will occur on average; partial weight regain is associated with an increase in HbA1C, but HbA1C remains below pre-intervention levels, and the reduction remains clinically meaningful (20).

Strength of Evidence: Moderate

Rationale: The Look AHEAD study enrolled over 5000 patients with type 2 diabetes and has achieved a follow up rate of 93 and 94 percent in the intensive lifestyle and diabetes support and education groups, respectively. Although only a single study, the number of observations is approximately equal to that obtained in the available SRs/MAs, none of which addressed part "c" of this question, "What is the effect of sustained weight loss for 2 or more years in individuals who are overweight or obese, on CVD risk factors, CVD events and health and psychological outcomes?" The ILI cohort had maintained a mean weight loss of 4.7 percent at 4 years, compared with a 1.1 percent weight loss in the diabetes support and education group. The pattern of weight

regain between 1 and 4 years in the intensive lifestyle group was mirrored by gradual increases in HbA1C, although the need for anti-diabetic medication remained lower in the intensive lifestyle group over all 4 years. At the end of 4 years of treatment, those in the intensive lifestyle group were more likely to meet goals for HbA1C and LDL-C than those receiving diabetes support and education. Those receiving intensive lifestyle treatment were also less likely to have started anti-diabetic medication (including insulin) and more likely to have discontinued diabetes medications. Intensive lifestyle treatment patients were more likely to have discontinued antihypertensive medications and less likely to have started lipid lowering medication than diabetes support and education patients.

Evidence Statement 6. In observational cohort studies, overweight and obese adults with type 2 diabetes who intentionally lost 9 to 13 kg had a 25 percent decrease in mortality rate compared to weight stable controls. (36,54).

Strength of Evidence: Low

Rationale: One aspect of this CQ was to address whether and how much weight loss is associated with reduced mortality rates in those with CVD risk factors. Poobalan et al. (54), examined the literature for evidence that weight loss reduces mortality. There was evidence that intentional weight loss in both men and women with diabetes reduced mortality rates. One of the studies included in this systematic review indicated that women with obesity-related illnesses who intentionally lost >20 pounds of weight had reduced mortality rates within 1 year, whereas this was not seen for men who intentionally lost weight. Because none of the studies included were prospective, randomized trials of lifestyle treatment to achieve weight loss we considered these findings to have low strength of evidence. After these evidence statements were developed,the

Look AHEAD trial was stopped because of the low likelihood of a difference in cardiovascular events between the ILI group compared with the diabetes support and education control group. Both groups received aggressive medical management of cardiovascular risk factors, a situation not comparable to the observational studies reviewed by Poobalan et al.

Evidence Statement 7--In overweight and obese adults with type 2 diabetes, orlistat compared to placebo, both with lifestyle treatment, results in 2–3 kg greater weight loss at 1 and 2 years. The addition of orlistat is associated with greater reductions in fasting blood glucose averaging 11 and 4 mg/dL at 1 and 2 years as well as an average greater reduction in HbA1C of 0.4 percent at 1 year (14,39,49).

Strength of Evidence: High

Rationale: One aspect of this question was to address whether "reduction in body weight with lifestyle and *pharmacological* interventions affect CVD risk factors, CVD events, morbidity, and mortality", however, the only agent that was FDA approved for long-term treatment of obesity at the time of the literature review was orlistat. Therefore, we reviewed the SR/MA that examined the published orlistat results. Four publications analyzed the effects of orlistat on fasting blood glucose and HbA1C. Avenell et al. (38,39) reported that orlistat at the standard prescribed dose of 120 mg three times daily with meals resulted in an average extra 1–3 kg weight loss at 1 and 2 years compared with placebo, and that this was associated with greater reductions in fasting blood glucose of 11 mg/dL and 4 mg/dL at 1 and 2 years, respectively, and a 0.3 percent greater reduction HbA1C at 1 year. Norris et al. (49) reported that 1 year of orlistat therapy resulted in an average 2 kg greater weight loss than placebo, a 13 mg/dL greater reduction fasting blood glucose and a 0.4 percent greater reduction HbA1C compared with placebo. Similar findings were

reported by O'Meara et al (14): standard orlistat therapy for one year resulted in an average 2.4 kg greater weight loss, 11 mg/dL greater fasting blood glucose reduction glucose and a greater 0.4 percent A1C reduction vs. placebo.

3.6 Weight Loss and Impact on Cholesterol/Lipid Profile—Spreadsheet 1.5

Seven SRs/MAs and 3 reports from the Look AHEAD Research Group were used to examine the effects of weight loss on lipid outcomes achieved in overweight and obese adults with lifestyle interventions or weight loss drugs combined with lifestyle modification. The literature available to us did not specifically address whether age, sex, ethnicity or waist circumference influence the response to weight loss in terms of CVD risk reduction. The Look AHEAD trial provides evidence of the effect of weight loss on lipids and lipid-lowering medication use at one to four years of follow-up achieved by comprehensive lifestyle intervention in overweight and obese individuals with type 2 diabetes.

Evidence Statement 1. In overweight or obese adults with or without elevated CVD risk, there is a dose-response relationship between the amount of weight loss achieved by lifestyle intervention and the improvement in lipid profile (19,55). The level of weight loss needed to observe these improvements varies by lipid.

- At a 3 kg weight loss, a weighted mean reduction in triglycerides of at least 15 mg/dL is observed.

- At 5–8 kg weight loss, LDL-C reductions of approximately 5 mg/dL and increases in HDL-C 2–C3 mg/dL are achieved (19,20,38,40,42).

- With less than 3 kg weight loss more modest and more variable improvements in triglycerides, HDL- and LDL-C are observed (61).

Strength of Evidence: High

Rationale: SRs, MAs, and selected reports from the Look AHEAD Study were used to determine if there is was a dose-response relationship between the amount of weight loss achieved by lifestyle intervention and the improvement in lipid profile in overweight or obese adults with or without elevated CVD risk (19,55), and the level of weight loss needed to observe improvements lipids (19,20,38,40,42,61). Some of the MAs reported the weighted mean difference between lifestyle intervention and control, yet the weighted mean difference in lipids was based on a subsample of the studies reporting weight loss. Thus, it was difficult to directly match the weight loss with the changes in lipid in some papers. When possible the weight loss and lipid data were matched from studies identified in these MAs, and in those cases the range of weight loss and lipid change was examined to address this critical question. In situations where the weight loss and lipid data were not able to be matched, data from those MAs were not used to support the evidence statement or recommendation made by the committee.

The systematic review conducted by Poobalan et al. (55) and the report from the Look AHEAD Study (19) were used to determine if there was a dose-response relationship between the amount of weight loss achieved by lifestyle intervention and the improvement in lipid profile In overweight or obese adults with or without elevated CVD risk. While Poobalan et al. (55) included studies that reported on weight loss from either lifestyle or surgical approaches, we were able to identify the lifestyle studies on scatterplots illustrating the relationship between weight loss and change in lipids. These scatterplots showed a significant positive association between the mean difference

in weight change and the change in LDL-C and triglycerides, with no identifiable association with change in HDL-C. However, the Look AHEAD study investigators showed a clear dose-response relationship between the amount of weight loss and the increase in HDL-C, with no relationship between weight loss and change in LDL-C.

The amount of weight loss resulting in detectable improvements varied by lipid. With regard to triglycerides, Avenell et al. (38,40) reported that weight losses of approximately 3-12 kg compared to control over a period of 12 months reduced fasting plasma triglyceride concentrations by approximately 15-50 mg/dL (38,40). A similar magnitude of change in triglycerides in response to weight loss was reported by Galani et al. (42). In a study by Witham 2010 reporting on older adults, weight loss of less magnitude (1.5–2.0 kg) resulting from a lifestyle modification was not associated with a significant reduction in triglycerides in overweight and obese adults ≥60 years of age (61).

With regard to LDL cholesterol, Avenell et al. (38,40) reported that a weight loss of 5–8 kg over 12 months was associated with reductions in LDL-C of approximately 5–8 mg/dL (38,40); similar findings were reported by Galani et al. (42). Among overweight and obese adults ≥60 years of age, lifestyle modifications that produced modest average weight loss of 1.5–2.0 kg over a period of 12 months compared to control did not change LDL-C (61). Moreover, among overweight and obese adults with type 2 diabetes aged 45–75 years, 8.0 percent weight loss at 1 year and 5.3 percent weight loss over 4 years compared to control did not result in a reduction in LDL-C comparable to controls. However, this difference in weight loss results in lower initiation of lipid lowering medication (20,46).

Among overweight and obese adults, lifestyle modification that produces weight loss of approximately 3.0–12.0 kg compared to control over a period of 12 months resulted in an increase in HDL-C of 2–4 mg/dL (38,40). However, among overweight and obese adults ≥60 years of age, lifestyle modifications that produces weight loss of only 1.5–2.0 kg over a period of 12 months compared to control results in no change in HDL cholesterol mg/dL (61). Moreover, among overweight and obese adults with type 2 diabetes aged 45–75 years, 8.0 percent weight loss at 1 year and 5.3 percent weight loss over 4 years compared to control increases HDL by an additional 2 mg/dL (20) and 1.6 mg/dL (20), respectively.

Evidence Statement 2. Among overweight and obese adults with type 2 diabetes, 8.0 percent weight loss at 1 year and 5.3 percent weight loss over 4 years compared to usual care control results in greater average increases (2 mg/dL) in HDL and greater average reductions in triglycerides.

Strength of Evidence: Moderate

Rationale: The Look AHEAD study enrolled over 5000 patients with type 2 diabetes and has achieved a follow up rate of 93 and 94 percent in the intensive lifestyle and diabetes support and education (DSE) groups, respectively. Although only a single study, the number of observations is approximately equal to that obtained in the available SRs/MAs, none of which specifically addressed the effect of weight loss on changes in lipids in overweight and obese adults with type 2 diabetes. The ILI achieved a weight loss of 8.6 percent of initial body weight at 1 year compared to 0.7 percent in DSE, which served as the usual care control in this study (46). Across 4 years of intervention the mean weight loss was 6.2 percent in the ILI versus 0.9 percent in DSE (20). These magnitudes of weight loss resulted in HDL increasing by 3.0 mg/dL in ILI and 1.0 mg/dL in

DSE at 1 year, with a mean increase of 4.0 mg/dL in ILI vs. 2.0 mg/dL in DSE when averaged across the 4 years of intervention. Triglycerides decreased by 30.0 mg/dL in ILI and 15.0 mg/dL in DSE at 1 year, with the mean decrease across 4 years being 26.0 mg/dL in ILI vs. 20.0 mg/dL in DSE.

Evidence Statement 3. A mean 5 percent weight loss achieved over 4 years by lifestyle intervention in overweight or obese adults with type 2 diabetes is associated with a reduction in newly prescribed lipid lowering medications compared with controls.

Strength of Evidence: Moderate

Rationale: The Look AHEAD Research Group reported that the ILI produced significantly greater weight loss at 1 year and across 4 years of intervention compared to DSE. However, the reduction in LDL cholesterol was not significantly different between ILI and DSE at 1 year (46) after adjusting for lipid-lowering medication across 4 years (20). Yet, the percentage of participants not prescribed lipid-lowering mediation at baseline who then initiated lipid-lowering medication across the 4 years of intervention was significantly less in ILI (47.2 percent) compared to 53.2 percent in DSE (20). There was no difference between ILI and DSE for the percentage of participants who were prescribed lipid-lowering medication at baseline and continued to be prescribed lipid-lowering medication at 4 years (ILI = 90.9 percent; DSE=90.4 percent) (20).

Evidence Statement 4. Among overweight and obese adults with type 2 diabetes, there is a dose-response relationship between the amount of weight loss and the increase in HDL-C that is most pronounced in those who are the least overweight at baseline.

Strength of Evidence: Low

Rationale: As described above, the Look AHEAD study enrolled over 5000 patients with type 2 diabetes. The Look AHEAD Research Group reported that there was an interaction between baseline weight and weight change categories for HDL-C in patients with type 2 diabetes , such that the slope (increase in HDL-C as a function of weight loss) was steepest in those who weighed least at baseline (19).

Evidence Statement 5. Compared to placebo, the addition of orlistat to lifestyle intervention in overweight and obese adults results in an average 3 kg greater weight loss together with an 8-12 mg/dL reduction in LDL- cholesterol, a 1 mg/dL reduction in HDL- cholesterol and variable changes in triglycerides.

Strength of Evidence: High

Rationale: Among overweight and obese adults, an intervention that included lifestyle intervention plus orlistat versus placebo produced weight loss of approximately 1.0-4.0 kg over a period of at least 1 years and resulted in a decrease in LDL-C of approximately 11 mg/dL (38,49). This type of intervention over a period of 2 years that produced weight loss of approximately 3.0-4.0 kg compared to placebo decreased LDL-C by approximately 8 mg/dL (38). A similar magnitude of change in LDL-C was reported by Rucker et al. (56) when examining studies that were at least 1 year in duration. In patients with type 2 diabetes, Hutton et al. (44) reported that a weighted mean difference for weight loss of 2.5 kg was associated with a reduction in LDL-C of approximately 10 mg/dL. Moreover, Norris et al. (49) reported that in patients with type 2 diabetes, an intervention that included orlistat and produced weight loss of approximately 1.0–4.0 kg compared to control over a period of 12 to 57 weeks resulted in a decrease in LDL-C of approximately 12 mg/dL (49).

Among overweight and obese adults, an intervention that included lifestyle intervention plus orlistat, and produced weight loss of approximately 1.0–4.0 kg compared to placebo over a period of at least 1 year, resulted in a non-significant decrease in HDL-C of approximately 1 mg/dL (38). An intervention that included orlistat, and produced weight loss of approximately 3.0–-4.0 kg compared to control over a period of two years, resulted in a decrease in HDL-C of approximately 1 mg/dL (38). In patients with type 2 diabetes, Hutton et al. (44) reported that a weighted mean difference for weight loss of 2.5 kg was associated with a reduction in HDL-C of approximately 1 mg/dL.

There are variable changes in triglycerides associated with weight loss resulting from an intervention that included orlistat. Among overweight and obese adults, an intervention that included orlistat, and produced weight loss of approximately 1.0–4.0 kg compared to control over a period of at least 1 year, resulted in a decrease in triglycerides of approximately 3 mg/dL (38,49). An intervention that included Orlistat and produced weight loss of approximately 3.0-4.0 kg compared to placebo over a period of 2 years resulted in a decrease in triglycerides of approximately 4 mg/dL (38). A similar magnitude of change in triglycerides was reported by Rucker et al.(56) when examining studies that were at least 1 year in duration. In patients with type 2 diabetes, Hutton and Fergusson (44) reported that a weighted mean difference for weight loss of 2.5 kg was associated with a reduction in triglycerides of approximately 17 mg/dl. Moreover, in patients with type 2 diabetes, an intervention that included orlistat and produced weight loss of approximately 1.0-4.0 kg compared to control over a period of 12 to 57 weeks resulted in a decrease in triglycerides of approximately 20 mg/dL (49).

The Look AHEAD group reported that there was an interaction between baseline weight and weight change categories for HDL-C in patients with type 2 diabetes, such that the slope (increase in HDL-C as a function of weight loss) was steepest in those who weighed least at baseline.

3.7 Weight Loss and Hypertension Risk—Spreadsheet 1.6

Eight SRs/MAs and 3 reports from the Look AHEAD Research Group were used to examine the effects of weight loss on blood pressure outcomes achieved in overweight and obese adults with elevated CVD risk (including diagnosis of hypertension and type 2 diabetes) achieved by diet or lifestyle interventions or weight-loss drugs combined with calorie-restricted diets or lifestyle modification. The literature available to address this question did not specifically examine whether age, sex, gender, ethnicity, BMI, or waist circumference influences the effect on blood pressure of weight loss achieved by alternative non-surgical methods. The Look AHEAD trial provides evidence of the effect of weight loss on blood pressure medication use at one to four years of follow-up achieved by comprehensive lifestyle intervention in overweight and obese individuals with type 2 diabetes.

Evidence Statement 1. In overweight or obese adults with elevated CVD risk (including type 2 diabetes and hypertension), there is a dose-response relationship between the amount of weight loss achieved for up to 3 years by lifestyle intervention alone or combined with orlistat and the lowering of blood pressure.

- At a 5 percent weight loss, a weighted mean reduction in systolic and diastolic blood pressure of approximately 3 and 2 mm Hg, respectively, is observed.

- At less than 5 percent weight loss, there are more modest and more variable reductions in blood pressure.

Strength of Evidence: High

Rationale: Eight SR/MAs (37-39,43,45,47,49-51,56,58) and the Look AHEAD Study (19,20,46) provided evidence on the effect of weight loss achieved by diet, physical activity and orlistat combined with energy-restricted diets on systolic and diastolic blood pressure levels in overweight and obese adults with elevated CVD risk including individuals with type 2 diabetes and hypertension. Three of the reports (37-39) formally modeled the linear relationships between weight loss achieved by lifestyle or orlistat and blood pressure outcomes in overweight and obese adults with elevated CVD risk. The studies reviewed in the SRs/MAs varied considerably in research design, including study subject characteristics and quality ratings; nonetheless, the focused nature of the reviews allowed conclusions regarding weight loss effects on blood pressure in subjects with elevated CVD risk including the presence of the diagnosis of hypertension or type 2 diabetes. Further distinctions on the relative effectiveness of weight loss on blood pressures of subjects with specific combinations of risk factors or co-morbidities were not feasible from this literature. Our examination of weight loss drug trials was limited to those involving orlistat since other weight-loss drugs were not in clinical use at the time of this review. Surgical interventions for weight loss are not reviewed here because the effects of bariatric surgery results are addressed in CQ5. The authors of the SRs/MAs noted that bias may have been introduced in certain trials due non-compliance with protocols or loss to follow-up. Despite this, relatively consistent, modest and favorable effects on systolic and diastolic blood pressure levels were demonstrated across this literature as a result of weight loss by non-surgical interventions in overweight and obese adults with elevated CVD risk.

Aucott et al.'s (36) Health Technology Assessment report which addresses obesity treatments and health improvements examined 8 trials involving 4533 overweight and obese adults at high CVD risk; all trials involved orlistat combined with energy-restricted diets (with or without physical activity or other lifestyle behavioral interventions). Weight losses ranged from -1.30 kg to -4.2 kg at 12 to 24 months and resulted in a weight mean reduction of -2.02 mmHg and -1.64 mmHg in systolic and diastolic blood pressure, respectively. Four trials of lifestyle intervention alone involving over 550 overweight and obese subjects with elevated CVD risk also demonstrated that weight losses ranging from -2 to -8 kg at 12 to 24 months resulted in mean 0-9 mmHg lowering of systolic blood pressure and 1-12 mmHg reductions in diastolic blood pressure. Formal modeling of the combined orlistat and lifestyle intervention effects suggested linear relationships between weight reduction and blood pressure; a 5 percent change in weight was associated with a decline of 3 mmHg in systolic blood pressure and 2 mmHg in diastolic blood pressure. Rucker (56) and (51) reviewed 30 original studies which examined lifestyle alone or drug trials typically combined with lifestyle intervention for weight loss in 10,631 overweight and obese adults. Weighted mean differences (WMDs) in weight loss at 12 month follow-up or longer were -1.3 percent to 4.3 percent and resulted in WMD of -1.5 mmHg in systolic and -1.4 mmHg in diastolic blood pressure. Subgroup analyses in subjects with diabetes suggested that weight loss may be more modest. Johansson et al. (45) examined 12 trials of weight loss drugs combined with lifestyle interventions involving 5540 overweight and obese subjects with elevated CVD risk; WMD in weight loss of -2.8 kg achieved at 12 months in non-diabetic and diabetic subjects. In non-diabetic subjects, WMDs on systolic and diastolic blood pressure were -2.2 mmHg and -1.6 mmHg for systolic and diastolic blood pressure, respectively; blood pressure effects in adults with type 2 diabetes were more modest. Norris (49) examines 8 weight loss trials of orlistat combined with lifestyle

intervention involving 2,036 overweight and obese subjects with type 2 diabetes. A subset of four trials with combined weight loss and blood pressure outcomes demonstrated WMD weight losses ranging from about -1 to -4 kg which resulted in WMDs of -3 mmHg in systolic and -4 mmHg in diastolic blood pressure. Aucott (37) reviewed 11 trials of orlistat combined with energy-restricted diets in 489 overweight or obese adults with hypertension; at two years, WMD in weight (compared to placebo) were about -3.0 kg and were associated with a -3 mmHg improvement in systolic blood pressure and a 0 to -2 mmHg in diastolic blood pressure. Formal modeling of the weight loss effects indicated that a 5 kg reduction in weight in overweight or obese adults with hypertension was associated with a 3 mmHg reduction in systolic blood pressure and a 2 mmHg lowering of diastolic blood pressure. In subgroup analyses of 4 lifestyle interventions for weight loss of up to 5 years duration in 670 overweight and obese adults with elevated CVD risk, higher levels of weight loss (up to -12 kg) were consistently associated with improvements in systolic and diastolic blood pressure. Siebenhofer (58) and Horvath (43)reviewed drug trials for weight loss involving 3132 adults with hypertension and noted that a 4 kg weight loss is needed to achieve a 2.5 mmHg reduction in blood pressure and a 2 mmHg reduction in diastolic blood pressure. Horvath (43) also conducted a sub-group analysis of dietary interventions for weight loss of 6-36 month duration in 2,219 adults with hypertension. The observed WMDs in body weight of -5 to -6 kg that were associated with a 6 mmHg reduction in systolic blood pressure and a 3 mmHg led the authors to conclude that dietary intervention alone for weight loss may be more effective in lowering blood pressures than weight loss drugs combined with energy-restricted diets. The Look Ahead Group (19,20,46) examined the 1–4 year outcomes associated with comprehensive lifestyle intervention for weight loss in 5345 overweight and obese adults with type 2 diabetes. At 12 months, the 8 percent mean weight loss (minus controls) was associated

with a -4 mmHg reduction in systolic blood pressure and a - 1 mmHg reduction in diastolic blood pressure. At 4 years, a 5 percent weight loss was retained but blood pressure effects were attenuated (-2 mmHg systolic and -0.4 mmHg diastolic blood pressure). Norris (49,50) examined non-pharmacological interventions for weight loss in 4699 adults with type 2 diabetes and found that WMDs ranging from -2.8 to 4 kg at 1-2 years were associated with a 2 mmHg reduction in systolic blood pressure and no change in diastolic blood pressure.

Evidence Statement 2. A 5 percent mean weight loss difference achieved over four years by intensive lifestyle intervention in overweight or obese adults with type 2 diabetes is associated with a lower prevalence of patients who are prescribed antihypertensive medications compared with controls.

Strength of Evidence: Moderate

Rationale: The Look Ahead Group (19,20,46) provided evidence at 1 to 4 year follow-up in 5145 overweight and obese adults with type 2 diabetes that comprehensive lifestyle intervention for weight loss results in reduced blood pressure medication use. Fewer adults involved in intensive interventions initiated or continued hypertensive medications over 1-4 years.

3.8 Recommendations

The recommendations in this report are numbered to correspond with the numbering used in the guideline report. The panel decided that the recommendations from CQ1 should follow the recommendations made by CQ2, thus the following recommendation is numbered "Recommendation 2". Recommendation 1 is included in the CQ2 section of the report,

3.8.1. Recommendation 2: Counsel overweight and obese adults with cardiovascular risk factors

(high blood pressure, hyperlipidemia and hyperglycemia), that lifestyle changes that produce even modest, sustained weight loss of 3%-5% produce clinically meaningful health benefits, and greater weight losses produces greater benefits.

a. Sustained weight loss of 3%-5% is likely to result in clinically meaningful reductions in triglycerides, blood glucose, hemoglobin A1c and the risk of developing type 2 diabetes;
b. Greater amounts of weight loss will reduce blood pressure, improve LDL-C and HDL-C, and reduce the need for medications to control blood pressure, blood glucose and lipids as well as further reduce triglycerides and blood glucose.

(Grade A, Strong); ACC/AHA COR I, LOE A

Rationale: The body of evidence was clearly in favor of a dose-response relationship between intentional weight loss and reduction in cardiovascular risk factors. By focusing on outcomes at 1 or more years after the beginning of treatment we were more confident that the reported improvements were related to the reduced weight/body fat, not due to the acute or sub-acute effects of negative energy balance. The amount of weight loss needed to detect a clinically meaningful improvement was not the same for all risk factors. Glycemia-related risk and triglyceridemia were responsive to modest (3–5 percent), sustained weight loss. For those at risk of developing type 2 diabetes, 3–5 percent sustained weight loss reduced the incidence of diabetes. This finding was perhaps the most clinically meaningful. Patients at risk for developing type 2 diabetes can substantially reduce that risk by sustaining a modest weight loss over time. Given the morbidity and cost of treatment for type 2 diabetes, and given that this degree of weight loss is readily achievable with lifestyle treatment, this group seems particularly suited to benefit from participating in comprehensive lifestyle interventions. On average, 3–5 percent weight loss also

is associated with clinically meaningful reductions in serum triglyceride concentrations, as well as lowering of fasting glucose and HbA1C in patients with type 2 diabetes. Greater degrees of weight loss result in greater reductions in fasting glucose and HbA1C, despite the need for less anti-diabetic medication, and further lowering of serum triglyceride concentrations. On average, clinically meaningful reductions in systolic and diastolic blood pressure, lowering of LDL-C and increases in HDL-C are seen in those who sustain weight losses of ≥5 percent of body weight. These improvements are greater in those who achieve greater amounts of weight loss via lifestyle interventions, despite the need for less medication to treat hyperlipidemia and hypertension. As the panel was completing its work it was announced that the Look AHEAD trial would be discontinued because, after up to 11 years of lifestyle intervention, it was judged the likelihood of detecting a significant difference in cardiovascular mortality between the lifestyle and control groups was too low. Both the intensive lifestyle group and the diabetes support and education group had many fewer cardiovascular events than had been previously reported in populations of type 2 diabetes, possibly due to the aggressive pharmacotherapy for known cardiovascular risk factors. The group treated with intensive lifestyle required fewer medications, had less sleep apnea, better quality of life and greater physical mobility. Our interpretation of this announcement is that pharmacotherapy, together with diabetes support and education interventions, is equal to comprehensive lifestyle interventions in reducing cardiovascular events. The data indicate that ILI reduce medication need and improve quality of life compared to a control intervention.

3.9 Gaps in Evidence and Future Research Needs

The literature available to CQ1 did not specifically address whether age, sex, race or baseline BMI/waist circumference modify the beneficial effects of weight loss as regards cardiovascular risk factors. Likewise, the SRs/MAs did not specifically address the issue of how baseline comorbid conditions and cardiovascular risk factors modify the response to weight loss. Thus, although the group was able to address parts "b" and "c", they could not address all of part "a". Because only SRs/MAs and the Look AHEAD data were used, however, it is possible that there is high quality literature that does address these issues. Given that caveat, future research in this area should address the following issues:

1. Do the observed improvements in cardiovascular risk factors, need for medications and improved quality of life associated with weight loss differ by age, sex, race and BMI/waist circumference?

2. What is the cost-effectiveness of modest weight loss as a preventative strategy for those at risk of developing type 2 diabetes?

3. What is the best approach to identify and engage those who can benefit from weight loss?

4 CRITICAL QUESTION 2

4.1. Statement of the Question

CQ2 has three parts:

A. Are the current cutpoint values for overweight (body mass index (BMI) 25.0 to 29.9) and obesity (body mass index (BMI) ≥30) compared with BMI 18.5 to 24.9 associated with elevated CVD-related risk (defined below)?

   Are the waist circumference cutpoints of >102 cm (M) and >88 cm (F) associated with elevated CVD-related risk (defined below)?

   How do these cutpoints compare with other cutpoints in terms of elevated CVD-related risk and overall mortality?

   1. Fatal and non-fatal CHD, stroke, and CVD (CHD and stroke)
   2. Overall mortality
   3. Incident type 2 diabetes
   4. Incident dyslipidemia
   5. Incident hypertension

B. Are differences across population subgroups in the relationships of BMI and waist circumference cutpoints with CVD, its risk factors, and overall mortality sufficiently large to warrant different cutpoints? If so, what should they be?

   1. Fatal and non-fatal CHD, stroke, and CVD
   2. Overall mortality
   3. Incident type 2 diabetes
   4. Incident dyslipidemia

5. Incident hypertension

Groups being considered include:

1. Age

2. Sex (both M and F)

3. Race/ethnicity (African American, Hispanic, Native American, Asian, White Caucasian)

C. What are the associations between maintaining weight and weight gain with elevated CVD-related risk in normal weight, overweight, and obese adults?

4.1.1. Subgroup Analyses

- **By Population Subgroups**
  - Age
  - Sex
  - Socioeconomic status – *no evidence anticipated*
  - Race/Ethnicity
  - BMI cutpoints [Overweight (BMI 25.0 to 29.9) vs. obese (BMI ≥30.0) vs. normal (BMI 18.5 to 24.9), or whatever the evidence dictates]
  - Waist circumference cutpoints

- **By CVD Risk Factors**
  - Fatal and non-fatal CHD, stroke, CVD
  - Overall mortality
  - Incident dyslipidemia
  - Elevated blood pressure, hypertension
  - Incident cases of type 2 diabetes
- **By Amount of Weight loss**
  - Different cutpoints
- **By Weight Loss Maintenance**
  - Different cutpoints
- **Modifiers to Take into Account**
  - Smoking status (as an effect modifier only)
  - Diminished cardiorespiratory fitness (as an effect modifier only)
  - Depression (as an effect modifier only)
  - Metabolic syndrome (as a mediator)

4.2 Selection of the Inclusion/Exclusion Criteria

Panel members identified I/E criteria in 10 categories for CQ2 (see Table 4). The criteria included the PICOTS criteria as the first six and then also several others related to study design, type of publication, and time frame for publication:

- Population
- Intervention
- Comparator
- Outcomes
- Time
- Setting
- Study Design
- Language
- Publication Type
- Publication Time Frame

For each of these criteria, the panel members developed detailed specifications related to each component. The population of interest for CQ2 is American adults. For this CQ, intervention studies were not included.

Table 4.0 Criteria for Selection of Publications for CQ2

	Inclusion Criteria	Exclusion Criteria
Population	Adults • Normal weight (BMI 18.5 to 24.9) • Overweight (BMI 25.0 to 29.9) • Obese (BMI ≥30.0)	• Children • Animals studies • Studies on specific populations (e.g. sample with coronary artery disease, cancer)
Intervention	No interventions	
Comparator	• BMI: must compare 2 or more BMI categories or include BMI as a continuous variable • Waist circumference: must compare 2 or more waist circumference categories or include waist circumference as a continuous analysis	
Outcomes	*Study must report BMI or waist circumference as an independent variable* Must have one or more of the following *outcomes:* *CVD Events* • Myocardial infarction • Heart failure • Hospitalization for heart failure • Stroke *CVD Risk* • Elevated systolic blood pressure or diastolic blood pressure • Dyslipidemia as measured by total cholesterol, HDL-C, LDL-C, non-HDL-C, triglycerides • Dysglycemia as measured by fasting insulin, fasting glucose, HbA1c (includes prediabetes), incident cases of type 2 diabetes *Morbidity* • CHD/CVD • Diabetes *Mortality* • CVD-related	• Studies focused on predicting risk

	Inclusion Criteria	Exclusion Criteria
	• Overall	
Timing	• Intervention or exposure period: no limits • Follow-up period is 6 months or more	Follow-up of less than 6 months
Setting	The majority (greater than 50 percent) of studies in MAs, SRs, or pooled analyses from Westernized countries: • United States • Canada • Europe • Australia • New Zealand • Israel Any clinical or research setting	
Study Design	• SRs (qualitative summary or narrative review article); or MAs (quantitative summary of published data); or pooled analyses (an analysis of independent primary studies that do not have identical protocols for all measures and are collected in more than one distinct examination center), focusing only on CHD, CVD, and mortality as outcomes • Sample size: – For fatal and non-fatal CHD, stroke and CVD, overall mortality, type 2 diabetes, dysglycemia, impaired glucose tolerance, impaired fasting glucose, prediabetes): sample size ≥1000 incident outcomes or ≥500 for minority groups – For abnormal lipids (LDL, HDL, triglycerides), hypertension, or increased blood pressure and elevated CRP: sample size ≥ 500	• Case series, case reports • Cross-sectional studies
Language	• Full-text must be available in English	• Studies where the abstract only, and not the full text, is available in English

	Inclusion Criteria	Exclusion Criteria
Publication Type	• Published SRs/MAs and pooled studies	• Studies examining a single cohort • Other unpublished literature – Unpublished data – Unpublished industry-sponsored trials • U.S. Food and Drug Administration (FDA) Medical and Statistical reviews • Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Publication Time Frame	• Studies published between 2000 and 2011 • Supplemental searches for SRs/MAs and pooled studies were conducted between 2000 and 10/2011	• Studies published before 2000

4.3 Introduction and Rationale for Question and Inclusion/Exclusion Criteria

Overall, CQ2 evaluates the utility of two well-established measures in obesity—BMI and waist circumference. Specifically, CQ2 addresses the CVD health risks associated with overweight (BMI 25 to 29.9 kg/m^2) and obesity (BMI $\geq$30 kg/m^2) defined by the current cutpoints. These cutpoints were established in the 1998 Obesity Clinical Practice Guidelines (4) and have been widely established as the standard in clinical practice and research settings. As a result, the classification for BMI has been broadly applied across the population. CQ2 also seeks to determine if the current cutpoints defining persons as overweight and obese are equally appropriate for key subgroups within the U.S. population. Lastly, CQ2 attempts to address the issue of elevated waist circumference, as defined by current cutpoints, and its association with CVD health risks. Waist circumference cutpoints of >102 cm (>40 in.) for men and >88 cm (>35 in.) for women were recommended in the 1998 Clinical Guidelines to identify "increased risk in most adults with a BMI of 25 to 34.9 kg/m^2." A 2008 report of a WHO Expert Consultation (63) identified these waist circumference cutpoints as associated with "substantially increased" risk,

while cutpoints of >94 cm in men and >80 cm in women were identified as associated with "increased" risk. Other alternative waist circumference cutpoints include those by the International Diabetes Federation for Europids (≥94 cm for men and ≥80 cm for women), for South Asians, and Chinese (≥90 cm for men and ≥80 cm for women) and for Japanese (≥85 cm for men and ≥90 cm for women). The panel searched for evidence on all of these cutpoints as they relate to elevated CVD risk.

The utility of BMI and waist circumference cutpoints is of interest because it is important for PCPs to be able to understand how to use easily obtained measures that serve as surrogates of body fatness (BMI) and the distribution of that body fat (waist circumference) in decision making. It is important to know whom to identify as a potential candidate for weight reduction therapy or further evaluation of other CVD risk factors. Ultimately, the goal is to produce clear guidance for the practitioner to efficiently provide meaningful recommendations to patients likely to be at high risk, thus those most likely to benefit from a weight control intervention. Note that the panel did not review the literature evaluating the diagnostic performance of BMI compared to more valid measures of percent body fat (e.g., dual energy X-ray absorptiometry); these are not as simple or inexpensive to use as BMI in clinical settings.

4.4 Methods for Critical Question 2

The Obesity Panel formed subcommittees for each of its five CQs. For CQ2, the subcommittee was chaired by an epidemiologist, and also included physicians and researchers representing universities, the NHLBI, and the NIDDK.

CQ2 addresses the association of BMI and waist circumference with CVD events and CVD-related outcomes such as mortality, type 2 diabetes, dyslipidemia, and hypertension. Other

indices, such as waist-to-hip ratio, waist-to-height ratio or sagittal abdominal diameter, were not examined here. The methodology team assisted by applying the PICOTS criteria and also worked with CQ2 panel members to develop and refine the detailed I/E criteria. Due to resource limitations, CQ2 limited its literature search and evidence review to SRs, MAs, and pooled analyses to limit the number of individual articles to be searched, reviewed, and quality rated. The evidence review was limited to studies that were published between the years of 2000 and 2011. Thus, the evidence statements and rationales for this critical question reflect the status of the literature as of the dates of the search, but some conclusions may change or be refined as new data become available. Panel members excluded studies that focused on specific subpopulations with a disease or condition (e.g., women with breast cancer, adults on maintenance hemodialysis) and constructed spreadsheets from the identified articles. Then the methodology team reviewed and checked the spreadsheets for accuracy.

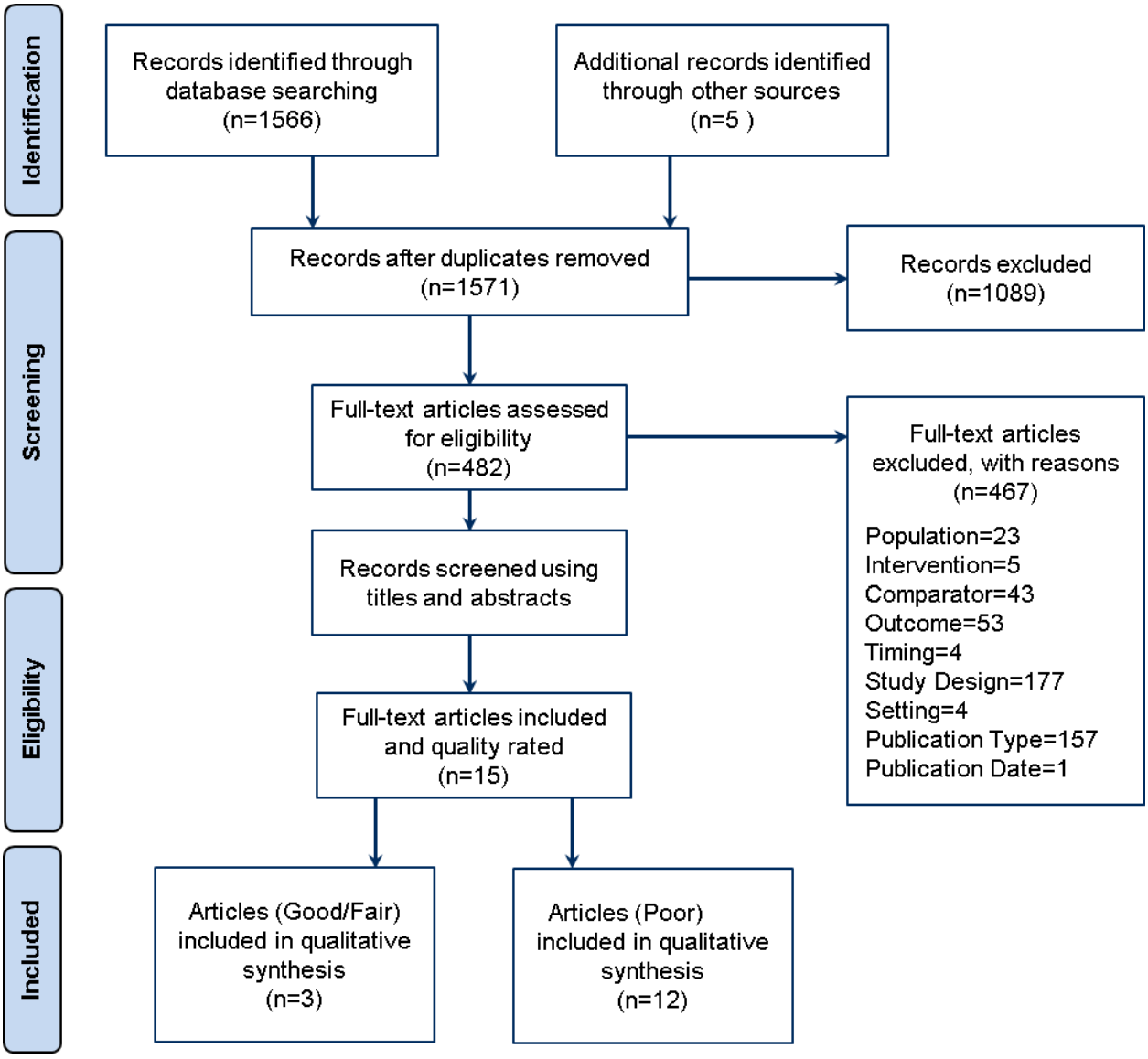
The literature search for CQ2 included an electronic search of the Central Repository for SRs, MAs, and pooled analyses published in the literature from January 2000 to October 2011. The Central Repository contains citations pulled from seven literature databases: PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts. The literature search produced 1,566 citations, with 5 additional citations identified from non-search sources (i.e., by the panel members). Three of the 5 citations met the criteria and were eligible for inclusion in the CQ2 Evidence Base (64-66). In contrast, the other two citations did not meet the criteria and were excluded from the CQ2 Evidence Base (67,68).

Figure 6, the PRISMA diagram outlines the flow of information from the literature search through the various steps used in the systematic review process.

Two reviewers independently screened the titles and abstracts of 1,571 publications against the I/E criteria, which resulted in 1089 publications being excluded and 482 publications being retrieved for full-text review to further assess eligibility. Next, two reviewers independently screened 482 full-text publications and assessed eligibility by applying the I/E criteria; 467 of these publications were excluded based on one or more of the I/E criteria (see specified rationale as noted in the PRISMA).

Fifteen of the 482 full-text publications met the criteria and were included. The quality (internal validity) of these 15 publications was assessed using the quality assessment tool developed to assess SRs, MAs, and pooled analyses (see Appendix 2). Of these, 12 publications were rated as poor quality (64-66,69-77); however, they were used as part of the evidence base since NHLBI policy indicated that poor studies could be used as part of this evidence base if the majority of included studies were not rated good or fair. Rationales for the poor quality studies are included in Appendix 3. Panel members reviewed the final articles on the included list, along with their quality ratings, and had the opportunity to raise questions. They appealed some pooled analyses previously deemed to be of poor quality which were subsequently upgraded to fair quality upon closer review by the methodology team, who made the final decision (78,79). Three SRs/MAs were ultimately rated good or fair quality (78-80) and included in the evidence base that was used to formulate the evidence statements and recommendations. Panel members created spreadsheets, containing key information from the SRs, MAs, and pooled analyses; these (cross-checked by the methodology and SR teams) formed the basis for panel deliberations.

Figure 6. PRISMA Diagram Showing Selection of Articles for Obesity Question 2



Some papers included in this evidence review examined BMI using the current cutpoints, and therefore the panel was able to evaluate the performance of those cutpoints for CVD risk prediction. Other included papers evaluated BMI as a continuous variable, and the results were used to support categorical analyses, but not alone to evaluate the current cutpoints. To give some basis of comparison to categorical studies, when continuous BMI was used, the panel calculated the risk estimate for a BMI of 27.45 (midpoint of overweight range) and 34.95 (midpoint of obese

class I and II ranges) compared to 21.70 (midpoint of normal weight range) as the reference. To calculate these risk estimates, the panel took the natural log of the RR (risk ratio or hazard ratio (HR)) reported in the study of continuous BMI and divided it by the number of BMI units that it represented to estimate the beta coefficient per 1 unit of BMI. Then, the panel multiplied the result by 5.75, which is the distance between the midpoint of normal weight (21.70) and the midpoint of overweight (27.45), to estimate the contrast between overweight and normal weight. Similarly, the panel multiplied the beta coefficient per 1 unit of BMI by 13.25, which is the distance between the midpoint of normal weight (21.70) and the midpoint of obesity class I and II (34.95). Lastly, the panel exponentiated these values to convert them to RRs. For example, Wormser et al. reported an HR of 1.29 per 4.56 units of BMI for incident CHD (78). The panel calculated risk estimates for overweight and obesity compared to normal weight as follows (81):

$$HR\ for\ overweight\ compared\ to\ normal\ weight = e^{\left(\frac{\ln(1.29)}{4.56} \cdot 5.75\right)} = 1.38$$

$$HR\ for\ obesity\ compared\ to\ normal\ weight = e^{\left(\frac{\ln(1.29)}{4.56} \cdot 13.25\right)} = 2.10$$

If interactions were tested, the results were used to determine effect modification. Plots and figures were studied carefully, but interpreted with caution unless the results shown used current cutpoints and included confidence intervals (CIs). BMI below 18.5 kg/m^2 was not examined as underweight was not part of CQ2 .

Preference was given to estimates from studies that used measured rather than self-reported height and weight. Self-reported body weight is highly correlated with measured body weight with many studies showing correlations between the two measures of over 0.9 (82-85). Nevertheless, adults tend to underreport their weight, and the amount of underestimation is greater in heavier

than in lighter individuals (83,84,86). Also, since height is often over reported, especially in men (87), BMI calculated from self-report measures can underestimate measured BMI. It has been shown that self-reported and measured BMI values were equally correlated with CVD risk factors in cross-sectional studies (83). Nevertheless, when the goal is to examine risk at a specified BMI cutpoint, as is the case here, the bias in self-reported data results in misclassification and could be problematic (88). Some papers in the search included only studies that used measured weights and heights, while other MAs, pooled analyses, or SRs included results from some individual studies that did not. The panel used both self-reported and measured data for evaluation of BMI as a continuous variable; however, when addressing cutpoints the panel did not use the evidence from a study if it used measured height and weight to calculate BMI in less than 85 percent of studies included in a MA or less than 85 percent of individuals in pooled analyses. The criterion value of 85 percent was arbitrary and based only on expert opinion.

Crude, unadjusted results and results adjusted for mediators of the effect of BMI or waist circumference on outcomes were not used. Thus, the panel did not use the included study by Guh et al. because that study only presented unadjusted risk estimates (71). This review included studies that adjusted their analysis at least for age; analyses that adjusted for age, gender, and smoking were used when available.

The panel was cautious in the interpretation of ratio estimates of risk (such as HRs or RR) used to compare obesity-associated risk by age group. It is well known that ratio estimates are inflated in groups in which the incidence of the outcome is rare in the reference group compared to groups in which the incidence is more common in the reference group (89,90). Thus, even if the absolute increase in the number of events is higher in older than younger obese adults, ratio estimates of obesity risk can be higher in young adults than older adults if younger adults of normal weight are

much less likely to have the event than older adults of normal weight (and therefore the denominator of the ratio can be much smaller in the younger group). This circumstance applies to CVD, mortality, and type 2 diabetes since older normal weight adults are much more likely to experience events than younger normal weight adults.

Since for CQ2 the search was limited to SRs, pooled, or MAs of observational studies, the strength of evidence was not considered to be high because only observational study designs were used rather than randomized controlled trials (RCTs). The panel also limited its analysis to studies that were conducted in countries with predominantly Western cultures, limiting conclusions in some race groups.

Areas of insufficient evidence. The panel was not able to address parts of CQ2 due to lack of SRs, MAs, and pooled analyses identified in the systematic search. The panel members were aware of a large body of literature from individual studies examining the associations between BMI or waist circumference and hypertension or dyslipidemia, but they have not been summarized in MAs, pooled analyses, or SRs that met the panel's criteria. In addition, there were no studies in the search that compared alternative cutpoints to current cutpoints as they relate to risk of CHD, stroke, CVD, overall mortality, and diabetes. There were no studies identified that examined current waist circumference cutpoints as they relate to the risk of all outcomes addressed in CQ2; however, the panel examined studies that used waist circumference as a continuous variable. For several outcomes, there were no analyses in retrieved studies that examined current BMI and waist circumference cutpoints stratified by age, gender, and race-ethnicity. Finally, there was a lack of these types of studies examining the associations between maintaining weight and weight gain with elevated CVD risk in normal weight, overweight, and obese adults. For this reason, the panel did not develop evidence statements addressing questions related to these areas.

The methodology team and systematic review team worked closely with panel members to ensure the accuracy of data and the application of systematic evidence-based methodology.

4.5 Evidence Statements and Summaries

This section will describe the evidence statements and their rationale for CQ2a and 2b. Fifteen studies met the final I/E criteria (Spreadsheet 2.1.) (64-66,69-80). CQ2c could not be addressed in this report due to lack of SRs, pooled, or MAs examining the associations between maintaining weight and weight gain with elevated CVD risk in normal weight, overweight, and obese adults.

4.5.1 BMI Cutpoints and CVD-Related Risk

4.5.1.1 Fatal and Non-Fatal Coronary Heart Disease

Areas of Insufficient Evidence: The available evidence from SRs, pooled analyses, and MAs did not provide sufficient evidence to adequately address all sections of CQ2 pertaining to the relationship between BMI and fatal and nonfatal CHD. Specifically, the panel was unable to address the adequacy of current BMI cutpoints for overweight and obesity in comparison to alternative cutpoints. In addition, the panel was unable to determine if age-specific or race-specific BMI cutpoints for overweight and obesity are warranted to delineate elevated risk of fatal and non-fatal CHD. *Therefore, there will not be evidence statements addressing these areas.*

4.5.1.1.1 Current BMI Cutpoints – Spreadsheet 2.2.1a-b

- ***Evidence Statement 1:*** Among overweight and obese adults, analyses of <u>continuous</u> BMI show that the greater the BMI, the higher the risk of fatal CHD and combined fatal and non-fatal CHD. The current <u>cutpoints</u> for overweight (BMI ≥25.0 kg/m2) and obesity (BMI

≥30 kg/m2) compared with normal weight (BMI 18.5 to 24.9 kg/m2) are associated with elevated risk of combined fatal and non-fatal CHD.

Strength of the Evidence: Moderate

Rationale: Associations between continuous BMI and combined fatal and nonfatal CHD were studied in two pooled analyses (69,78) and two MAs (Spreadsheet 2.2.1a.) (75,77). Pooled analyses using studies from predominantly Western developed countries were conducted by Bogers et al. in 21 cohorts and the Emerging Risk Factors Collaboration (ERFC) in 58 cohorts. The MAs by Owen et al. included 15 cohorts and by Whitlock et al. included 46 cohorts. The pooled studies were adjusted for age, gender, and smoking; the MAs included adjustments for age and gender. The studies showed risk estimates associated with a 5 kg/m^2 (69), a 1 standard deviation (SD) (4.56 kg/m^2) (78), a 1 kg/m^2or 1 SD (2.5 kg/m^2) (75), and a 2 kg/m^2 (77) increase in BMI. All four studies indicated an increased risk of incident CHD with increasing BMI. Using continuous analyses from these four studies, the panel calculated risk estimates for the midpoints of overweight (BMI=27.45) and obesity (BMI=34.95) compared to the midpoint of the normal weight (BMI=21.7). Compared to the midpoint of the normal weight range, the calculated risk estimate for the midpoint of overweight ranged from 1.32 to 1.56, while the calculated risk estimate for the midpoint of obesity ranged from 1.88 to 2.77. These estimates were consistent with the estimates from the categorical analyses.

The Prospective Studies Collaboration (PSC) presented pooled analyses on BMI associations with fatal CHD that included 57 studies and adjusted for age, gender, and smoking (Spreadsheet) 2.2.1b) (79). In the PSC study examining the BMI as a continuous variable (per 5 kg/m^2), the authors found positive associations with BMI. Using continuous analyses from Whitlock 2009, the panel calculated risk estimates for the midpoints of overweight (BMI=27.45) and obesity

(BMI=34.95) compared to the midpoint of the normal weight (BMI=21.7) (see Methods). The calculated risk estimates for overweight and obesity were 1.46 and 2.39, respectively, as compared to the midpoint of the normal BMI range. The PSC also examined the association between BMI and fatal CHD within 2 BMI strata and found that the slope was steeper with a BMI above 25 compared to a BMI of below 25.

Only the meta-analysis by Whitlock *et al.* investigated fatal and non-fatal CHD separately and found that the risk estimates for the two outcomes were similar (Spreadsheets 2.2.1a. and 2.2.1b.) (77). Using the continuous analyses by Whitlock et al., the panel calculated risk estimates for the midpoints of overweight (BMI=27.45) and obesity (BMI=34.95) and compared them to the midpoint of the normal weight (BMI=21.7) (see Methods). The calculated risk estimates were 1.49 for overweight and 2.52 for obesity when compared to normal weight.

Two pooled analyses examined BMI using current cutpoints (74,78). The study by Wormser et al. indicated increased risk of combined fatal and non-fatal CHD at BMI levels higher than 25 compared to lower levels. The risk tended to be higher in the obese (BMI ≥30) when compared to the overweight group (BMI 25 to 29.9) (Spreadsheets 2.2.1a.). McGee et al. presented a pooled analysis of 26 studies with 100 percent measured BMI that examined BMI associations with fatal CHD (Spreadsheets 2.2.1b) (74). This study adjusted for age and smoking and stratified their analysis by gender. McGee et al. found a small increase in the BMI 25 to 30 category and a larger increase in the BMI ≥30 category when compared to a BMI 18.5 to 24.9 in both men and women. The corresponding risk estimates were 1.097 (95% CI: 1.001 to 1.201) and 1.624 (95% CI: 1.459 to 1.806) for women; and 1.159 (95% CI: 1.088 to 1.235) and 1.508 (95% CI: 1.362 to 1.670) for men.

4.5.1.1.2 Age-, Gender-, and Race-Specific BMI Cutpoints – Spreadsheets 2.2.1a-b

None of the studies included in our search examined current BMI cutpoints in relation to CHD risk stratified by age or race.

- ***Evidence Statement 2:*** Among overweight and obese adults, analyses of continuous BMI show that the greater the BMI, the higher the risk of fatal CHD and combined fatal and non-fatal CHD in both men and women. The current BMI cutpoints for overweight (BMI ≥25.0 kg/m2) and obesity (BMI ≥30.0 kg/m2) compared with normal weight (BMI 18.5 to 24.9 kg/m2) are associated with elevated risk of fatal CHD in both sexes.

Strength of the Evidence: Moderate

Rationale: Wormser et al. and Whitlock et al. examined the associations between continuous BMI and combined fatal and non-fatal CHD and fatal CHD, respectively (Spreadsheets 2.2.1a. and 2.2.1b) (78,79). Both studies found that risk was significantly higher with increasing BMI in both men and women, and BMI-gender interactions were null (p=0.643 and p=0.2, respectively). In the study by Wormser et al., the HRs per 1 SD (4.56 kg/m^2) were 1.24 (95% CI: 1.14 to 1.35) in women and 1.26 (95% CI: 1.18 to 1.34) in men. In the study by Whitlock et al., the HRs per 5 kg/m^2 were 1.35 (95% CI: 1.28-1.43) in women and 1.42 (95% CI: 1.35–1.48) in men. Using continuous analyses from these two studies, the panel calculated risk estimates for the midpoints of overweight (BMI=27.45) and obesity (BMI=34.95), comparing them to the midpoint of the normal weight (BMI=21.7) (see Methods). Compared to the midpoint of the normal weight range, the calculated risk estimates for the midpoints of overweight and obesity were 1.34 and 1.96 in men and 1.31 and 1.87 in women, respectively, in the study by Wormser et al. The respective calculated risk estimates were 1.50 and 2.53 in men and 1.41 and 2.22 in women in the study by Whitlock et al.

McGee et al. (74) was the only study that investigated current BMI cutpoints in relation to fatal CHD stratified by gender (Spreadsheets 2.2.1b). The authors did not formally test gender interactions, but the CIs for the gender-specific risk estimates overlapped indicating that the estimates were not different from each other. In women, the risk estimates were 1.10 (95% CI: 1.00–1.20) for overweight and 1.62 (95% CI: 1.46–1.81) for obesity. The corresponding risk estimates for men were 1.16 (95 CI: 1.09–1.24) and 1.51 (95% CI: 1.36–1.67), respectively. Thus, evidence does not indicate a need for gender-specific BMI cutpoints for CHD.

4.5.1.2 Fatal and Non-Fatal Stroke

Areas of Insufficient Evidence: The available evidence from SRs, pooled analyses, and MAs did not provide sufficient evidence to adequately address all sections of CQ2 related to the relationship between BMI and fatal and nonfatal stroke. Specifically, the panel was unable to address issues related to changing current BMI cutpoints for overweight and obesity when compared to alternative cutpoints. In addition, the panel was unable to determine if age-, sex-, or race-specific BMI cutpoints for overweight and obesity are warranted to delineate elevated risk of fatal and non-fatal stroke. Therefore, there will not be evidence statements addressing these areas.

4.5.1.2.1 Current BMI Cutpoints – Spreadsheets 2.2.2a-b

- ***Evidence Statement 3:*** Among overweight or obese adults, analyses of <u>continuous</u> BMI show that the greater the BMI, the higher the risk of fatal stroke overall as well as ischemic and hemorrhagic stroke. The same relationship holds for combined fatal and non-fatal ischemic stroke but across the entire BMI range, not just in overweight and obese adults. There is no

evidence from MAs, pooled analyses, and SRs to change current BMI cutpoints as they relate to risk of stroke.

Strength of the Evidence: Moderate

Rationale: One pooled analysis examined associations between BMI and stroke mortality from 57 cohorts: 894,576 adults predominantly from Europe, Israel, United States (including at least one study in Hawaii), and Australia with less than 10 percent from Japan (Spreadsheet 2.2.2b) (79). The underlying cause of death was obtained from death certificates, and confirmation was sought from other sources (e.g.,autopsy findings or medical records) in some but not all studies. There were 6,128, 1,395, and 1,107 deaths from overall, ischemic, and hemorrhagic strokes, respectively, that were reported over a mean 13 years of follow-up; the first 5 years were excluded to limit reverse causality. All but three studies used measured height and weight. This analysis adjusted for study, age at risk, and smoking status. For BMI in the range of 25 to less than 50 kg/m^2, each 5 kg/m^2 higher BMI was associated with an increased risk of overall stroke mortality (1.39; 1.31 to 1.48) and death from ischemic (1.38; 1.23 to 1.56) and hemorrhagic (1.53; 1.32 to 1.78) stroke. However, for BMI in the range of 15 to less than 25, there was no increased risk of overall stroke (0.92, 0.82 to 1.03) and death from ischemic (0.87, 0.68 to 1.10) or hemorrhagic (0.75, 0.58 to 1.00) stroke. Findings did not differ for either BMI range when analyses were restricted to participants who had never smoked; however, the magnitude of risk for hemorrhagic stroke was less for BMI 25 to 50 (1.37, 1.09 to 1.73), although still significant.

Another pooled analysis (78) examined the relation of BMI and combined fatal and non-fatal ischemic stroke but did not examine overall stroke or other stroke subtypes (Spreadsheet 2.2.2a). This study used data from 21 studies including 85,169 participants (2,431 cases) in 17 countries, who were predominantly European with 4 percent of participants each from Australia and Japan.

There were 2,906 ischemic stroke outcomes; 43 of 58 possible studies reported diagnosis of strokes on the basis of brain imaging and attributed stroke subtype. In ischemic stroke analyses, 21 studies were used with a total of 2,582 outcomes over a median of 5.7 years. Almost all studies used measured height and weight, but the exact number for stroke analyses was not provided. Each ~5 kg/m^2 higher BMI was associated with an increased risk of fatal and non-fatal ischemic stroke after adjusting for age, sex, and smoking status.

Both studies examined risk of stroke by BMI in figures. In the 2009 study by Whitlock et al. (79), yearly death rates per 1000 indicated greater risk of overall stroke mortality among participants with obesity (rates read from graphs were about 1.5 to 3) than overweight and normal weight participants (rates about 1.0 to 1.5), with non-overlapping CIs (Spreadsheet 2.2.2.b). These relationships were similar for ischemic and hemorrhagic stroke. Wormser et al. presented risk of combined fatal and non-fatal ischemic stroke for BMI quintiles but not for other stroke outcomes (Spreadsheet 2.2.2a) (78). Compared to the lowest BMI quintile (between 20 and 25 kg/m^2), a higher risk was observed in the quintiles overlapping the current overweight category (HR~1.2 to 1 4) after adjustment for age, sex, and smoking status. The risk for the highest quintile (BMI >30) was higher (HR~1.5 to 1.6) than those in the overweight category, but the 95% CI overlapped one of the quintiles in the overweight category. Although not entirely consistent, there is no evidence from MAs, pooled analyses, and SRs to change current BMI cutpoints as they relate to risk of stroke.

4.5.1.2.2 Age-, Gender-, and Race-Specific BMI Cutpoints

None of the studies included in our search examined current BMI cutpoints in relation to stroke risk stratified by age, gender, or race.

4.5.1.3 Fatal and Non-Fatal CVD

Areas of Insufficient Evidence: The available evidence from SRs, pooled analyses, and MAs did not provide sufficient evidence to adequately address all sections of CQ2 related to the relationship between BMI and fatal and nonfatal CVD. Specifically, the panel was unable to address issues of the adequacy of current BMI cutpoints for overweight and obesity in comparison to alternative cutpoints. Given the lack of absolute risk estimates, the panel was unable to determine if age-specific BMI cutpoints for overweight and obesity are warranted to delineate elevated risk of fatal and non-fatal CVD.

4.5.1.3.1 Current BMI Cutpoints – Spreadsheets 2.2.3a-b

- ***Evidence Statement 4:*** Among overweight and obese adults, analyses of continuous BMI show that the greater the BMI, the higher the risk of combined fatal and non-fatal CVD. The current cutpoint for obesity (BMI ≥30 kg/m2) compared with normal weight (BMI 18.5 to 24.9 kg/m2) is associated with an elevated risk of fatal CVD in men and women.

Strength of the Evidence: Moderate

Rationale: Only the ERFC pooled analysis gave results for combined fatal and nonfatal CVD (Spreadsheet 2.2.3a) (78). They used continuous BMI. The HR associated with a 4.56 kg/m^2 or 1 SD increase in BMI was 1.23 (95% CI: 1.17–1.29). The panel calculated risk estimates for the midpoints of overweight (BMI=27.45) and obesity (BMI=34.95) as compared to the midpoint of normal weight (BMI=21.7) as 1.30 and 1.82, respectively (see Methods).

No study showed overall associations between BMI and fatal CVD, but one study showed analyses stratified by age and race in women (64). Another showed associations stratified by gender (74) (Spreadsheet 2.2.3b). Abell et al. examined African American and White women <60 and ≥60

years of age (n=2,843), adjusting their analysis for age and smoking. The RR of obesity compared to normal weight ranged from 1.18 in African American women ≥60 years to 2.49 in White women <60 years. No associations were detected for overweight compared to normal weight.

The analysis of this McGee et al. study, stratified by gender, is presented above. The RR of obesity compared to normal weight was 1.529 (95% CI: 1.381 to 1.692) in women and 1.453 (95% CI: 1.327 to 1.590) in men. Overweight was associated with an elevated risk of fatal CVD in men (HR=1.10; 95% CI: 1.03 to 1.16) but not in women.

4.5.1.3.2 Age-, Gender-, and Race-Specific BMI Cutpoints – Spreadsheet 2.2.3b

None of the studies included in the panel's search examined current BMI cutpoints in relation to CVD risk stratified by age alone.

- ***Evidence Statement 5:*** In men but not women, the current BMI cutpoint for overweight (BMI 25.0 to 29.9 kg/m2) compared to normal weight (BMI 18.5 to 24.9 kg/m2) is associated with an elevated risk of fatal CVD. In both men and women, obesity (BMI ≥30.0 kg/m2) compared with normal weight is associated with an elevated risk of fatal CVD.

Strength of the Evidence: Low

Rationale: The pooled analysis by McGee et al. (74) investigated the effect of current BMI cutpoints on fatal CVD stratified by gender and estimated similar RR for men and women for overweight and obesity (Spreadsheet 2.2.3b). The RRs were 1.096 (1.034 to 1.163) and 1.453 (1.327 to 1.590) in men and 1.029 (0.948 to 1.116) and 1.529 (1.381 to 1.692) in women for overweight and obesity, respectively. However, the RR for overweight among women was not significant. The gender-BMI interaction was not tested. Only one study included in the

systematic review by Lenz et al. was relevant to answering this question. It calculated CVD mortality rates (standardized mortality rates (SMRs)); standardized to the overall German population) for high BMI levels (36.0 to 39.9 and ≥40.0) for men and women separately (Spreadsheet 2.2.3b) (80). The SMRs were larger in men than women; however, the levels of BMI investigated are above the current overweight and obesity cutpoints.

- ***Evidence Statement 6:*** Using current BMI cutpoints, the relative risk of fatal CVD was higher in obese White than in obese African American women compared to normal weight women. In overweight women, there was no increase in risk of fatal CVD compared to normal weight women in either race group.

Strength of the Evidence: Low

Rationale: Abell et al. examined the effect of measured BMI on fatal CVD for White and African American women stratified by age (<60 and ≥60 years; Spreadsheet 2.2.3b) (64). They found that there was no increase in risk in overweight compared to normal weight women of either race. However, the risk associated with obesity was higher in White women than in African American women in both age categories. In women <60 years, risk of fatal CVD associated with obesity was 2.49 (1.91–3.22) in White women and 1.46 (1.07–2.01) in African American women. For women ≥60 years, the respective estimates were 1.44 (1.25 to 1.65) and 1.18 (0.90 to 1.55). Race interactions were not tested in women, and there was no evidence in men.

4.5.1.4 Incident Type 2 Diabetes

Areas of Insufficient Evidence: The available evidence from SRs, pooled analyses, and MAs did not provide sufficient evidence to adequately address all sections of CQ2 related to the relationship between BMI and type 2 diabetes. Specifically, the panel was unable to address

issues of the adequacy of current BMI cutpoints for overweight and obesity in comparison to alternative cutpoints. In addition, the panel was unable to determine if age-, gender-, or race/ethnic-specific BMI cutpoints for overweight and obesity are warranted to delineate an elevated risk of type 2 diabetes. Therefore, there will not be evidence statements addressing these areas.

4.5.1.4.1 Current BMI Cutpoints – Spreadsheet 2.2.4

- ***Evidence Statement 7***: Analyses of <u>continuous</u> BMI across the entire BMI range show that the greater the BMI, the higher the risk of type 2 diabetes, without an indication of a threshold effect.

Strength of the Evidence: Moderate

Rationale: Two MAs (72,76) examined the association between BMI and incident type 2 diabetes (Spreadsheet 2.2.4). Vazquez et al. conducted a meta-analysis of 32 prospective cohort studies (9 from Europe, 12 from the United States, 4 from Asia, and 7 others). The pooled RR for incident type 2 diabetes was 1.92 (95% CI: 1.70 to 2.17) per SD of BMI (4.3 kg/m^2). In a meta-analysis of 31 prospective cohort studies, Hartemink et al. found a linear association between increasing BMI and type 2 diabetes risk; the pooled RR was 1.19 (95% CI 1.17 to 1.21) per one unit increase in BMI. Neither study examined BMI as a categorical variable.

These MAs indicate a linear relationship between BMI and type 2 diabetes, with no indication of any threshold effects. Even higher BMI within the normal range are associated with increased type 2 diabetes risk as compared to those with lower BMI levels.

4.5.1.4.2 Age, Gender, and Race-Specific BMI Cutpoints

None of the studies included in our search examined current BMI cutpoints in relation to type 2 diabetes stratified by age, gender, or race.

4.5.1.5 All-Cause Mortality

Areas of Insufficient Evidence: The available evidence from SRs, pooled analyses, and MAs did not provide sufficient evidence to adequately address all sections of CQ2 related to the relationship between BMI and all-cause mortality. Specifically, the panel was unable to address issues of the adequacy of existing BMI cutpoints for overweight and obesity to delineate elevated risk of all-cause mortality for adults above the age of 65 or ethnic minority groups. Therefore, there will not be evidence statements addressing the need for age- or race-specific BMI cutpoints for overweight and obesity.

4.5.1.5.1 Current BMI Cutpoints – Spreadsheet 2.2.5

- ***Evidence Statement 8:*** Among overweight and obese adults, analyses of continuous BMI show that the higher the BMI, the greater the risk of all-cause mortality. The current category for overweight (BMI 25 to 29.9 kg/m2) is not associated with elevated risk of all-cause mortality; but, a BMI at or above the current cutpoint for obesity (BMI ≥30 kg/m2) is associated with an elevated risk of all-cause mortality, compared with normal weight (18.5 to 24.9 kg/m2),

Strength of the Evidence: Moderate

Rationale: The relationship between continuous BMI and all-cause mortality was examined in two pooled analyses (Spreadsheet 2.2.5) (65,79). The pooled analyses included adult populations of 1.5 million (65) and 894,576 individuals (79) and were adjusted for age, sex, and smoking

status. Weight was self-reported in all but one of the 19 cohorts from the de Gonzalez et al. pooled analysis. In the largest study, Whitlock et al. (79) examined mortality risk associated with BMI among both men and women with a BMI >25 kg/m^2 and found a risk ratio of 1.29 (95% CI: 1.27, 1.32) per 1 BMI unit. This indicated that among overweight and obese individuals the higher the BMI the greater the risk of all-cause mortality. These findings were confirmed with similar point estimates of risk for higher BMI from the de Gonzalez et al. study that used primarily self-reported weight. Between a BMI of 15 and 25, BMI was inversely associated with all-cause mortality risk (0.79; 95% CI: 0.77, 0.82). In smoking-stratified models shown in a figure, mortality was higher in BMI categories over 30 kg/m^2 compared to <30 kg/m^2, but this association was more consistent in the never smokers than in the current smokers. Results in the smokers may have been confounded.

The relationship between the categories of overweight and obesity defined by the current BMI cutpoints and all-cause mortality was examined based on data from three studies, including one systematic review (73) and two pooled analyses (66,74) (Spreadsheet 2.2.4.). Weight was self-reported in 5 of the 13 studies included in the Heiat et al. systematic review. The pooled analysis included 388,622 adults and was adjusted for age, sex, and smoking status (74) The European Prospective Investigation into Cancer and Nutrition (EPIC) study by Pischon et al., which included 359,387 individuals, stratified by gender and used age as the underlying time variable and models were adjusted for smoking. The studies included a predominance of European and American Whites, but also included African Americans, Asians, and Hispanics.

The BMI category defined as obese (BMI ≥30 kg/m^2) was clearly associated with an increased risk of all-cause mortality. Pischon et al. compared mortality risk in men and women using six BMI categories. They found that risk was increased in both genders in two BMI categories (30 to <35

kg/m^2 and ≥35 kg/m^2) compared to a BMI of 23.5 to 25.0 kg/m^2. McGee et al. reported a significant increase in mortality risk in the obese BMI category (≥30 kg/m^2) compared to the normal weight category in both men (1.201; 95% CI: 1.119, 1.289) and women (1.275; 95% CI: 1.183, 1.373). Taken together this evidence supports that a BMI including and above the current cutpoint value for obesity (BMI ≥30 kg/m^2) compared with a BMI 18.5 to 24.9 kg/m^2 (i.e., normal weight) is associated with an elevated risk of all-cause mortality.

While the association between obesity and increased risk of all-cause mortality was well supported by the available evidence, there was no clear association between being in the overweight category (BMI 25 to 29.9 kg/m^2) and an increased risk of all-cause mortality. Pischon et al. did not find an increased risk in three categories in the overweight range (25 to <26.5, 26.5 to <28, 28 to <30) compared to a BMI of 23.5 to 25.0 kg/m^2. Using current cutpoints for overweight and normal weight, McGee et al. did not find that overweight was associated with an increased risk of all-cause mortality in men and women separately. McGee et al. found the lowest risk of all-cause mortality to be a BMI between 25.0 and 29.9 in women and between 18.5 and 29.9 in men. The findings from Heiat et al., which included a significant proportion of self-reported weights, were consistent with these results, showing no effect of overweight on mortality in a study population limited to adults who were age 65 and older. The EPIC study (66) indicated that a BMI between 23.5 and 28.0 tended to be associated with lowest risk of mortality in women and men. In the study by Whitlock et al. (79), the lowest mortality appeared to be in categories between 20.0 and 27.5 in never smokers, thus having some overlap between the normal weight and overweight categories.

The normal weight range (BMI 18.5 and 24.9 kg/m^2) appears to be a transition zone where the risk of all-cause mortality associated with BMI reaches a nadir. However, the nadir is part of a

J-shaped relationship between BMI and all-cause mortality, where all-cause mortality risk rises as BMI decreases or increases beyond this point. As noted above, the lowest risk of all-cause mortality was often inclusive of the normal weight category but not completely so in all studies reviewed. In the PSC (79), the point of lowest risk of all-cause mortality appears to be between a BMI of 22.5 and 24.9 kg/m^2 for both men and women, according to a figure presented in this paper. Risk of all-cause mortality appears to rise in a linear fashion as BMI decreases below 22.5 kg/m^2. Conversely, there is a fairly linear increase in all-cause mortality risk as BMI moves above 25 kg/m^2. Therefore, the normal weight category appears to consistently be associated with the lowest risk of all-cause mortality but begins a transition to increased risk that goes through the overweight category. The increase in risk that occurs in the overweight category relative to the normal weight category does not appear to be a significant increase. However, once BMI reaches the obese category, the increased risk is significant and consistent for this category. Although there is some evidence that significant elevation in mortality risk is not observed until a BMI of 27.5, there is a lack of compelling evidence from this set of MAs, pooled analyses, and SRs to recommend new BMI cutpoints for normal weight, overweight, and obesity.

4.5.1.5.2 Age-, Gender-, and Race-Specific BMI Cutpoints – Spreadsheet 2.2.4

None of the studies included in the panel's search examined BMI cutpoints in relation to all-cause mortality risk stratified by age or race.

- ***Evidence Statement 9:*** Sex-specific analyses of <u>continuous</u> BMI among overweight and obese men and women, show that the greater the BMI, the higher the risk of all-cause mortality. The risk of all-cause mortality associated with the current <u>cutpoints</u> of obesity was similar for men and women.

Strength of the Evidence: Moderate

Rationale: Whitlock et al. (79) examined mortality risk associated with BMI as a continuous variable among men and women with a BMI of 25 to 50 kg/m^2 and found risk ratios of 1.32 (1.29, 1.36) in men and 1.26 (1.23, 1.30) in women per 5 BMI units (Spreadsheet 2.2.4.). Between a BMI of 15 and 25, BMI was inversely associated with risk in both genders, and risk estimates were similar (0.79; 95% CI: 0.76, 0.82 in men and 0.80; 95% CI: 0.75, 0.85 in women). Findings from the study by de Gonzalez et al. used self-reported weights and reported similar findings for men and women as those seen in the Whitlock study, which used primarily measured weights (HR=1.28; 95% CI: 1.26 to 1.31 for women and HR=1.36; 95% CI: 1.32 to 1.40 for men for a BMI between 25 and 50) (Spreadsheet 2.2.4.).

Pischon et. al. compared mortality risk in men and women using six BMI categories (Spreadsheet 2.2.4.). They found that risk was increased in both genders in two BMI categories (30 to <35 kg/m^2 and ≥ 35 kg/m^2) compared to a BMI of 23.5 to 25.0 kg/m^2. The authors did not formally test the gender-BMI interaction; the CIs overlapped. Similarly, CIs overlapped in the study by McGee, who reported a significant increase in mortality risk in the obese BMI category (≥30 kg/m^2) compared to the normal weight category in both men (1.201; 95% CI: 1.119, 1.289) and women (1.275; 95% CI: 1.183, 1.373) (Spreadsheet 2.2.4.). These studies indicate that there is no need for sex-specific BMI cutpoints based on the association with mortality risk.

4.5.2 Waist Circumference Cutpoints and CVD-Related Risk

Areas of Insufficient Evidence: The available evidence from SRs, pooled analyses, and MAs did not provide sufficient evidence to adequately address the relationship between current waist circumference cutpoints and any of the outcomes in CQ2. Specifically, the panel was unable to

address issues of the adequacy of current waist circumference cutpoints for overweight and obesity in comparison to alternative cutpoints. The panel was also unable to determine if age-, gender- or race-specific waist circumference cutpoints are warranted to delineate elevated risk of all outcomes examined in CQ2. However, evidence from SRs, pooled analyses, and MAs did address the relationship between continuous waist circumference and several CQ2 outcomes. Because the panel was unable to address issues of the adequacy of current waist circumference cutpoints for overweight and obesity in comparison to alternative cutpoints, the choice of cutpoints to apply in patient evaluation is somewhat arbitrary. The absence of evidence from the available SRs, MAs and pooled analyses for waist circumference cutpoints is not the same as the evidence of absence of usefulness. The panel acknowledges that this absence does not mean that waist circumference does not provide useful information. This evidence was summarized by the panel but not linked to any evidence statements per se: it did not directly address the questions in CQ2.

4.5.2.1 Fatal and Non-Fatal CHD – Spreadsheet 2.3.1-5

Rationale: One pooled analysis (78) investigated the effect of continuous waist circumference on combined fatal and non-fatal CHD overall and stratified by age, sex, and race-ethnicity (Spreadsheet 2.3.1.). This study estimated a significant increase in CHD risk per 1 SD (12.6 cm) increase in waist circumference (HR=1.31, 1.24 to 1.37) in unstratified analyses. This result was not adjusted for BMI. The authors presented HRs for continuous waist circumference associations with combined fatal and non-fatal CHD in 3 age groups (40 to 59, 60 to 69 and ≥70 years); risk estimates declined with age (78). The HRs in the 3 age groups were 1.50 (95% CI: 1.37 to 1.63); 1.28 (95% CI: 1.20 to 1.37); and 1.13 (95% CI: 1.06 to 1.21), respectively; the interaction was significant ($p<0.0001$). The HRs among men and women were 1.24 (1.17 to 1.32) and 1.31 (1.21 to 1.43), respectively, with a borderline significant ($p=0.056$) gender-waist

circumference interaction. Risk was significantly elevated in both Whites and non-Whites with HRs of 1.35 (95% CI: 1.27 to 1.44) and 1.33 (95% CI: 1.17 to 1.51), respectively, per 1 SD (12.6cm) increase in waist circumference. However, the interaction between waist circumference and race for combined fatal and non-fatal CHD was null (78).

Fatal and Non-Fatal Stroke: One pooled analysis (78) investigated the association of waist circumference and combined fatal and non-fatal ischemic stroke (Spreadsheet 2.3.2.) but did not present data for overall stroke or other stroke subtypes. Each 12.6 cm increase in waist circumference was associated with an increased risk of ischemic stroke (1.25; 1.18 to 1.33) after adjusting for age, sex, and smoking status; the risks were increased among both men (1.32; 1.22 to 1.42) and women (1.27; 1.12 to 1.43). Estimates of risk of combined fatal and non-fatal ischemic stroke for continuous waist circumference (per 12.6 cm) in three age strata (40 to 59, 60 to 69, ≥70y) were 1.45 (95% CI=1.30 to 1.60); 1.29 (95% CI=1.20 to 1.40); and 1.10 (95% CI=1.03 to 1.18) per 12.6 cm, respectively, with a significant interaction (p=0.001) (78).

Wormser et al. presented HRs for continuous waist circumference with combined fatal and non-fatal ischemic stroke stratified by sex (Spreadsheet 2.3.2.). Risk estimates for continuous waist circumference (per 12.6 cm) were not different for men (1.33, 95% CI=1.21 to 1.46) as compared to women (1.20, 95% CI=1.05 to 1.37)(p=0.43). The authors also presented risk estimates for ischemic stroke in waist circumference quintiles in a supplemental figure. Among men, HRs ranged from 1.1 to 1.4 between 90 cm and 100 cm and were about 1.75 at about 110 and 115 cm compared to men with waist circumference of about 80 cm. Among women, HRs ranged from 1.3 to 1.5 between 80 and 95 cm and about 1.75 around 110 cm compared to women with a waist circumference of about 70 cm. These data show a graded relationship for waist

circumference with ischemic stroke, but because 95% CIs overlap across sex-specific quintiles, no clear cutpoints were indicated.

Fatal and Non-fatal CVD: Only one meta-analysis of 15 cohort studies examined the effect of continuous waist circumference on combined fatal and non-fatal CVD (70), and it estimated a HR of 1.27 (95% CI: 1.20-1.33) per 1 SD (12.6 cm) increase in waist circumference, adjusted for age, gender, and smoking (Spreadsheet 2.3.3.). The authors also showed risk ratios for the association between continuous waist circumference and combined fatal and non-fatal CVD for men and women separately (70). They reported that the RR was 1.02 (0.99 to 1.04) in men and 1.05 (1.00 to 1.09) in women for a 1 cm increase in waist circumference. A formal interaction test was not presented, but CLs overlapped indicating a similar slope of the association between men and women.

All-Cause Mortality: Pischon et al. present data from the EPIC study (66), which examined the relationship between waist circumference and all-cause mortality (Spreadsheet 2.3.4.). The EPIC study examined waist circumference cutpoints stratified by gender, but did not use current cutpoints. In this study waist circumference was analyzed in quintiles and, thus, the authors used lower cutpoints for women (<10.1; 70.1 to <75.6; 75.6 to <81.0; 81.0 to <89.0; and ≥89.0) than men (<86.0, 86.0 to <91.5; 91.5 to <96.5; 96.5 to <102.7; and ≥102.7). In models that included adjustment for BMI, there was a consistent increase in RR the greater the waist circumference. At the highest quintile for women, a waist circumference ≥89 cm was associated with an all-cause mortality risk of 1.78 (1.56 to 2.04); for men in the highest quintile (waist circumference ≥102.7 cm) risk of all-cause mortality was 2.05 (1.80 to 2.33). In both men and women, risk was higher with increasing waist circumference cutpoints, and risk estimates were similar between men and women despite the different cutpoints used.

Incident Type 2 Diabetes: One MA examined the association between continuous waist circumference and incident type 2 diabetes (76) and found that the RR for type 2 diabetes was 1.87 (95% CI 1.58, 2.20) per SD of waist circumference (11.6 cm; Spreadsheet 2.3.5.). This meta-analysis indicates a linear relationship between waist circumference and type 2 diabetes risk. The authors also reported pooled RR stratified by age (76). The pooled RRs of type 2 diabetes per SD of waist circumference (11.6cm) were 1.6 (95% CI 1.4, 1.9) and 2.0 (95% CI 1.6, 2.7) in cohorts with a mean age <50 and ≥50 years, respectively. Although the point estimate appears to be higher for the older age group, the 95% CIs between the two groups largely overlap. The pooled RRs for 1 SD increase in waist circumference (11.6 cm) were 2.3 (2.0 to 2.6) in women and 2.9 (1.8 to 4.9) in men. Although the RR is larger in men than in women, the CIs overlap, but the study did not formally test for sex and waist circumference interaction. The RRs of type 2 diabetes per SD of waist circumference (11.6 cm) were 2.4 (95% CI 1.5, 4.0) for studies in Asians, 1.9 (95% CI 1.4, 2.5) for studies in the United States (largely Caucasian participants), and 2.1 (95% CI 1.7, 2.6) for studies in Europe (largely Caucasian participants). Although the RRs appear to be higher for Asians than for U.S. or European populations, the 95% CIs overlap.

4.6 Recommendations

4.6.1. Recommendation 1a: Measure height and weight and calculate BMI at annual visits or more frequently.

(Grade E, Expert Opinion); ACC/AHA COR I, LOE C

4.6.2. Rationale: An essential component of office visits is to use routinely measured height and weight to calculate BMI and discuss with patients the disease risks associated with overweight and obesity. In a recent nationally representative survey of primary care physicians, only 49 percent

reported recording BMI regularly, and fewer than 50 percent reported always providing guidance on diet, physical activity, or weight control (91). BMI is a simple tool that uses data already being measured and can be easily calculated using widely available, downloadable programs. BMI also is calculated as part of electronic medical records systems and its use is likely to become widespread as those systems come into use.

4.6.3. Recommendation 1b. Use the current cutpoints for overweight (BMI 25.0-29.9 kg/m2) and obesity (BMI ≥30 kg/m2) to identify adults who may be at elevated risk of CVD and the current cutpoints for obesity (BMI ≥30 kg/m2) to identify adults who may be at elevated risk of mortality from all causes.

(Grade A, Strong); ACC/AHA COR I, LOE B

Rationale: To identify adults 18 years and older who have an elevated risk of developing CVD, the panel recommend the continued use of cutpoints for overweight and obesity that were recommended in the 1998 Obesity Clinical Practice Guidelines (4). The 1998 Guidelines classified normal weight as 18.5 to 24.9 kg/m2, overweight as 25.0 to 29.9 kg/m2, and obesity as ≥30 kg/m2. The current review found that overweight and obesity, as defined by these cutpoints, are associated with an elevated risk of combined fatal and non-fatal CHD and stroke as well as fatal CVD (64,69,70,74,75,77-80). The panel found few or no SRs, MAs, and pooled studies that explored alternative cutpoints that might be better at predicting elevated CVD risk. Thus, the panel concludes that there is currently no evidence to change the cutpoints for overweight and obesity to identify individuals who may have elevated CVD risk. Further, these cutpoints are used internationally to define overweight and obesity and are well-accepted in both clinical and research settings.

The Panel's review using only SRs, MAs, and pooled studies found that obesity as currently

defined (BMI ≥30 kg/m2) is associated with an elevated risk of mortality from all causes compared with a normal weight (65,66,73,74,80). We found few or no SRs, MAs, and pooled studies that explored alternative cutpoints that might be better at predicting elevated risk of dying from all causes. There was no difference in the association of obesity, as defined by a BMI ≥30, with an elevated mortality risk between sexes, leading the panel to conclude that there is no need for sex-specific cutpoints. For those in the overweight category, an increase in risk of mortality from all causes was not seen in the evidence reviewed. However, as previously noted, the overweight category is associated with increased risk of CVD.

The Panel also suggests that the same cutpoints continue to be used for all age, sex, and race-ethnic subgroups, given that the studies generally included data from various age groups, both sexes, and a variety of countries (predominantly Western but including African Americans, Asians, and Hispanics) and thus, appear to be generally applicable. However, in this review using only SRs, MAs, and pooled studies there was insufficient evidence to evaluate whether different cutpoints based on age, sex, and race/ethnicity were better at predicting elevated CVD risk or all-cause mortality than the current ones.

Recommendation 1c: Advise overweight and obese adults that the greater the BMI, the greater the risk of CVD, type 2 diabetes, and all-cause mortality.

(Grade A, Strong); ACC/AHA COR I, LOE B

Rationale: The evidence among adults 18 years and older from SRs, MAs, and pooled studies consistently showed the continuous relationship between increasing BMI and increasing risks - that the greater the BMI, the greater the risk of elevated CVD, diabetes, and all-cause mortality (64-66,69,70,72-80).

Recommendation 1d: Measure waist circumference at annual visits or more frequently in overweight and obese adults.

Advise adults that the greater the waist circumference, the greater the risk of CVD, type 2 diabetes, and all-cause mortality. The cutpoints currently in common use (from either NIH/NHLBI or WHO/IDF) may continue to be used to identify patients who may be at increased risk until further evidence becomes available.

(Grade E, Exper Opinion); ACC/AHA COR IIa, LOE B

Rationale: The 1998 Obesity Clinical Practice Guidelines (4) recommended that a waist circumference >102 cm (>40 in.) among men and >88 cm (>35 in.) among women be used to identify "increased risk in most adults with a BMI of 25 to 34.9 kg/m2". The WHO Expert Consultation (63) concluded that these same waist circumference cutpoints were associated with "substantially increased" risk and recommended using lower cutpoints (>94 cm in men, >80 cm in women) to identify adults at "increased" risk. The same lower cutpoints were also recommended by the International Diabetes Federation to identify Europids with central abdominal obesity, but the Federation suggested that different cutpoints be used among South Asians and Chinese (>90 cm for men, >80 cm for women) and for Japanese (>85 cm for men and >90 cm for women). This search, using only SRs, MAs, and pooled studies, found that there was no evidence on any of the waist circumference cutpoints in categorical analyses as they relate to an elevated risk of CVD, all-cause mortality, and type 2 diabetes in adults. For this reason, the panel did not formulate evidence statements on specific waist circumference cutpoints to identify elevated risk of CVD, diabetes, and all-cause mortality.

However, there is clear evidence supporting the linear, continuous relationship between abdominal adiposity as measured by waist circumference and risk for CVD, type 2 diabetes and

all-cause mortality. The SRs, pooled analyses, and MAs reviewed by CQ2 provided evidence on the continuous relationship between increasing waist circumference and increasing risk for CVD, type 2 diabetes and all-cause mortality (70,76,78,80). This evidence was summarized by the panel but not linked to any evidence statements as it did not directly address the questions about waist circumference cutpoints in CQ2. The panel made this recommendation because of the consistency of the continuous relationship between increasing waist circumference and increased risk of CVD, diabetes, and all-cause mortality.

4.7 Gaps in Evidence and Future Research Needs

Evidence-based BMI and waist circumference cutpoints are essential for health care practitioners to identify patients with elevated risk for CVD (including fatal and non-fatal CHD, stroke, and CVD), mortality, and incident type 2 diabetes, dyslipidemia, and hypertension. Since the panel's review of the evidence was limited to SRs, MAs and pooled analyses, this section will also only focus on the research gaps in these study types.

The panel's literature review indicated that more research is needed to compare current BMI and waist circumference cutpoints to alternative cutpoints for predicting CVD risk. In particular, studies need to compare simultaneously the predictive value of the National Institutes of Health (NIH) (4) and WHO waist circumference cutpoints. Research should clearly explicate the methods and logic for decision making to guide the choice of cutpoints for adiposity-related variables such as BMI and waist circumference. From a practical perspective, assigning risk using categorical classification schemes based on predictor-outcome relationships that are linear without obvious thresholds can be useful for informing decisions about cost/benefit or risk/benefit

balance. The panel's current classification schemes for BMI and waist circumference have a supporting evidence base, but additional research is needed to optimize the specificity of these cutpoints for higher risk of CVD. Future research should also examine the independent and combined effects of BMI and waist circumference to determine whether waist circumference adds to the prediction of chronic disease incidence and mortality by BMI, and identify BMI levels at which waist circumference is most informative for disease prediction. The combined effect between BMI and waist circumference has been hypothesized to distinctly affect CVD risk and both might be essential to correctly identify patients at elevated CVD risk.

Studies that use more valid measures of percent body fat may help optimize the use of measures of BMI and waist circumference in clinical settings. Associated research on percent body fat and changes in percent body fat on CVD risk could improve the fundamental understanding of the risk associated with waist circumference and simple-to-use BMI in the overall population and in subgroups. In addition, studies using BMI and waist circumference compared to more valid measures of percent body fat are needed to examine the predictive role of various adiposity measures. Further, the development and validation of new tools that are easy to use in clinical settings and more accurately measure body fat is needed.

The panel found that studies on appropriate cutpoints for BMI and waist are needed that show analyses stratified by age, gender, or race-ethnic groups. Studies that compare associations in different age groups using absolute risk measurements (such as events per persons at risk in a defined timeframe) would be useful, and this work would be facilitated by the development of software to more easily estimate covariate adjusted absolute risk estimates and CIs for time-to-event analyses. There is a critical lack of studies on race-ethnic differences in Western

countries to determine whether different cutpoints for subgroups might be appropriate. In this context, the lack of work is most striking in Asian Americans and Hispanic Americans.

There is an absence of SRs, MAs, and pooled analyses examining the associations between maintaining or gaining weight and risk of CVD, all-cause mortality, diabetes, hypertension, and dyslipidemia among normal weight, overweight, and obese adults. Research on methods to better identify the intentionality of weight change in observational studies would be an important contribution. Studies that test how weight change or maintenance modifies the association of baseline BMI status with the outcomes addressed in CQ2 are also needed. Likewise, studies are needed to examine whether changes in waist circumference over time, as a marker of changes in fat distribution, predict subsequent disease outcomes, independent of weight change. For studies using mortality as an outcome, special attention should be paid to address potential biases due to confounding by smoking and reverse causation by preexisiting chronic diseases.

There are a substantial number of published individual studies examining the associations between BMI or waist circumference and hypertension, dyslipidemia, and diabetes; yet, no SRs, MAs, and pooled analyses on these topics were identified during the literature search. This absence constitutes a lost opportunity to provide combined estimates and a means of better understanding appropriate BMI and waist circumference cutpoints and their clinical implications. Future research should include efforts to conduct SRs, MAs, and pooled studies to provide broader and more comprehensive evidence on the associations highlighted above, as well as the relationship between waist circumference cutpoints and all outcomes examined in CQ2.

In reviewing the evidence, the panel and methodology team identified few well-designed, well-executed SRs and MAs. The majority of studies were rated as poor using the quality rating

tool for SRs and MAs (see Appendix 2). This indicates a need for more rigorous research that complies with standard criteria for assessing the quality of such studies, including systematically rating the quality of the original individual component studies and applying other established criteria. In addition, improved methods for evaluating the quality of studies based on pooled individual-level data need to be developed. Given its distinct methodology and research approach, the panel believes that evaluation of pooled analysis may benefit from the development of different rating criteria from those used for MAs or SRs.

5 CRITICAL QUESTION 3

5.1 Statement of the Question

CQ3 has two parts:

A. In overweight or obese adults, what is the comparative efficacy/effectiveness of diets of differing forms and structures (macronutrient content, CHO and fat quality, nutrient density, amount of energy deficit, dietary pattern) or other dietary weight loss strategies (e.g., meal timing, portion controlled meal replacements) in achieving or maintaining weight loss?

B. During weight loss or weight maintenance after weight loss, what are the comparative health benefits or harms of the above diets and other dietary weight loss strategies?

5.2 Selection of the Inclusion/Exclusion Criteria

Panel members developed eligibility criteria, based on a PICOTS approach, for screening potential studies for inclusion in the evidence review. Table 5.0 presents the details of the PICOTS approach for CQ 3.

Table 5.0 Criteria for Selection of Publications for CQ3

	Inclusion Criteria	Exclusion Criteria
Population	Adults, overweight (BMI 25.0–29.9) or obese (BMI ≥30.0)	• Children • Animals studies • Population not overweight (BMI 25.0–29.9) or obese (BMI ≥30.0) at baseline
Intervention	Diet: • Low-calorie • Very low-calorie count (VLCD) • Low-fat • High-fiber • High-protein • High-CHO • Low-CHO • Scheduling (meals & meal pattern) • CHO counting • Meal replacement • Low-glycemic index • Glycemic load • Dietary Approaches to Stop Hypertension (DASH) • Omni • Atkins • Vegetarian • Therapeutic Lifestyle Changes • Portfolio • Ketogenic • Mediterranean • South Beach • Zone • Ornish • Pritikin • Energy density • Portion control • Volumetrics	• All other non-diet weight loss interventions
Comparator	No dietary intervention Other dietary intervention Multi-component intervention—if physical activity and behavioral components standardized across treatment groups	• Bariatric surgical interventions (laparoscopic tric banding; laparascopic RYGB; open RYGB; BPD/duodenal switch; GS) • Physical activity

	Inclusion Criteria	Exclusion Criteria
		• Pharmacotherapy • Multi-component interventions
Outcomes	Reduction in body weight as measured by: • Weight (kg, lbs., %) • Body mass index (BMI) and BMI change • Waist circumference • Waist-hip ratio • % body fat • % reduction of excess weight • Weight loss maintenance Must have one or more of the following outcomes: Body weight measures CVD Events • Myocardial infarction • Heart failure • Hospitalization for heart failure or stroke CVD Risk Factors • Systolic blood pressure or diastolic blood pressure • Total cholesterol, HDL-C, LDL-C, Non-HDL-C, triglycerides • Fasting insulin, fasting glucose, HbA1c • CRP Morbidity • CHD/CVD • Chronic renal failure Mortality • CVD-related • All-cause	Outcomes by measure of self-report
Timing	Intervention period ≥3 months and follow-up period ≥6 months as measured from randomization	• Intervention less than 3 months • Follow-up of less than 6 months
Setting	Westernized countries: • United States • Canada • United Kingdom • European Union • Australia • New Zealand	Countries not applicable to western weight goals and diets

	Inclusion Criteria	Exclusion Criteria
	• Israel Any clinical or research setting	
Study Design	• RCTs Sample size at least 15 subjects per treatment arm	• SRs of RCTs or controlled clinical trials • Case series, case reports, before-after studies • Results are not compared according to randomized treatment assignments • Dropout rate ≥40 percent after 6 months
Language	• Abstract must be available in English	• Studies where the abstract only, and not the full text, is available in English • Full text translation into English must be feasible
Publication Type	• Published studies	• SRs/MA • Unpublished literature – Unpublished industry-sponsored trials – Other unpublished data • FDA Medical and Statistical reviews – Theses – Studies published only as abstracts – Letters – Commentaries and opinion pieces – Non-SRs
Publication Time Frame	• Studies published in years1998–2009. • Sentinel articles published after 2009 were also screened, provided they were randomized clinical trials and had ≥100 participants per treatment arm.	Studies published before 1998

5.3 Introduction and Rationale for Question and Inclusion/Exclusion Criteria

Patients are interested in many types of popular diets that are promoted for weight loss and turn to their PCPs as authoritative sources for information and referral to evidence-based intervention and

treatment. They play critical roles as advocates of sound preventive weight management in clinical practice. CQ3 asks which types of diet and dietary strategies are helpful and efficacious to achieve weight loss. The rationale for the panel's inclusion and exclusion (I/E) criteria was to find evidence relevant to dietary habits prevalent in the United States and to be sure that the evidence was relevant to a typical dietary intervention prescribed by U.S, practitioners. In addition, to evaluate the value of the dietary component of the intervention, *per se*, only dietary intervention comparisons were allowed; the other components of the intervention (exercise, behavioral tools) had to be held constant across treatment comparisons. Thus, *all* trials included in the evidence review compared dietary interventions; some were comprehensive, including a diet component along with a physical activity and/or behavioral component. In those studies, the comparators had the same additional components; i.e., treatment groups differed by diet alone.

The panel chose a search strategy that was broad and included descriptors for popular diets and for strategies that employed all conceivable approaches. The search was to identify diets that might be broadly applicable to the overweight and obese U.S. population who were trying to lose weight with diet approaches. The targeted evidence was around weight loss and included assessments of risk factors and health benefits, in the context of weight-reducing diets. The search excluded diets for children as the focus was on developing recommendations for diets to reduce weight in the overweight and obese adult U.S. population. When this process began, the 2008 HHS *Physical Activity Guidelines for Americans* had recently been released and were based on a comprehensive review of the evidence. Therefore, the panel focused their efforts on other questions that needed that level of review.

5.4 Methods for Critical Question 3

The Obesity Panel formed subcommittees for each of its five CQs. For CQ3 the subcommittee was chaired by a physician and was composed of physicians and investigators representing academic institutions across the U.S.

As noted in Chapter 4, Process and Methods Overview, a standardized approach to systematically reviewing the literature was conducted for all CQs. Panel members participated in developing the CQ, and its I/E criteria and reviewed the included/excluded papers and their quality ratings. Contractor staff worked closely with panel members to ensure the accuracy of data abstracted into evidence and summary tables and the application of systematic evidence-based methodology.

The literature search for CQ3 included an electronic search of the Central Repository for randomized clinical trials or controlled clinical trials published in the literature from January 1998 to December 2009. The Central Repository contains citations from seven literature databases: PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts. The search produced 1416 citations, with six additional citations identified from non-search sources, i.e., by the panel members or hand search of SRs/MA (obtained through the electronic search). Two of the six citations were published after December 31, 2009. Per NHLBI policy, certain lifestyle and obesity intervention studies published after the closing date could be allowed as exceptions. These studies must be RCT's in which each study arm contained at least 100 participants and was identified by experts knowledgeable of the literature. One of the two citations published after December 2009 met the criteria and was eligible for inclusion in the CQ3 Evidence Base (92). In contrast, the other citation did not meet the criteria and was excluded from the CQ3 Evidence Base (93). The remaining 4 citations were identified through non-search

sources (i.e., hand search) by cross-checking the references listed in 28 SRs/MA. The SRs/MA were only used for manual searches and were not part of the final evidence base. This manual cross-check was done to ensure that major studies were not missing from the evidence base. As a result of this cross-check, two of six studies were screened and found eligible for inclusion (94,95). Subsequently, the quality of the studies were rated as poor.

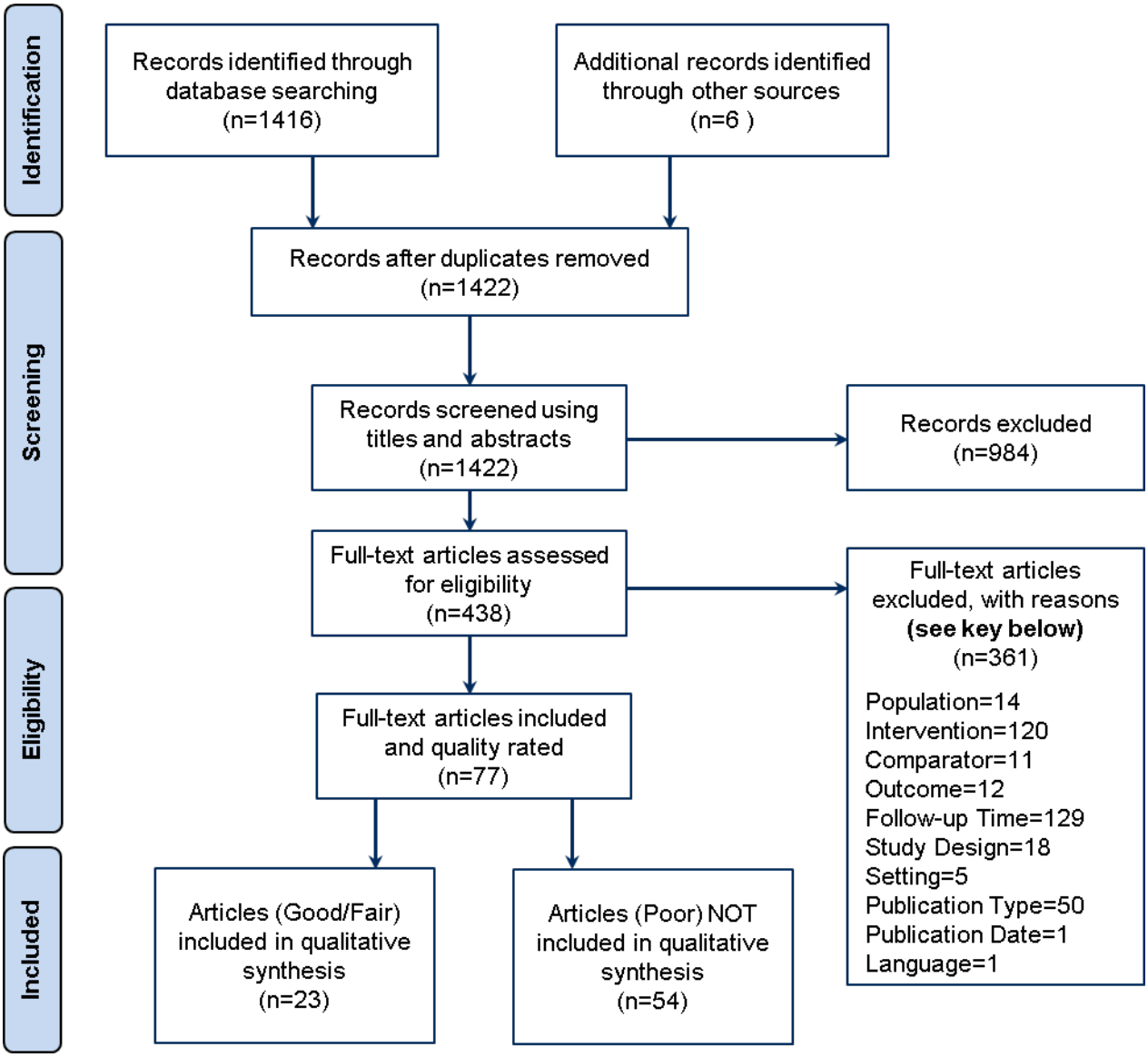
Figure 7, the PRISMA diagram, outlines the flow of information from the literature search through various steps used in the systematic review process for CQ3.

The titles and abstracts of 1422 publications were independently screened against the I/E criteria by two reviewers, resulting in 984 publications being excluded and 438 publications being retrieved for full-text review to further assess eligibility. Four hundred and thirty eight full-text publications were independently screened by two reviewers, who assessed eligibility by applying the I/E criteria; 361 of these publications were excluded based on one or more of the I/E criteria (see specified rationale as noted in the PRISMA). Furthermore, the CQ3 work group noted that since the focus of the CQ is solely on the effect of different dietary approaches to weight loss, other possible interventions could not differ. So, studies were excluded if treatment arms differed in their behavioral approach, i.e., the amount of participant contact, and amount or method of prescribed physical activity.

Seventy-seven of the 438 full-text publications met the criteria and were included. The quality (internal validity) of these 77 publications was assessed using the quality assessment tool developed to assess RCTs (see Appendix 2). Of these, 54 publications were excluded because they were rated as poor quality (94-147); 52 of these studies were rated poor due to the intention-to-treat (ITT) and attrition rates. Rationales for all the poor quality studies are included

in Appendix 3. The remaining 17 RCTs (23 articles) were rated good or fair quality (92,107,142,148-167) and included in the evidence base that was used to formulate evidence statements and recommendations. Panel members reviewed the 17 RCTs, along with their quality ratings, then, had the opportunity to raise questions. Some trials previously deemed to be of fair or good quality were downgraded to poor quality upon closer review of evidence tables. These trials used completers analyses rather than ITT analysis and had overall attrition rates exceeding 10 percent. If the study reported only an analysis of completers and had attrition at <10 percent, it was allowed in the evidence base. Methodologists worked with the systematic review team to reevaluate these trials and make a final decision. Evidence tables and summary tables consisted only of data from the original publications of eligible RCTs; these tables formed the basis for panel deliberations.

Figure 7 PRISMA Diagram Showing Selection of Articles for Obesity Question 3



5.5 Evidence Statements and Summaries

A total of 17 trials (23 articles) satisfied the final inclusion criteria for CQ3 and were rated fair or good quality (92,107,142,148-150,152-168). Most trials compared dietary interventions (92,142,148,149,152,153,155,156,159,160,162-167) and some compared the use of meal replacements or liquid diets (150,154,157,158,168). Some of the dietary interventions were comprehensive (92,142,148,149,152,153,155,156,159-167), including a diet component along with a physical activity and/or behavioral component. In those studies, the comparators had the same behavioral and physical activity components; treatment groups differed by diet alone. From these trials, three overarching evidence statements may be made regarding counseling to achieve dietary intervention. Additional statements address comparative effectiveness/efficacy of specific dietary approaches. The stated strength of evidence applies to the overall evidence statement, including any bulleted items.

Summary Tables 3.1 through 3.9 present summary data on the 17 included studies. First, Summary Table 3.1 provides the dietary interventions that form the basis for overarching evidence statements and recommendations. Second, Summary Tables 3.2–3.9 are organized around dietary form, structure, or pattern. Some studies appear in more than one summary table; they address more than one framework of analysis (e.g., macronutrient or dietary composition).

5.6 Overall Dietary Intervention and Composition—Summary Table 3.1

5.6.1 Creating Reduced Dietary Energy Intake

Evidence Statement 1. To achieve weight loss, an energy deficit is required. The techniques for reducing dietary energy intake include the following:

- Specification of an energy intake target that is less than that required for energy balance, usually 1,200 to 1,500 kcal/day for women and 1,500 to 1,800 kcal/day for men (kcal levels are usually adjusted for the individual's body weight and physical activity levels;

- Estimation of individual energy requirements according to expert guidelines (169-171) and prescription of an energy deficit of 500 kcal/day or 750 kcal/day or 30 percent energy deficit; and

- *Ad libitum* approaches where a formal energy-deficit target is not prescribed, but lower calorie intake is achieved by restriction or elimination of particular food groups or provision of prescribed foods.

Strength of the Evidence: High

Rationale: Twelve trials (18 articles)(92,107,142,148,149,152,153,155,156,159-162,164-167)provided evidence on dietary intervention and weight loss. Summary Table 3.1 summarizes the design characteristics and results of these trials. The diets included a range of macronutrient compositions or patterns. Three were rated good quality; nine were rated fair quality. The 12 studies described in 3.1 all confirm that to lose weight, a reduction in caloric intake is required. The energy balance equation requires that for weight loss, one must consume less energy than one expends or expend more energy than one consumes. Most weight loss programs reduce dietary intake by lowering energy consumption by 500 to 1,000 kcal per day (3,500 to 7,000 kcal per week) and increasing energy expenditure with moderate levels of physical activity, which will result in a weight loss of 1 to 2 lb/week.

Several strategies can achieve an energy deficit. First, one can assume that a total daily energy intake of 1,200 to 1,500 kcal for women and 1,500 to 1,800 kcal for men (with levels varying by the individual's body weight) will produce that deficit, and the dieter need only aim for that prescribed intake. That approach was used in some of the reports listed in Summary Table 3.1 (92,160,164,167).

The second approach tailors the prescription further, using an equation for daily energy requirements based on sex, weight, and age, such as the Harris Benedict Equation (169), Mifflin-St Jeor Equation (170), or the formula promoted by the World Health Organization (WHO 172). The WHO formula promoted the following process: 1) calculates daily caloric requirements by estimating an individual's energy requirement at rest (total calories), and then making adjustments for habitual physical activity, and 2) subtracts a sufficient amount of calorie from the daily calorie requirements to achieve the desired caloric deficit and weekly weight loss goal. This technique was used in two studies listed in Summary Table 3.1 (142,165). In one study (166), resting energy expenditure was measured via indirect calorimetry to calculate an individual's daily energy requirement, which was then adjusted for activity to set the weight loss calorie deficit.

None of the studies the Obesity Panel examined directly compared any methods of estimating the targeted calorie deficit to others. These studies are all randomized trials and compare a test dietary intervention implemented by highly trained or professional staff with a control diet. *All* dietary approaches were associated with weight loss when dietary energy deficits were achieved. To maintain dietary compliance, subjects in all trials participated in educational and/or behavioral therapy of varying intensity. In addition, they were to monitor food and calorie intake and physical activity.

Some of the studies examined did not require dieters to achieve a set calorie deficit target; in these trials, however, the approaches incorporated recommendations to avoid specific groups or classes of foods which led to voluntary reductions in energy intake with resulting weight loss (92,152,159,161-163). In addition, several studies provided subjects with foods required for the prescribed diet, with either an energy deficit (107,161) or *ad libitum* approach (152,155). Whether the latter approaches could be applied widely in free-living environments was not tested.

The weight loss trajectory in the studies examined is not linear and, after a few weeks, it does not reflect the targeted energy deficit resulting in pounds lost. This is the effect of both metabolic adaptation and suboptimal dietary adherence (173). As weight loss occurs, energy requirements decrease, out of proportion to the reduction accounted for in lowered weight. Consequently, targeted energy intake needs to be decreased if continued weight loss is to be achieved.

From the dietary approaches used to create energy deficits detailed in the studies of 3.1, the panel concludes that all can be successful in promoting weight loss. None offers superior short- or long-term success relative to the comparator energy-deficit diet. The existing literature, however, does not exhaustively compare all strategies against each other. Most existing randomized trials of fair and good quality compare test diets to an energy-restricted AHA Step 1 or 2 diet or the NHLBI Adult Treatment Panel (ATP) III dietary protocols. Each approach that reduced food and calorie intake was associated with weight loss, but none achieved greater benefits when tested against the energy-restricted AHA or ATP III diets when assessing weight, metabolic, or CVD risk factor outcomes.

5.6.2 Diets of Differing Forms and Structures (Macronutrient Content, Carbohydrate and Fat Quality, Nutrient Density, Amount of Energy Deficit, Dietary Pattern) or Other Dietary Weight Loss Strategies (e.g., Meal Timing, Portion Controlled Meal Replacements)

***Evidence Statement 2*.** A variety of dietary approaches can produce weight loss in overweight and obese adults. The following dietary approaches (listed in alphabetical order below) are associated with weight loss when a reduced dietary energy intake is achieved:

- A diet from the European Association for the Study of Diabetes (EASD) Guidelines, which focuses on targeting food groups, rather than formal prescribed energy restriction while still achieving an energy deficit;

- Higher protein diet (25 percent of total calories from protein, 30 percent of total calories from fat, 45 percent of total calories from carbohydrate) with provision of foods that realized energy deficit

- Higher protein Zone™-type diet (5 meals/day, each with 40 percent of total calories from carbohydrate, 30 percent of total calories from protein, 30 percent of total calories from fat) without a formal prescribed energy restriction diet but with realized energy deficit;

- Lacto-ovo-vegetarian-style diet with prescribed energy restriction

- Low-calorie diet with prescribed energy restriction;

- Low-carbohydrate diet (initially less than 20 g/day carbohydrate), without formal prescribed energy restriction but with a realized energy deficit;

- Low-fat, vegan-style diet (10 to 25 percent of total calories from fat), without prescribed energy restriction but with realized energy deficit;

- Low-fat diet (20 percent of total calories from fat), without formal prescribed energy restriction but with realized energy deficit;

- Low-glycemic load diet, either with formal prescribed energy restriction or without formal prescribed energy restriction but realized energy deficit;

- Lower fat (≤30 percent fat), high dairy (4 servings/day) diets with or without increased fiber and/or low glycemic index/load foods (low-glycemic load), with prescribed energy restriction;

- Macronutrient-targeted diets (15 percent or 25 percent of total calories from protein; 20 percent or 40 percent of total calories from fat; 35 percent, 45 percent, 55 percent or 65 percent of total calories from carbohydrate) with prescribed energy restriction;

- Mediterranean-style diet with prescribed energy restriction;

- Moderate-protein diet (12 percent of total calories from protein, 58 percent of total calories from carbohydrate, 30 percent of total calories from fat) with provision of foods that realized energy deficit;

- Diet of high-glycemic load or low-glycemic load meals with prescribed energy restriction;

- The American Heart Association Step 1 diet (with prescribed energy restriction of 1,500 to 1,800 kcal/day, <30 percent of total calories from fat, <10 percent of total calories from saturated fat).

Strength of the Evidence: High

Rationale: Twelve studies described in 18 reports (92,107,142,148,149,152,153,155,156,159-162,164-167)provided evidence about different dietary interventions and weight loss. Summary Table 3.1 summarizes the design, characteristics, and results of these trials. The diets included a range of macronutrient compositions or dietary patterns. Three studies were rated good quality, and nine were rated fair quality. The 12 studies in Summary Table 3.1 inform evidence statements regarding macronutrient content (fat, carbohydrate, and protein), some dietary patterns, and carbohydrate quality (glycemic index/load). However, adequate numbers of good or fair quality studies were not found to make statements about the following dietary weight loss approaches: fat quality; simple or complex carbohydrates; diets of varying nutrient density (including energy density); or alternative levels of energy deficits, meal timing, or meal replacements. Well-executed, large-scale studies (with high subject retention and dietary compliance levels) in overweight and obese free-living individuals of varying age ranges and ethnic diversity, as well as an analysis of those studies on an ITT methodology, are needed to inform future guidelines. Further research is needed in optimal dietary patterns, both for high-risk populations and the general population.

For the different dietary approaches (either with or without comprehensive lifestyle change) that the CQ3 panelists evaluated, it is evident that all prescribed diets that achieved an energy deficit were associated with weight loss. There was no apparent superiority of one approach, when behavioral components were balanced in the treatment arms.

The availability of such a wide range of options with established efficacy offers health care practitioners many evidence-based strategies to suggest to their patients who are overweight and

obese. Notably, these approaches were all found effective, however, only under conditions where multidisciplinary teams of medical, nutrition, and behavioral experts and other highly trained professionals worked intensively with individuals on weight loss management. With a similar level of attention to patient education and counseling, practitioners should expect comparable success (independent of diet's effect on other aspects of health factors) regardless of the energy-restricted dietary approach or targeted food-based method.

5.6.3 Pattern of Weight Loss Over Time With Dietary Intervention

Evidence Statement 3. With dietary intervention in overweight and obese adults, average weight loss is maximal at 6 months with smaller losses maintained for up to 2 years, while treatment and follow-up tapers. Weight loss achieved by dietary techniques aimed at reducing daily energy intake ranges from 4 to 12 kg at a 6-month follow-up. Thereafter, slow weight regain is observed, with a total weight loss at one year of 4 to 10 kg and at 2 years of 3 to 4 kg.

Strength of the Evidence: High

Rationale: The characteristics of the 12 studies (92,107,142,148,149,152,153,155,156,159-162,164-167) that form the evidence basis for statements and recommendations on the duration of the dietary intervention are displayed in Summary Table 3.1. Of the studies, three were rated good quality, while nine were rated fair quality. All 12 studies that were evaluated and displayed in Summary Table 3.1 produced maximal weight loss at 6 months following initiation of the intervention, with some weight regain occurring up to 2 years, but with some level of weight loss retention achieved from baseline. Of note, the amount of weight loss at these time points was variable, and the interventions often had

physical activity components. These studies did not evaluate the mechanisms of weight regain after initial weight loss; both behavioral and biologic factors contribute to weight regain. Over time, dieters can grow fatigued with the dietary prescriptions and find it difficult to maintain interest and commitment. Behavioral factors, metabolic adaptation, and changes in neurohormonal regulation can thwart maintenance of lost weight. Overweight and obese individuals who lose weight can have disproportionately reduced energy requirements (including resting energy expenditure) and increased appetitive signals, compared to those of the same age, sex, and weight who have not lost weight. Future studies are needed to identify strategies that prevent or minimize weight regain after successful dieting.

5.7 Low-Fat Approaches—Summary Table 3.2

Evidence Statement 4a. In overweight and obese adults, there is comparable weight loss at 6 to 12 months with instruction to consume a calorie-restricted (500 to 750 kilocalories deficit per day) lower fat diet (<30 percent of total calories from fat) compared to a higher fat (>40 percent of total calories from fat) diet. Comprehensive programs of lifestyle change were used in all trials. Comparator diets had 40 percent or more of total calories from fat, either with a low- carbohydrate or low-glycemic load diet or one that targets higher fat with either average or low protein.

Strength of the Evidence: Moderate

Evidence Statement 4b. With moderate weight loss, lower fat, higher carbohydrate diets, compared to higher fat, lower carbohydrate diets have the following differential effects:

- Greater reduction in LDL-C,
- Lesser reduction in serum triglycerides, and

- Lesser increases in HDL-C.

Strength of the Evidence: Moderate

Evidence Statement 4c. There is inconsistent evidence regarding blood pressure differences between lower fat, higher carbohydrate diets and higher fat, lower carbohydrate diets.

Strength of the Evidence: Low

Rationale: Three trials (two good quality and one fair quality) address interventions with low-fat approaches (92,162,166). Summary Table 3.2 summarizes these trials. Weight loss and CVD outcomes were reported in all three studies over 6 to 24 months. In addition to diet, all included a behavioral or counseling component. The three studies that examine low-fat diets are displayed in Summary Table 3.2. During the 1980s and 1990s, an evidence base emerged on the efficacy of a lower fat diet for chronic disease risk reduction. Various expert guidelines advocated the adoption of such protocols for disease prevention and health promotion (Grundy et al. 174,175-177). Since fat is energy-dense with 9 kcal/g compared to protein and carbohydrate with 4 kcal/g, high-fat foods tend to be high calorie. Individuals who eat lower fat diets tend to consume more volume and weight of foods, compared to a higher fat diet. However the satiety of lower fat or fat-free foods might wane over time since these foods may not offer the flavor or same hedonic attributes of fat-containing foods. Similarly, higher fat diets may become monotonous, making long-term compliance more difficult.

This review yielded three good or fair quality studies (92,162,166), comparing the prescription of low-total and low-saturated fat diets to low-glycemic load or low-carbohydrate approaches. A low-fat diet is generally defined as containing 20 to 30 percent of total calories from fat; those

levels were used in the studies. The lower carbohydrate approaches used in comparative studies consist of ≤ 45 percent of calories from carbohydrates (considerably higher than the very low-carbohydrate approaches). One 6-month study (162) prescribed an *ad libitum* approach, albeit with restriction of certain food choices, which resulted in an energy restriction of approximately 400 to 500 kcal/day. Whereas two longer studies (92,166) prescribed a calorie restriction (deficit of 750 kcal/day or 1,200 to 1,500 kcal/day for women and 1,500 to 1,800 kcal/day for men). All studies demonstrate comparable weight loss with lower or higher fat dietary approaches, given that other factors (food restrictions, instructions on amount of calorie deficit) are held constant.

5.8 Higher Protein (25–30 percent of Energy) Approaches—Summary Table 3.3

Evidence Statement 5a. In overweight and obese adults, recommendations to increase dietary protein (25 percent of total calories) as part of a comprehensive weight loss intervention results in equivalent weight loss as compared with a typical protein diet (15 percent of total calories), when both diets are calorie restricted (500 to 750 kcal/day deficit).

Strength of the Evidence: High

Evidence Statement 5b. In overweight and obese adults, when compared to typical protein diets (15 percent of total calories), high protein diets (25 percent of total calories) do not result in more beneficial effects on CVD risk factors, in the presence of weight loss and other macronutrient changes.

Strength of the Evidence: Low

Evidence Statement 5c. Based on studies conducted in settings where all food provided delivers increased protein (25 percent of total calories), either as part of caloric restriction or with *ad libitum* energy consumption, there is insufficient evidence to inform recommendations for weight loss interventions in free-living overweight or obese individuals.

Rationale: Five RCTs (10 articles) included interventions with higher protein (25 to 30 percent of total calories) approaches (107,148,149,153,155,159,161,165,166). Table 3.3 summarizes the design, characteristics, and results of these trials. One trial was rated good quality; four were rated fair quality. In two trials (107,148,149,153,155,161), all food was provided. All trials reported outcomes for weight change and CVD risk factors. Duration of follow-up ranged from 6 months to 2 years.

The five RCTs (10 articles) included interventions with higher protein (25 to 30 percent of total calories) are shown in Summary Table 3.3. Physiologic experiments and human diet studies (177,178) point to dietary protein as promoting satiety with a potential increase in resting energy expenditure. Thus, a strategy to improve weight loss and maintenance of lost weight would be to promote satiety and resting energy expenditure while on reduced caloric intake. Some investigators have increased dietary protein from levels typically seen in the American diet (15 percent of total calories as protein) as a pathway to more efficacious dieting strategies for weight loss. In real world settings, however, prescription of increased protein can be difficult to achieve due to the wide availability of palatable foods and snacks that are low in protein and high in carbohydrates and fat. Therefore, to follow a diet of increased protein consumption, one must simultaneously reduce consumption of fat and carbohydrate, primary elements of many lower cost and convenient foods and snacks.

These studies took two different approaches to testing the effect of increased dietary protein on weight loss: 1) prescribing an energy deficit and specific macronutrient targets with increased protein to 25 percent of total calories (165,166) or 30 percent of total calories (159), and 2) providing most or all foods that met specified energy targets (25 percent (107,153,155) or 30 percent (107,161) of total calories as protein).

When a prescription was given for both energy deficit and specific macronutrient targets (increasing protein to 25 percent of total calories) as in the POUNDS LOST and SMART studies, the macronutrient targets for protein were not reached. In addition, there was no difference in weight loss between groups assigned to energy-restricted lower or to higher protein intake; however, both groups successfully achieved weight loss. A study by McAuley et al., tested a diet popularized by The Zone™ popular diet book (179). Each of five meals per day was required to have a specified 30 percent of energy as protein. This diet was tested against an Atkins-type low-carbohydrate diet and an EASD-endorsed (European Association for the Study of Diabetes) food group diet. The study did not test higher or lower protein levels *per se*, but rather the two diets described in the Zone™ diet book and the Atkins diet book.

CALERIE (107,161) tested 30 percent dietary energy restriction in a metabolic ward setting and tested changes in glycemic load and protein. There was no significant difference in weight loss between group assignments of high glycemic load and 20 percent of total calories as protein or low glycemic load and 30 percent of total calories as protein. These were not free-living individuals, and the enforced total calorie restriction (all food provided in a metabolic ward) of 30 percent of estimated requirements, whether assigned to 20 percent or 30 percent of the reduced total calories as protein, was likely the major determinant of weight loss.

A Denmark study (148,149,153,155) tested increasing dietary protein and reducing glycemic load using the unique methodology of providing all foods in a university-setting supermarket, where dietitians instructed participants in selecting foods with appropriate macronutrient content. Participants could eat *ad libitum* from the selected foods and were not given an energy deficit target. The higher protein, lower glycemic load approach demonstrated a weight loss benefit. This study, while intriguing, cannot be translated to real world guidance without evidence that free-living individuals can achieve the dietary regimen and that the regimen produces weight loss.

As to the effect of higher and lower protein levels on CVD risk factors, these studies did not show ascertainable differences in lipids or blood pressure due to protein alterations alone, although manipulations of fat content and carbohydrate content will result in changes in lipids.

5.9 Low Carbohydrate Approaches (<30g/Day)—Summary Table 3.4

Evidence Statement 6a. In overweight and obese adults, there are no differences in weight loss at 6 months with instructions to consume a carbohydrate-restricted diet (20 g/day) for up to three months, followed by increasing levels of carbohydrate intake up to a point at which weight loss plateaus) in comparison to instruction to consume a calorie-restricted, low-fat diet. The comparator diets on which this statement is based were either calorie-restricted, higher CHO and lower protein (55 percent of total calories from carbohydrate, 30 percent of total calories from fat, 15 percent of total calories from protein) or a lower fat EASD (European Association for the Study of Diabetes) food group dietary pattern (40 percent of total calories from CHO, 30 percent of total calories from fat, and 30 percent of total calories from protein).

Strength of the Evidence: Low

***Evidence Statement 6b*.** There is insufficient evidence to comment on the CVD risk factor effects of low carbohydrate diets.

Rationale: Two RCTs addressed interventions with low-carbohydrate approaches (92,159). Summary Table 3.4 presents a brief description of these trials. The first, a good quality trial conducted in the United States, reports on weight loss and CVD risk factors at 6 and 12 months. The second, a fair quality trial, was conducted in an academic setting in New Zealand for 24 weeks. The two studies addressing low-carbohydrate weight loss diets are shown in Summary Table 3.4. Low-carbohydrate approaches to dieting, as endorsed by The Atkins Diet books (180), have been popular among consumers for many decades. This is, in part, due to the initial rapid weight loss, which occurs in the first few weeks of the low-carbohydrate diet because of glycogen depletion. Glycogen is stored with two molecules of water; fat is anhydrous. As glycogen is depleted, water is released, and weight loss is amplified. The low-carbohydrate diet prescribes an initial period of only 20 grams of daily carbohydrate intake. In the studies examined (92,159), this was sustained for 3 weeks to 3 months. Then, carbohydrate is re-introduced at 5 grams per day per week until stable and desirable weight loss is achieved. Another effect of the low-carbohydrate diet is to eliminate certain food types or food groups, especially packaged and processed foods, from the diet. Diet books using the low-carbohydrate approach emphasize what one *can* eat (such as steak, chicken, fish, shrimp, eggs, hollandaise sauce, asparagus, lettuce, whipped cream) rather than what one *cannot* eat (breads, sweets, chips, potatoes, rice, apples).

The first (92) of two studies we examined was rated good quality and compared the low-carbohydrate diet with a low-fat (<30 percent of total calories as fat), energy restricted approach. The other aspects of the intervention (contact time and exercise instruction) were controlled across groups. There was no difference in weight loss between groups at 6 and 12

months; in fact, both groups lost more than 10 kg, on average, at 1 year. The second study (159) was rated fair quality and compared a low-carbohydrate diet to a Zone™ diet (179) and to an EASD food group diet (181) in obese, insulin-resistant women. While the study reports greater weight loss at 6 months with the EASD diet compared to the other two, the amount does not reach the study's *a priori* definition of clinical significance (-3 kg).

The number of good or fair quality studies to address low-carbohydrate approaches is disappointing. Maintaining long-term compliance can be difficult because of the restriction in food choices; retention is often problematic. Since the two included studies show that the low-carbohydrate dietary approach does not produce weight loss greater than calorie-restricted, low-fat approaches over 6 to 12 months, it would be useful to have more observations to better evaluate this popular approach.

5.10 Complex Versus Simple Carbohydrates—Summary Table 3.5

Evidence Statement 7. There is insufficient evidence to comment on the value of substituting either simple or complex carbohydrates for dietary fat for overweight or obese adults for achieving weight loss.

Rationale: Only one fair quality randomized trial comparing *ad libitum* intake of either complex or simple carbohydrates satisfied eligibility criteria for inclusion (152). Summary Table 3.5 summarizes the design, characteristics, and results of this trial. The study addressing complex vs. simple carbohydrates for weight-reduction diets, shown in Summary Table 3.5, included a control arm; however, the attrition rate in this arm was substantially higher than in the two test diet arms. Only the results from the test diet arms were included as part of this panel's evidence base. Since the study provided food constituting more than 60 percent of energy requirements, the

generalizability to free living conditions is limited. Weight loss was greater at 6 months with the low-fat, high-complex carbohydrate diet than the low-fat, high-simple carbohydrate diet. Because there is only one study, no evidence statement can be made.

5.11 Glycemic Load Dietary Approaches—Summary Table 3.6

Evidence Statement 8. In overweight and obese adults, both high- and low-glycemic load diets produce a comparable weight loss with a similar rate of loss over 6 months.

Strength of the Evidence: Low

Rationale: Two randomized trials, described in three papers (107,161,162), met the inclusion criteria; both trials were conducted in the United States and were rated fair quality. One trial (107,161) was conducted for 12 months; however, only the six-month results are discussed as the 12-month results were not included due to the use of completers analysis and an overall withdrawal rate exceeding 10 percent. The second trial reports the results on a number of CVD risk factors at 6, 12, and 18 months (162). The two trials that tested low-glycemic load approaches are shown in Summary Table 3.6. Diets that manipulate glycemic load have become popular because they attempt to modify insulin secretion. The available evidence suggests that insulin secretion can be stimulated by foods that contain rapidly absorbed carbohydrates. Low-glycemic load foods tend to be higher in fiber and have higher levels of complex carbohydrates and lower levels of simple carbohydrates. The rationale for low-glycemic load diets is that they will produce a lower and more moderated insulin response and result in less hunger in the long term, although this has never been convincingly shown. The low-glycemic load approach is popular in patients with diabetes and pre-diabetes.

Because of the widespread prescription of low-glycemic load diets for people with insulin resistance, the panel sought studies comparing low- and high-glycemic load approaches. Unfortunately, the available evidence from good or fair quality studies is sparse; it shows that both high- and low-glycemic load diets can be successful for weight loss over 6 to 18 months. One study (107,161) conducted in a metabolic ward with all food provided and an imposed caloric deficit resulted in no difference in weight loss among diets of high- and low-glycemic load. Another study (162) of *ad libitum* food intake among free-living individuals showed no difference in weight loss between a low-glycemic load diet (40 percent carbohydrate, 35 percent fat, 25 percent protein) and a low-fat diet (55 percent carbohydrate, 20 percent fat, 25 percent protein). However, that study did demonstrate significant differences at 6 and 18 months in LDL-C favoring the low-fat diet and in HDL-C and triglycerides favoring the low-glycemic load diet. There were no differences in blood pressure, glucose, or insulin between diets.

Because of the widespread use of diets that manipulate glycemic load in populations with diabetes and pre-diabetes, the panel identified the need for studies of glycemic load (or glycemic index) in free-living individuals, with attention to retention, compliance, and ITT analysis of outcomes. See section 7.17.

5.12 Dietary Patterns (Mediterranean Style and Vegetarian and Other Dietary Pattern Approaches)—Summary Table 3.7

Evidence Statement 9. In overweight and obese adults, a variety of calorie-restricted dietary patterns (i.e., Mediterranean-style, lower fat lacto-ovo-vegetarian or vegan-style, or lower fat high dairy/calcium with added fiber and/or low-glycemic index/load foods) produce weight loss and

cardiovascular benefits that are comparable to an energy restricted, lower fat (25–30 percent of total calories from fat, ATP III or AHA Step 1) dietary pattern.

Strength of the Evidence: Low

Rationale: Four RCTs (one good quality, three fair quality) described in six articles met inclusion criteria for strategies focusing on alternative types of dietary patterns for weight loss (142,156,160,163,164,167). Summary Table 3.7 summarizes the design, characteristics, and results of these trials. The good quality trial compared a Mediterranean-style diet to a low-fat dietary pattern (164) and followed subjects in a university setting for 4 years. Two fair quality trials compared a vegetarian-style dietary pattern intervention (156,160,163,167) to a lower fat dietary pattern. Only two of the trials reported on CVD risk factor outcomes in addition to weight change. The fourth trial evaluated lower fat, higher dairy/calcium, and higher fiber and lower glycemic index/load dietary pattern approaches (142). Summary Table 3.7 displays the four studies and six articles describing dietary pattern approaches. Recent epidemiological evidence from population-based prospective studies suggests that healthier overall dietary patterns are associated with lower rates of obesity and reduced chronic disease risk, including CVD and diabetes. Dietary patterns are generally defined in two different ways: 1) in terms of the population's *habitual* eating practices (also referred to as empirical or *a posteriori* patterns) such as Mediterranean or vegan/vegetarian dietary patterns, or 2) as patterns that are specifically designed to target certain foods, improve macronutrient profiles, and achieve higher nutrient density and overall improved dietary quality based upon existing expert evidence (also referred to as theoretical or *a priori* patterns) such as the DASH (182) DASH-Sodium (183), and AHA Step 1 (Grundy et al. 174) and National Cholesterol Education Program ATP III dietary patterns (175). The randomized clinical trials were designed to test the effectiveness of dietary patterns that

targeted specific foods and nutrients, based on evidence suggesting that they might promote weight loss and potentially improve other health outcomes (e.g., decrease CVD risk factors). In all the trials, the test dietary patterns were compared to lower fat (25–30 percent) protocols, which typically advocated fat restriction, higher complex carbohydrates, and whole grains. Energy intake was either explicitly restricted or achieved by subjects voluntarily. Trial arms were balanced in terms of physical activity recommendations and intensity of behavioral therapy managed by highly trained professionals.

For weight loss outcomes, observed advantages of the Mediterranean-style, low-fat, lacto-ovo-vegetarian-style, vegan, or low-fat, high-dairy/calcium with and without high fiber (low glycemic index/load) foods are inconsistent across available research studies and modest, at best (164). At follow-up ranging from 6 to 18 months, only one trial indicated that the Mediterranean-style dietary pattern resulted in greater weight losses (difference -2 kg) at 12 months and greater reductions in waist circumference (-1.3 cm) compared to the AHA Step 1 dietary pattern. One trial indicated that at 6 and 18 months, the energy-restricted, low-fat, lacto-ovo-vegetarian-style diet did not result in differences in weight, BMI, or waist circumference changes compared to the low-fat dietary pattern (160,167). One other trial suggested that the low-fat, vegan dietary pattern resulted in greater reductions in weight (-4.9 kg and -3.1 kg at both 12 and 24 months, respectively) compared to the low-fat National Cholesterol Education Program pattern (-1.8kg and -0.8kg, respectively). In one study, changes in weight loss and secondary weight outcomes (body fat, trunk fat, waist and hip circumferences) did not differ between a high-dairy diet and a diet high in dairy and fiber and with a low-glycemic index (142). At the 4-year follow-up, one trial demonstrated that shorter-term differences in weight outcomes between the Mediterranean-style and AHA Step 1 dietary patterns were attenuated (164).

For CVD risk factors, like weight loss outcomes, the evidence of modest favorable benefits of certain dietary patterns also is inconsistent. One study indicated that the Mediterranean-style dietary pattern compared to the AHA Step 1 dietary pattern at the 12-month follow-up resulted in modest but favorable changes in glucose control, lipids, and blood pressure, with a difference of -0.6 percent in HbA1c, -1.2 mmol/L in plasma glucose, +0.08mmol/L in HDL-C, -0.22 mmol/L in triglycerides, -3.1 mmHg in systolic blood pressure, and -1.0mmHg in diastolic blood pressure (164). At year 4, the Mediterranean-style diet changes remained favorable for glucose control and lipids, but the blood pressure impacts were attenuated (164). One study (167) indicated that LDL-C was lower at 6 months in a low-fat, lacto-ovo-vegetarian dietary group (-0.16 mmol/L) compared to the low-fat (+0.05 mmol/L) dietary pattern group. At 18 months, the LDL-C levels no longer differed in vegetarian and low-fat groups.

Diets that differ substantially from an individual's habitual dietary patterns may be difficult to adhere to and maintain long term and appear to result in lower dietary treatment compliance. Since calorie-restricted diets appear to be similar in their short- and long-term effects on weight, metabolic, and CVD outcomes with no consistent, strong evidence of the benefits of one dietary pattern over another, practitioners are advised to tailor dietary interventions for weight loss to the individual's habitual eating practices, when possible (160,164,167).

5.13 Meal Replacements and Adding Foods to Liquid Diets —Summary Table 3.8

***Evidence Statement 10a*.** In overweight and obese women, the use of liquid and bar meal replacements is associated with increased weight loss at up to 6 months, in comparison to a balanced deficit diet utilizing only conventional food. Longer term evidence of continued weight loss advantage is lacking.

Strength of the Evidence: Low

Evidence Statement 10b. There is insufficient evidence to comment on the value of adding various types of foods to a low-calorie liquid diet.

Rationale: Three studies (rated fair quality) used meal replacements with differing counseling approaches (157,168) and with adding specific solid food to a liquid diet (154) (Summary Table 3.8). The two studies that evaluated meal replacements compared dietitian-led counseling with and without the use of liquid or bar meal replacements. Those studies evaluated only women and neither trial reported data on CVD risk factors. The study that evaluated the addition of various types of foods to a liquid diet allowed male and female subjects to add either almonds or a food of equivalent caloric content from a food list. Summary Table 3.8 describes the three studies evaluating meal replacements. Meal replacements are commercial, portion-controlled products. They are packaged as powders that can be reconstituted as shakes or soups, liquids, bars, or packaged or frozen entrees or snacks. In practice, meal replacements are usually employed to enforce caloric restraint, and they were used in this way in the Look AHEAD study (157). In the two studies described in Summary Table 3.8, the use of liquid and bar meal replacements resulted in greater weight loss at 6 months (151) and 20 weeks (157), although no significant difference in weight loss was documented by 40 or 60 weeks in one of the studies (157), although no significant difference in weight loss was documented by 40 or 60 weeks in one of the studies (157).

Although most meal replacement diets replace one to two meals and are usually prescribed as part of a 1,200 to 1,500 kcal/day low-calorie diet, one fair quality study (154) addressed the strategy of liberalizing the diet while on a liquid diet for all three meals. That study involved adding targeted foods to an energy-restricted liquid formula. Summary Table 3.8 summarizes the design,

characteristics, and results of this trial. The issue of helping patients sustain compliance while on meal replacement diets has practical implications. However, just one small study addresses the issue.

5.14 Very Low-Calorie Diet Approaches—Summary Table 3.9

Evidence Statement 11a. There is insufficient evidence to comment on the value of liquid protein supplementation following the VLCD induction of weight loss as an aid to weight loss maintenance.

Evidence Statement 11b. There is insufficient evidence to comment on strategies to provide more supervision of VLCD adherence or to liberalize VLCD therapy with the addition of conventional foods as an aid to the induction of weight loss.

Rationale: Two studies (rated fair quality) addressing VLCDs for weight loss net inclusion criteria and are characterized in Summary Table 3.9 (150,158). They evaluated VLCDs as an initial phase for weight loss maintenance programs. In addition, CQ 4 addressed VLCDs as part of behavioral interventions, assessing different behavioral approaches as additions to VLCDs (184-187). The two studies describing VLCDs are found in Summary Table 3.9. VLCDs are usually defined as diets providing <800 kcal/day (< 3,347 kilojoules) and are designed to produce rapid weight loss while preserving lean body mass. The macronutrient content of these diets therefore typically consist of 0.8 to 1.5 grams of protein/kg of ideal body weight per day. The protein usually is provided as a milk, soy, or egg-based powder, which is mixed with water and ingested as a liquid. These powders also contain carbohydrate (up to 80 g/day) and fat (up to 15 g/day) and include 100 percent of the recommended daily allowance for essential vitamins and minerals (188). Another method of obtaining a VLCD is to use the protein-sparing modified fast

(PSMF), which consists of lean meat, fish, and fowl. The PSMF must be supplemented with vitamins and minerals as well as large amounts of water and noncaloric fluids (4,189). VLCDs are considered safe and effective when used by individuals under carefully supervised medical monitoring.

Despite the popularity of VLCDs, only two studies using liquid diets in obese subjects (154,158) and rated fair were rated of adequate quality to be included in CQ3. They used VLCD without intensive lifestyle intervention (ILI) and both had weight loss and weight maintenance phases. Lejeune, et al. 2005 used a 2100 kj (500 kcal)/day VLCD [Modifast powders that were reconstituted with water into a milkshake, pudding, soup or cereal and supplemented with fruits, vegetables] during 4 weeks of weight loss followed by a 6 month maintenance phase where groups consumed a 'usual diet' and one group received an additional liquid, reconstituted pure protein powder supplement (30 g protein/day). Weight differences at 6 months favored the protein supplement group. Torgerson et al. 1999 used a 2100 kj (500 kcal)/day VLCD for 16 weeks using three different approaches: liquid-only diet inpatient, liquid-only diet outpatient, and outpatient with VLCD plus fruit and vegetable supplements. The study found no differences in weight losses.

The 1998 NIH Obesity Clinical Guidelines state that long-term (<1 year) weight loss with VLCDs is not different from that of low-calorie diets, despite superior initial weight loss. The equivalence of long-term weight losses was attributable to greater weight regain among the VLCD-treated subjects. Two studies (186,187) evaluated by CQ4 in this evidence review met inclusion criteria and addressed VLCDs for weight maintenance in the context of lifestyle intervention. Borg et al. 2002 used an intervention which included Nutrilett (2100 kj or 500 kcal)/day vs. control. Fogelholm et al. 2000 used the same Nutrilett program and had a similar

duration. Each study started with a weight loss program, which was 2 and 3 months in length for the VLCD, followed by maintenance and follow-up. The modest short-term weight loss was not sustained for a longer term (33 months), with average weight regains between 5.9 to 9.7 kg at 33 months. Exercise maintenance seemed to attenuate the weight regain.

Recommendations—Dietary Strategies for Weight Loss

Recommendation 3a. Prescribe a diet to achieve reduced calorie intake for obese or overweight individuals who would benefit from weight loss, as part of a comprehensive lifestyle intervention. Any one of the following methods can be used to reduce food and calorie intake:

a. Prescribe 1,200–1,500 kcal/day for women and 1,500–1,800 kcal/day for men (kilocalorie levels are usually adjusted for the individual's body weight);

b. Prescribe a 500-kcal/day or 750-kcal/day energy deficit; or

c. Prescribe one of the evidence-based diets that restricts certain food types (such as high-carbohydrate foods, low-fiber foods or high-fat foods) in order to create an energy deficit by reduced food intake.

(Grade A, Strong); ACC/AHA COR I, LOE A

Rationale: Foundational to weight loss is the necessity of creating a negative energy balance during the active weight loss period. To do this, the emphasis must be on reducing energy intake from food. This is a requirement since to create a substantial energy deficit by increasing energy expenditure in physical activity *alone* is, for most Americans, very difficult. Thus, for the active weight loss phase of weight management, the emphasis in lifestyle counseling is on constructing a healthy low-calorie diet that can produce weight loss of 1 to 2 lb/wk. We provide three recommended ways to achieve this aim, but health care providers must understand that the key to

achieving them is to give patients not only instructions but also tools to implement them. In the majority of the studies included in our review, registered dietitians provided the behavioral counseling. Therefore, practitioners who are not proficient and willing to devote the considerable time required should refer patients who would benefit from weight loss to a nutrition professional or to counselors trained in nutrition intervention, so that patients may benefit from behavioral intervention.

Evidence Statement 1 identified three pathways (used in the studies from the evidence base for CQ3) to achieve negative energy balance through reduced food intake and those pathways form the basis for Recommendation 1. The three pathways described in Recommendation 1 are all documented to produce weight loss. The provider should consider the patient's preference, ability, and health status to select a pathway to achieve negative energy balance. The most common technique is to limit intake to 1200 to 1500 kcal/day for women or 1500 to 1800 kcal for men (92,160,164,167). The higher limits are for individuals who have greater weights at baseline. In another technique, the baseline energy requirement is calculated with a formula, described above (169,170,172), and modified for patients' habitual exercise pattern. This "tailors" the estimation of baseline energy requirements; the calorie goal is determined by subtracting 500 to 750 kcal/day. Of course, the goal may be readjusted depending on actual weight loss. For both of these techniques, patients are then given tools and strategies to achieve daily caloric targets and monitor daily intake. As variants of these approaches, sometimes patients are provided with tools to monitor "points" that correspond to a calorie limit. Some diets are so called "ad libitum" approaches (92,152,159,161-163). However, these diets restrict certain food types or food groups. "Ad libitum" refers only to food intake of certain prescribed foods. It

must be emphasized that the "ad libitum" is illusory. In these approaches, reduced caloric intake is well documented, and the weight loss achieved is due to negative energy balance.

Recommendation 3b. Prescribe a calorie restricted diet, for obese and overweight individuals who would benefit from weight loss, based on the patient's preferences and health status and preferably refer to a nutrition professional[i] for counseling. A variety of dietary approaches can produce weight loss in overweight and obese adults, as presented in CQ3, Evidence Statement 2. *(Grade A, Strong); ACC/AHA COR I, LOE A*

Rationale: A myriad of dietary approaches to weight loss can be successful. The evidence supports all the approaches listed in Evidence Statement 2, above. Diets recommended for Americans by the AHA and American Diabetes Association (ADA) can produce weight loss and are nutritionally balanced (Grundy et al.174,175,176,190). Weight loss can be achieved with vegetarian or vegan diets (142,156,163) and with dietary patterns modeled after certain traditional cultures (164). Diets employed in the popular diet books can induce weight loss (179,180) but may not be nutritionally balanced. Although not considered in this evidence review, health care practitioners must consider overweight and obese patients with hypertension as good candidates for a calorie-restricted DASH diet, with nine servings of fruits and vegetables and three servings of low-fat dairy products (182,183,191). The charge to practitioners is to support patients' preferences and strong aversions and to guide their patients in selecting healthy dietary patterns that can be sustained over the longer term.

The message to the practitioner is three-fold. First, there are many options/choices that can work to help patients lose weight and achieve health benefits. Second, when selecting a weight-loss diet consider the contribution of the diet to management of other risk factors or diseases (e.g., type

2 diabetes, hypertension, gout). Also consider the long-term nutritional adequacy and sustainability of the diet, and tailor the dietary intervention to the needs, habitual patterns, and preferences of the individual. Third, no diet will be effective for weight loss without calorie reduction. Losing weight requires reduction in calorie intake, whether patients are tracking calories, points, grams of a macronutrient, or eating from a limited list of food choices. If a diet "doesn't work," then an analysis should reveal an excessive consumption of calories, relative to energy expenditure, and a modification of approach is indicated.

6.16 Gaps in Evidence and Future Research Needs

Dietary interventions are a critical element of any attempt to lose weight and maintain weight loss. While our review of the evidence supports that there are a variety of dietary patterns and alternative dietary forms, structures, or composition to achieve and sustain weight loss, further research is still needed.

Because long-term dietary adherence is problematic in weight management, studies should test pragmatic approaches to diet intervention delivery in free-living individuals for at least 2 years. What works over six months may not be durable over two years. The long-term outcome is of utmost importance to determine the best dietary approach to sustain weight loss over the long-term.

Additionally, studies are needed testing the impact of tailoring choice of dietary interventions on the individual's *ability to adhere long-term*. One of the findings of our assessment of the longer-term diet studies was that a minority of participants were adhering to dietary recommendations at two years. The diet can only have an effect if people will follow it.

And last, to fully understand and develop remedies for the challenges of long-term weight maintenance, studies are needed evaluating the physiologic and biologic adaptations to weight loss. These are physiologic studies of metabolic response to weight reduction. Understanding the physiologic response to weight reduction might enable us to define better dietary methods of caloric restriction during weight reduction and maintenance.

6. CRITICAL QUESTION 4

6.1 Statement of the Question

CQ4 has two parts:

A. Among overweight and obese adults, what is the efficacy/effectiveness of a comprehensive lifestyle intervention program (i.e., comprised of diet, physical activity, and behavior therapy) in facilitating weight loss or maintenance of lost weight?

B. What characteristics of delivering comprehensive lifestyle interventions (e.g., frequency and duration of treatment, individual vs. group sessions, onsite vs. phone/e-mail contact) are associated with greater weight loss or weight loss maintenance?

6.2 Selection of the Inclusion/Exclusion Criteria

Panel members developed eligibility criteria, based on a PICOTS approach, to use for screening potential studies for inclusion in the evidence review. Table 6.0 presents the details of the PICOTS approach for CQ4. Only RCTs were considered.

Table 6.0. Criteria for Selection of Publications for CQ4

	Inclusion Criteria		Exclusion Criteria
Population	Adults, overweight (BMI 25.0–29.9) or obese (BMI ≥30.0)		• Children • Animals studies • Population not over-weight (BMI 25.0–29.9) or obese (BMI ≥30.0) at baseline
Intervention	Comprehensive lifestyle interventions for weight loss, weight maintenance, or weight regain prevention, comprises three components: diet, physical activity, behavioral therapy		• Pharmacotherapy • Obesity surgery • Alternative medicine, including hypnosis and others
	4a	Components • Diet: calorie (energy) restriction/reduction • Physical activity: exercise, increased physical activity • Behavioral therapy: behavioral weight control, behavior therapy or treatment, behavior modification	
	4b	• Duration: short term (≤6 months), intermediate (>6 months and ≤12 months), long term (>1 year) • Delivery: – Sessions: group (i.e., meetings, treatment) or individual (i.e., meetings, treatment) – Format: face-to-face (onsite, clinic based); electronic (Internet Web site, e-mail, chat room, individual telephone, group telephone [conference call]); mail; or bibliotherapy • Frequency of contact: daily, weekly, biweekly, monthly, quarterly • Characteristics: self-monitoring, food records, activity records	
Comparator	• Usual care • Minimal or control intervention • No treatment intervention • Comprehensive intervention comprising three components: diet prescription, physical activity, behavioral therapy • Diet comparison trials, which examined the effects of different dietary interventions (in		• Pharmacotherapy • Obesity surgery • Alternative medicine, including hypnosis and others

	Inclusion Criteria	Exclusion Criteria
	the presence of the same physical activity and behavioral therapy components), were evaluated by CQ3.	
Outcomes	One or more of the following outcomes: • Weight (kg, lbs., percent) • Body fat measures (BMI and BMI change, waist circumference,, waist-hip ratio, percent body fat) • Weight loss maintenance • Percent reduction of excess weight	Outcomes by measure of self-report * Results are not reported according to randomized treatment or treatment groups *Note: Panel determined self-reported weight (only allowed in studies reporting CVD events; for risk factors, the studies have to report measured weight) is not appropriate for this CQ because these would be observational studies
Timing	Intervention: ≥3 months Follow-up: ≥6 months (defined from the start of randomization)	• Intervention less than 3 months • Follow-up of less than 6 months
Setting	Countries with westernized diets: • United States • Canada • European Union • Australia • New Zealand • Israel Any clinical or research setting	
Study Design	• For efficacy/effectiveness: RCTs. (SRs/MAs were used to identify papers potentially missed by the search.) Sufficient information must be presented about the intervention to replicate the study. • For adverse effects: RCTs, controlled clinical trials, cohort studies with a contemporaneous comparison group, case-control studies, large observational studies • Post hoc analyses of large RCTs if analyses of randomized comparisons are included • Sample size: must be ≥15 subjects per treatment arm	• SRs/MAs • Case series, case reports, before-after studies • Results are not compared according to randomized treatment assignments. • Dropout rate ≥40 percent after 6 months • Studies with <15 subjects per treatment arm

	Inclusion Criteria	Exclusion Criteria
Publication Type	Published studies	• SRs/MAs • Unpublished literature – Unpublished industry-sponsored trials – Other unpublished data • FDA Medical and Statistical reviews • Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Language	• Abstract must be available in English	• Full text translation into English must be feasible
Publication Time Frame	• RCTs published in years 1998–2009; RCTs published in 2010 and 2011 were included if they included ≥100 participants per treatment arm.	• Studies published before 1998

6.3 Introduction and Rationale for Question and Inclusion/Exclusion Criteria

Prior national and international expert panels [(e.g. (4,192-196)] have independently recommended that overweight and obese adults be provided a comprehensive lifestyle intervention to achieve weight loss. Comprehensive programs employ diet, physical activity, and behavior therapy, all in combination. CQ4 seeks to determine the short- and long-term weight losses that can be achieved with a comprehensive lifestyle intervention.

Traditionally, comprehensive lifestyle interventions have been delivered onsite, in frequent face-to-face meetings (i.e., high-intensity, onsite treatment). This approach is generally considered the state of the art for lifestyle intervention. In the past decade, however, comprehensive programs delivered by electronic means, including the Internet, e-mail, and text

messaging, as well as by person-to-person telephone counseling, have been emerging. Comprehensive interventions also are being delivered in new settings, which diverge from the academic centers in which most RCTs have been conducted. For example, health professionals who work in primary care settings have been implementing lifestyle interventions in their settings. Some commercially-based programs also have incorporated the components of a comprehensive lifestyle intervention into their programs, which they offer to the public through face-to-face and telephone- and electronically-based contacts. CQ4 describes the short- and long-term weight losses from RCTs that have examined the results of comprehensive interventions delivered through these different modalities and venues. In most cases, the efficacy of each comprehensive lifestyle intervention was compared with usual care (i.e., minimal treatment, attention-control group).

Few RCTs have directly compared the efficacy of comprehensive lifestyle interventions as delivered by one modality vs. another or as offered in one setting vs. another. For example, only one trial has directly compared the efficacy of the same lifestyle intervention delivered onsite (i.e., face-to-face) vs. by Internet. This prevented the panel, in several instances, from drawing definitive conclusions about the relative efficacy of the different interventions examined. This limitation also applied to the panel's efforts to draw conclusions about several characteristics of traditional onsite comprehensive interventions that the panel thought might influence short- or long-term weight losses. These characteristics included the intensity of the intervention (i.e., how frequently participants had counseling contacts), the duration of care, and whether participants received individual or group counseling. In the absence of RCTs that directly tested these issues, the panel examined the difference in mean weight loss between participants who were assigned to the intervention and those assigned to the usual care groups. Net-of-control difference for one

group of trials, such as those that offered high-intensity onsite treatment, were then compared with net-of-control differences for a second group of trials, such as those that provided low-intensity onsite treatment. Large differences between two groups of studies in their net-of-control differences suggested that one intervention approach was potentially superior (or inferior) to another. These comparisons, however, were not subjected to statistical analysis, thus, again limiting definitive conclusions in some areas.

RCTS that examined interventions to improve the maintenance of lost weight were of particular interest, given the widely acknowledged problem of weight regain following the end of lifestyle interventions. Later sections of this document describe the different study designs that are used to examine the induction vs. the maintenance of weight loss, as well as progress over the past decade in improving the maintenance of lost weight.

The panel did not attempt to isolate the effects in inducing weight loss of one intervention component (i.e., diet, physical activity, or behavior therapy) relative to others, given the review of this issue by prior expert panels, with the resulting consensus that all three components should be prescribed. Additional information about the effects on weight loss of diet composition and form are covered in CQ3, whereas findings concerning the contribution of different types of physical activity to weight reduction recently have been reviewed by another expert panel (197). Behavior therapy is used to facilitate participants' adherence to diet and physical activity recommendations; it is not used in isolation (by itself) for weight loss.

6.3.1. A Dictionary of Lifestyle Intervention Terms

This section defines select terms from Table 4.0.

6.3.1.1. Comprehensive Lifestyle Intervention

Comprehensive lifestyle interventions for overweight/obese adults include three principal components: 1) prescription of a moderately reduced calorie diet; 2) prescription of increased physical activity; and 3) a program of behavior change to facilitate adherence to diet and activity recommendations. (All three components, described later in greater detail, should be included.) Adherence to diet and activity recommendations also is facilitated by ongoing guidance and feedback from a trained interventionist.

6.3.1.2. Intervention Delivery

- **Onsite:** The intervention is delivered to participants by a trained interventionist in face-to-face meetings held at a clinic, community center, worksite, or other settings.

- **Electronic:** The intervention is delivered to participants by e-mail, Internet, mobile phone, text message, or similar electronic means. Interventionists may communicate personally with participants by electronic means (e.g., e-mail) but not by telephone (i.e., speaking with each other).

- **Telephone:** The intervention is delivered to participants by telephone (i.e., live person-to-person contact).

- **Commercial:** The intervention is delivered to participants who pay a fee to a proprietary weight-loss program. Interventionists, trained by the company, deliver the intervention.

- **Primary care:** The intervention is delivered to overweight/obese individuals in a primary care practice by health professionals and staff who work in the practice.

6.3.1.3. Intervention Intensity

The panel defined the intensity of lifestyle interventions by the number of treatment contacts provided in the first 6 months.

- **High** = 14 or more contacts. (Weekly contact for the first 3 to 6 months is common.)
- **Moderate** = 6 to 13 contacts (i.e., monthly to every-other-week contact).
- **Low** = 1 to 5 contacts (i.e., less than monthly).

6.3.1.4. Intervention Duration

The panel defined the duration of lifestyle intervention, as well as the time point at which body weight was last assessed after intervention (i.e., non-intervention follow-up) as follows:

- **Short term** $\leq$6 months
- **Intermediate term** >6 to $\leq$12 months
- **Long term** $\geq$12 months

6.3.1.5. Individual vs. Group Intervention

A trained interventionist may deliver a lifestyle intervention to a single participant (i.e., individual contact) or to a group of individuals (typically 10 to 20 participants).

6.3.1.6. Trained Interventionist

In the studies reviewed, trained interventionists included mostly health professionals (e.g., registered dietitians, psychologists, exercise specialists, health counselors, or professionals in training) who adhered to formal protocols in weight management. In a few cases, lay persons

were used as trained interventionists; they received instruction in weight management protocols (designed by health professionals) in programs that have been validated in high quality trials published in peer-reviewed journals.

6.3.1.7. Trials of Weight Loss Induction versus Maintenance of Lost Weight

- **Weight Loss Induction:** RCTs of weight loss induction assign participants to different interventions and examine changes in body weight (from baseline) at different intervals, which may include at the end of treatment delivery and then at 3 or more months after treatment has concluded (i.e., 3-month, non-intervention follow-up). Such trials, thus, often provide information about the effects of an intervention on both short- and long-term weight changes. Long-term changes in weight are sometimes referred to as the "weight loss maintenance" phase, although "long-term weight change" is a more appropriate term.

- **Maintenance of Lost Weight**: This term often is used interchangeably with "maintenance of weight loss" or "preventing weight regain," although there are differences between the terms. A major difference is that "maintenance of weight loss" suggests that the intervention is designed to facilitate participants' continued loss of weight, following the initial period of weight loss. "Maintenance of lost weight," by contrast, suggests that the goal is to keep off (or maintain) the weight loss that was achieved in the initial weight loss phase. "Prevention of weight regain" suggests trying to limit the amount of weight that is regained from the prior weight loss.

RCTs designed to address the maintenance of lost weight use a different experimental design than those that examine weight loss induction. In the former case, all participants must first lose a certain amount of weight (e.g., 5 percent of initial weight) to qualify for randomization in the

weight loss maintenance trial. The initial weight loss often is described as occurring during a "diet run-in" period. Success in the maintenance trial typically is measured by the percentage of the prior (run-in) weight loss that is maintained or by the absolute change in body weight from the randomization weight (achieved after the diet run-in). This latter assessment often translates into a measure of weight regain from randomization.

6.4 Methods for Critical Question 4

The Obesity Panel formed subcommittees for each of its five CQs. For CQ4 the subcommittee included one internal medicine physician and two clinical psychologists representing academic institutions across the U.S. Chairmanship rotated among the members.

The wording of the CQ evolved over time, from a comprehensive intervention initially including two or more components (i.e., dietary prescription, physical activity, or behavioral therapy) to one including all three components. Additional exclusion criteria were later put in place to remove trials that included comprehensive lifestyle interventions but were designed principally to compare different dietary interventions. The panel felt that these trials were more appropriately addressed under CQ3. One seminal RCT, the Diabetes Prevention Program, did not meet inclusion criteria because of the lower BMI inclusion criteria for the trial (24 kg/m^2, or 22 $kg/m^2$for Asians). However, because of the importance of this trial, an exception was made to include the Diabetes Prevention Program in the evidence base.

As noted in Chapter 4, Process and Methods Overview, a standardized approach to systematically reviewing the literature was conducted for all CQs. The panel members participated in developing CQ4 and its I/E criteria, and in reviewing the included/excluded papers and their quality ratings. Contractor staffs worked closely with panel members to ensure the accuracy of

data abstracted into evidence tables and summary tables and the accuracy of the application of systematic evidence-based methodology.

The literature search for CQ4 included an electronic search of the Central Repository for RCTs or controlled clinical trials published in the literature from January 1998 to December 2009. The Central Repository contains citations pulled from seven literature databases (PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts). The search produced 2145 citations, with 15 additional citations identified from non-search sources, i.e., by the panel members or hand search of SRs/MA (obtained through the electronic search). The SRs/MA were only used for manual searches and were not part of the final evidence base. This manual cross-check was done to ensure that major studies were not missing from the evidence base. Eleven of the 15 citations identified from non-search sources were published after December 31, 2009. Per NHLBI policy, certain lifestyle and obesity intervention studies published after the closing date could be allowed as exceptions. These studies were required to be RCTs in which each study arm contained at least 100 participants and were identified by experts' knowledgeable of the literature. Ten of the 11 citations published after December 2009 met the criteria and were eligible for inclusion in the CQ4 evidence base (20,198-206). In contrast, one of the 11 citations did not meet the criteria and was excluded from the CQ4 evidence base (207). The remaining four citations, identified through non-search sources, were published before 2009. Of these four, one citation had no abstract, two citations had no indication in the abstract or MeSH terms that they were related to overweight or obese populations, and one citation had no indication in the abstract or MeSH terms that the publication was related to comprehensive lifestyle interventions. Of the 15 citations identified through non-search sources, 14 were screened and found eligible for inclusion; two of these studies were subsequently rated as poor quality studies.

Figure 8, the PRISMA diagram outlines the flow of information from the literature search through the various steps used in the systematic review process for CQ4.

Two reviewers (i.e., independent contractors) independently screened the titles and abstracts of 2160 publications against the I/E criteria, which resulted in 1776 publications being excluded and 384 publications being retrieved for full-text review to further assess eligibility. Next, two reviewers independently screened three hundred and eighty-four full-text publications, assessing eligibility by applying the I/E criteria; 215 of these publications were excluded based on one or more of the I/E criteria (see specified rationale as noted in the PRISMA).

One hundred and forty-six of the 384 full-text publications met the criteria and were included. The quality (internal validity) of these 146 publications was assessed using the quality assessment tool developed to assess RCTs (see Appendix 2). Of these, 74 publications were excluded because they were rated as poor quality (104,112,116,145,151,168,198,208-273); of these, 43 studies were rated poor because they did not use an intention-to-treat (ITT) analysis and had high attrition rates. Rationales for all of the poor quality studies are included in Appendix 3 (206,274-279)(209,277-282)(209,277-282)(210,278-283)(210,278-283). The remaining 51 trials (72 articles) were rated good or fair quality (20,46,184-187,199-206,274-331) and included in the evidence base that was used to formulate the evidence statements and recommendations. Panel members reviewed the final studies on the include list, along with their quality ratings, and had the opportunity to raise questions. Some trials previously deemed to be of fair or good quality were downgraded to poor quality upon closer review of evidence tables. These trials used completers analyses rather than ITT analysis and had overall attrition rates exceeding 10 percent. If the study reported only an analysis of completers and had attrition at <10 percent, it was allowed in the evidence base. Methodologists worked with the systematic review team to re-evaluate

these trials and make a final decision. Evidence tables and summary tables consisted only of data from the original publications of eligible RCTs; these tables formed the basis for panel deliberations.

Creation of the evidence tables followed the methodology described in Appendix 2. For each RCT (all included articles combined into one entry) that met the inclusion criteria for this CQ and was rated good or fair quality, the following data were presented in an evidence table:

- **Study Characteristics:** author, year, study name, country and setting, funding, study design, research objective, year study began, overall study number, quality rating

- **Study Design Details:** treatment groups, descriptions of interventions, duration of treatment, duration of follow-up, number of contacts, format of intervention, provider, assessments or collection of outcome data

- **Criteria and Endpoints:** I/E criteria, primary outcome, secondary outcome, outcome ascertainment

- **Baseline Population Characteristics:** age, sex, race/ethnicity, BMI, weight, history of myocardial infarction, CHD, CVD, congestive heart failure, hypertension, diabetes, comments on demographics

- **Results:** outcomes of interest (weight change in kg, percent reduction in initial weight, weight change within specific percent change groups such as 5 or 10 percent) by time periods, adverse events, attrition at end of study, adherence. Because waist circumference, waist-hip ratio, and percent body fat were not consistently reported in many of the included studies, the panel elected to focus on direct measures of body weight only.

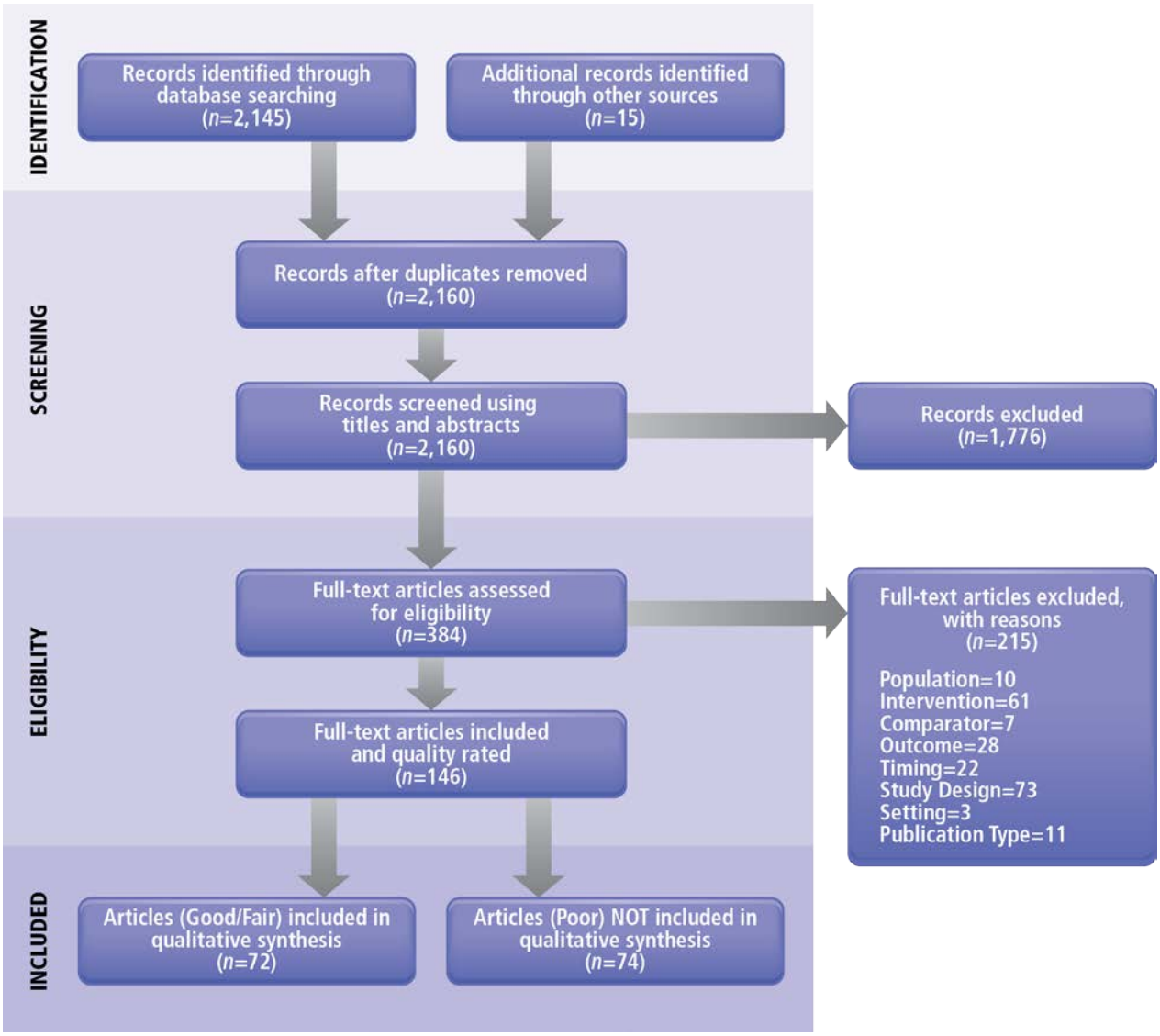
Summary tables for this CQ followed the same general format, as depicted below; however, the organization of trials or sections within each table varied by the panel's preference of how to present the evidence:

- **Study Characteristics:** study name, author, year, study name, study design, type of ITT analysis, country/setting, primary outcome quality rating
- **Intervention Groups and Component Details:** Interventions concisely describing key elements of the three required components
- **Study Duration, Contents, Health care practitioner:** duration of treatment and follow-up, description of contacts, practitioner
- **Sample Characteristics, Group Size, Baseline Characteristics:** brief sample description, intervention (not specified), weight, BMI
- **Outcomes:** These are presented in three separate columns: ≤6 months mean weight loss change (kg/percent change); >6– and ≤1–year mean weight loss change (kg/percent change); and ≥1–year mean weight
- **Attrition, Adherence:** withdrawals by group at study end, attendance at sessions

While preparing summary tables, it came to our attention that many included trials reported only completer's analysis data with greater than 10 percent attrition. These trials were downgraded to poor quality and removed from the analysis. (Trials with ≤ 10 percent attrition were retained in the analysis.)

Panel members developed very preliminary evidence statements prior to the development of evidence tables. This served to organize the studies into categories of questions addressed and to ensure that the appropriate data elements would be presented in the evidence tables and incorporated into the summary tables for the evidence synthesis.

Figure 8. PRISMA Diagram Showing Selection of Articles for Obesity Question 4



6.5 Evidence Statements and Summaries

A total of 51 trials (72 articles) met the final I/E criteria and were quality rated fair or good quality. The panel members decided to consider only RCTs for this question (in order to work from the original data and to reach their own conclusions). Of these, 27 trials (45 articles) compared a comprehensive intervention arm to usual care, minimal intervention, or no intervention. Thirteen trials (13 articles) had at least two or more comprehensive intervention arms compared to usual care, minimal intervention, or no intervention. The remaining 11 trials (13 articles) compared a comprehensive intervention to another comprehensive intervention (the latter included a different physical activity or behavior therapy component). Details regarding specific trials included for each summary table are presented below.

6.5.1. Introduction of Evidence Statements

The panel reviewed and summarized evidence in three key areas on the efficacy/effectiveness of a comprehensive lifestyle intervention for facilitating weight loss and maintaining lost weight. The first key area covers data on weight loss induction and programs providing extended interventions to facilitate adherence to the initial program. Comprehensive, high-intensity onsite interventions, the most widely studied models, were the focus. These models, considered state of the art for behavioral interventions, were primarily conducted in academic research settings. Using this evidence base, panel members reviewed different types of intervention programs and then drew conclusions about the effectiveness of the various approaches (i.e., commercial programs, very low-calorie diets, primary care-based programs, electronic interventions, and telephone-based counseling). The second area of evidence examines programs designed to help patients maintain lost weight. Included in this evidence base are RCTs that assigned participants to intervention

strategies after the initial weight-reduction period was completed. During this review, weight loss maintenance strategies were closely examined. Finally, the third area of evidence examines the delivery characteristics of interventions, including structural components of the interventions or modes of delivery associated with differences in outcomes. This area covers evidence on the intensity (i.e., frequency) of intervention contact (moderate and low intensity), individual vs. group counseling, and onsite vs. remote, electronically-delivered counseling.

6.6 Diet, Physical Activity, and Behavior Therapy Components in High-Intensity, OnSite Lifestyle Interventions—Summary Table 4.1

***Evidence Statement 1*.** The principal components of an effective high-intensity, onsite comprehensive lifestyle intervention include: (1) prescription of a moderately reduced calorie diet; (2) prescription of increased physical activity; and (3) the use of behavioral strategies to facilitate adherence to diet and activity recommendations. All three components should be included.

Reduced-calorie diet. In comprehensive lifestyle interventions, overweight/obese individuals typically are prescribed a diet designed to induce an energy deficit ≥500 kcal/day. This deficit often is sought by prescribing 1200 to1500 kcal/day for women and 1500 to 1800 kcal/day for men. Alternatively, dietary energy deficits can be determined by one of the methods described in CQ3.

Increased physical activity. Comprehensive lifestyle intervention programs typically prescribe increased aerobic physical activity (such as brisk walking) for ≥150 minutes per week (≥30 minutes a day, most days of the week). Higher levels of physical activity, approximately 200–

300 minutes per week, are recommended to maintain lost weight or minimize weight regain long-term (>1 year).

Behavioral strategies. Comprehensive lifestyle interventions usually provide a structured program that includes guidance on behavioral strategies and approaches to accomplish prescribed dietary intake and physical activity goals. One common strategy is regular self-monitoring, including monitoring of food intake, physical activity, and weight. These same behaviors are recommended to maintain lost weight, with the addition of frequent (i.e., weekly or more often) monitoring of body weight.

Strength of the Evidence: High

Rationale: The treatment components of high-intensity, onsite (i.e., face-to-face) comprehensive lifestyle interventions were identified from 10 RCTs (summarized in Summary Table 4.1) that compared a lifestyle intervention with a usual care control group (281,320,322). Six were rated good quality, while four were rated fair quality. (Several trials have two or more publications, which represent follow-up evaluations.) In 3 of the 10 trials, women were prescribed approximately 1200 to1500 kcal/day and men 1500–1800 kcal/day.(46,203,274,303) (This practice assumes that men have higher energy requirements than women, based on their generally greater body weight and greater amount of fat-free mass.) Alternatively, in three trials, energy intake was prescribed based on body weight, regardless of gender (46,203,274,303). If followed, both prescriptive methods are likely to help participants achieve an energy deficit of at least 500 kcal/day, independent of changes in physical activity. One trial recommended a 500 kcal/day deficit (311) and another a 300 to 400 kcal/day deficit (202). Another trial recommended reducing calorie and fat intake but did not specify the targeted goals (276,305).

Only one trial (321) did not recommend a calorie-restricted diet, instead proposing a reduced fat intake, with an increased intake of fruits, vegetables, and fiber.

Comprehensive interventions typically prescribe brisk walking (or similar aerobic activity) to increase participants' physical activity and, thus, energy expenditure. Of the 10 RCTs, eight recommended that participants gradually build to 90 to 225 minutes of walking per week, with the most common goal being 150 to 200 minutes per week (46,202,203,274,276,303,305,311,320,322). Participants were instructed to exercise on their own in 8 of 10 trials(46,202,203,274,276,303,305,311,320,322), with onsite supervision provided in the other two (281,321).

Behavior therapy provides overweight/obese participants with a set of skills to help them adopt recommended eating and activity behaviors. Self-monitoring is the most frequently recommended practice. In 9 of 10 trials, participants were instructed to monitor their food intake (usually including calories) (46,202,203,274,311,320), and 6 trials encouraged participants to monitor their physical activity (46,202,203,274,311,320). Regular monitoring of body weight also is recommended, often once or twice a week during initial weight loss (20,46,203,274,281,303). Individual trials in Summary Table 4.1 show that many interventions provided a behavior change program that included additional techniques such as stimulus control, slowing the rate of eating, problem solving, cognitive restructuring, and relapse prevention. Collectively, these techniques comprise a "behavioral package," different components of which may be emphasized in different trials.

6.7 Comprehensive Interventions Compared with Usual Care, Minimal Care, or No-Treatment Control—Summary Table 4.2

Evidence Statement 2A **(Short-Term Weight Loss).** In overweight and obese individuals in whom weight loss is indicated and who wish to lose weight, comprehensive lifestyle interventions consisting of diet, physical activity, and behavior therapy (all three components) produce average weight losses of up to 8 kg in 6 months of frequent (i.e., initially weekly), onsite treatment provided by a trained interventionist in group or individual sessions. Such losses (which can approximate reductions of 5–10 percent of initial weight) are greater than those produced by usual care (i.e., characterized by the limited provision of advice or educational materials). Comparable 6–month weight losses have been observed in treatment comparison studies of comprehensive lifestyle interventions, which did not include a usual care group.

Strength of the Evidence: High

Evidence Statement 2B **(Intermediate-Term Weight Loss).** Longer term comprehensive lifestyle interventions, which additionally provide weekly to monthly onsite treatment for another 6 months, produce average weight losses of up to 8 kg at 1 year, losses which are greater than those resulting from usual care. Comparable 1-year weight losses have been observed in treatment comparison studies of comprehensive lifestyle interventions, which did not include a usual care group.

Strength of the Evidence: Moderate

Evidence Statement 2C **(Long-Term Weight Loss).** Comprehensive lifestyle interventions which, after the first year, continue to provide bi-monthly or more frequent intervention contacts,

are associated with gradual weight regain of 1 to 2 kg per year (on average), from the weight loss achieved at 6 to 12 months. Long-term (>1 year) weight losses, however, remain larger than those associated with usual care. Comparable findings have been observed in treatment comparison studies of comprehensive lifestyle interventions, which did not include a usual care group.

Strength of the Evidence: High

Rationale: The three preceding evidence statements are based on findings from 10 RCTs that compared a high-intensity, comprehensive lifestyle intervention, delivered on site with a usual care or minimal treatment control group (i.e., characterized by the limited provision of advice or educational materials) (20,46,199,202-204,274,276,281,286,303,305,311,320-322,331). (Several trials have two or more publications, which represent follow-up evaluations.) Six were rated good quality, while four were rated fair quality. Comprehensive programs were delivered by trained interventionists, in group or individuals sessions, and provided recommendations on the following: consuming a low-calorie diet (e.g., 1200 to 1800 kcal/day based on body weight or gender); engaging in regular physical activity (e.g., 180 minutes per week of brisk walking); and using behavioral strategies to achieve these recommendations (e.g., self-monitoring, goal setting, problem solving). High-intensity interventions were defined as providing a minimum of 14 sessions during the first 6 months (i.e., the period of short-term weight loss). Most interventions provided weekly sessions for the first 3 months, and often at least every-other-week sessions from months 4 to 6. From months 7 to 12 (i.e., the period of intermediate weight loss), several of the high-intensity interventions continued to provide onsite counseling, with the frequency of contact varying from three sessions per month to only one session every two months. After 1 year (i.e., the period defined as long-term weight loss), the frequency of onsite contact provided in some of

these high-intensity trials ranged from monthly to every other month. (Some of these trials provided additional contacts by telephone or e-mail.)

Short-term. Six of the 10 studies (320,321) reported weight losses at 6 months. Four of these six trials reported mean losses of approximately 6 to 8 kg. Two other studies reported mean losses of 4.4 kg and 3.0 kg (320,321). The last trial (321) differed from the other eight in not prescribing a specific calorie target or requiring participants to record their food intake (although a curriculum of lifestyle modification was provided). In these 6 studies, the difference in weight loss between the intervention and control groups (i.e., net of control) at 6 months ranged from 3.2 kg to 8.6 kg (in favor of the intervention in all studies).

Intermediate-term. Three of the 10 RCTs reported weight loss at 12 months (46,202,274,303,331). All three trials reported a mean loss of approximately 7 to 8.5 kg at this time (equal to approximately a 7 percent to 8.5 percent reduction in initial weight). Two studies found that 61 percent and 68 percent of intervention participants lost $\geq$5 percent of initial weight, compared with 16 percent and 14 percent, respectively, in the usual care groups (46,202,331). The third study reported that 50 percent of intervention participants lost $\geq$7 percent (274,303). The similar weight-loss outcomes were achieved despite differences in the use of individual (274) versus group (46,202) sessions and different frequencies of onsite contact during months 7 to 12, ranging from three times monthly (46) to once every other month (274). The largest weight losses at 12 months were reported in a trial that included the use of meal replacement products during the first 4 months (e.g., liquid shakes and snack bars) to replace two meals and one snack daily (46). (Participants continued to replace one meal or snack daily thereafter.) In these three studies, the difference in weight loss between intervention and control groups at 12 months ranged from 4.3 to 7.9 kg (in favor of the intervention in all studies). These data suggest that, at 1 year,

overweight/obese individuals can maintain approximately the full amount of their initial weight loss (achieved in the first 6 months) when provided continuing onsite lifestyle counseling from months 7 to 12. On average, participants typically do not lose additional weight from 7 to 12 months.

Long-term. Eight of the 10 RCTs (20,46,202,203,274,276,303,305,311,320,321) reported weight losses beyond 1 year, ranging from 18 months (321) to 4 years (20). Mean weight losses ranged from 0.2 to 5.6 kg. The difference between intervention and control groups ranged from a mean of 2.0 to 5.5 kg (in favor of intervention in all studies). In all trials that reported weight losses for two or more follow-up assessment periods, weight losses were consistently smaller at long-term follow-up than at the 6- or 12-month assessments. Thus, even in studies in which participants were provided continued onsite counseling after the first year, overweight/obese individuals were not able to maintain their maximum weight loss, achieved in the first 6 to 12 months. Weight regain averaged approximately 1 to 2 kg per year. In a 4-year study (20,46) for example, participants lost a mean of 8.6 kg at 12 months and maintained a loss of 4.7 kg at 48 months. These findings indicate that further research is needed on facilitating maintenance of lost weight, as discussed in another section of this report. They also underscore that overweight/obese individuals need to continue to participate in a weight loss maintenance program following initial weight loss in the first 6 to 12 months.

Comparative treatment studies. Five additional RCTs (275,280,298,300,301) were identified that compared a high-intensity, comprehensive lifestyle intervention, delivered onsite, with other high-intensity, onsite interventions that varied the physical activity or behavior therapy component (usually by intensifying it). One study was rated good quality; four were rated fair quality. These five studies did not include a usual care or minimal-treatment control group. However,

they provide additional estimates of the efficacy of high-intensity, onsite interventions. (Trials that compared different dietary interventions, prescribed as part of comprehensive lifestyle interventions, are discussed in CQ3.)

Four of the five studies used a calorie-restricted diet and behavior therapy while varying the physical activity component, typically by increasing the duration and/or intensity of prescribed activity (298,300,301). In three studies (298,300,301), in which one group of participants received a conventional activity prescription (such as expending 1,000 kcal/week), participants achieved average weight losses of 8.1 to 8.3 kg at 6 months. Two such studies reported 12-month losses, which ranged from 6.1 to 6.3 kg (298,301). Two trials reported 18-month mean losses, which ranged from 4.1 to 5.8 kg (300,301). These short- and long-term weight losses are comparable to those described above for high-intensity, onsite interventions compared with usual care. One (301) of two trials that prescribed a higher dose of physical activity (i.e., expending 2500 kcal/week) observed significantly greater weight loss at 18 months, compared with the conventional dose of activity (i.e., expending 1000 kcal/week); the other trial (298,299) did not observe a significant difference in short- or long-term weight loss for higher vs. lower doses of physical activity. Posthoc analyses (which are not shown in Summary Table 4.3) performed in three studies revealed that higher (participant-reported) long-term levels of physical activity were associated with larger long-term weight losses (independent of participants' original assignment to physical activity groups) (280,298,300).

A fifth study (275) examined the addition of motivational interviewing to a high-intensity lifestyle intervention. (Motivational interviewing is designed to help participants resolve ambivalent feelings they may have about changing their behavior.) All participants had type 2 diabetes. Those in the traditional high-intensity intervention lost 3.1, 2.7, and 1.7 kg at 6, 12, and 18 months,

respectively. The addition of motivational interviewing increased weight loss significantly at each time by 1.6 to 2.1 kg.

6.8 Efficacy/Effectiveness of Electronically Delivered, Comprehensive Interventions in Achieving Weight Loss—Summary Table 4.3

Evidence Statement 3. Electronically delivered, comprehensive weight-loss interventions developed in academic settings, which include frequent self-monitoring of weight, food intake, and physical activity—as well as personalized feedback from a trained interventionist—can produce weight loss of up to 5 kg at 6 to12 months, a loss that is greater than that resulting from no or minimal intervention (i.e., primarily knowledge-based) offered on the Internet or in print.

Strength of the Evidence: Moderate

Rationale: Summary Table 4.3 presents 13 randomized trials in which weight-loss interventions, or weight-loss maintenance interventions, developed primarily in academic settings, were delivered by one or more of the following methods: counseling via electronic mail (e-mail), text messaging, interactive Internet websites, and automated phone calls. During initial weight loss, nine of these trials used Internet Web sites, e-mail, or text messaging (279,282,291,293,297,314,324,325). Seven were rated good quality; six were rated fair quality.One study (200) compared group sessions held on site (face-to-face) to group sessions held virtually using an Internet Web site (with a chat room). As in other parts of this report, consideration of initial weight-loss interventions has been separated from consideration of weight-loss maintenance interventions. For this reason, five studies listed in Summary Table 4.3 (277,284,294,323) are not discussed here but are reviewed in the weight-loss maintenance section of this report.

Three RCTs compared an Internet-delivered program, which included personalized feedback (from a trained interventionist) by e-mail, with information-only control groups (297,314,324). Hunter et al. (297) reported a significantly greater 6–month weight loss in intervention vs. control participants (-1.5 kg vs. +0. 5 kg) and that significantly more participants in the former group lost ≥5 percent of initial weight (22.6 percent vs. 6.8 percent). Morgan et al reported mean 6-month losses of -5.3 and -3.5 kg for intervention and control groups, respectively, which did not differ significantly. Tate et al. (324) compared a static Internet program (which included an Internet website with a tutorial on weight loss and a message board, plus weekly non-personalized e-mails with weight loss tips and reminders) with a more intensive intervention that included all of the features of the basic program, plus regular e-mail communications with a trained interventionist, and entry of food diaries on the website. At 12 months, the intensive Internet program produced significantly greater weight loss than the static program (4.4 kg vs. 2.0 kg). A fourth trial (293) compared a no-treatment control condition to a weight-loss intervention delivered by telephone text messages and an Web site. Differences in weight loss at 12 months (-0.7 and -3.1 kg, respectively) did not differ significantly.

Five additional randomized trials compared various combinations of electronically delivered weight loss interventions without also including a no-treatment or minimal-treatment control condition (200,279,282,291,325). A primary finding of these trials is that interventions that are more intensive, that is, have more frequent contacts and provide personalized feedback to participants, tend to be more effective in achieving weight loss. One of these trials (291) compared a commercial, Internet-based intervention program to a more intensive Internet- and e-mail-based intervention developed for this project. The primary difference between these two interventions was that the more intensive program included weekly advice and personalized

feedback from a professional health counselor over a 6-month initial intervention period. Mean weight loss at 12 months for participants in the commercial program was significantly less than the mean weight loss for the more intensive personalized program (5.1 kg vs. 2.6 kg). In another trial (279) comparing the same commercial Internet-based program to an intervention that included a detailed weight loss manual and occasional individual meetings with a weight loss counselor, participants assigned to the in-person program had significantly greater mean weight loss at 12 months than those assigned to the Internet program (4.0 kg vs. 1.1 kg).

Tate et al. (325) randomly assigned participants to intervention programs at three levels of intensity (325). The lowest intensity program included the following: a 1-hour group session; exercise advice; a personalized calorie target; instruction on using structured meals and meal replacements; a recommendation for using two meal replacements per day; a week's supply of meal replacements; coupons for discounts on future purchases of meal replacements; and encouragement to use an interactive weight loss Web site that included self-monitoring, e-mail prompts to report weight weekly, weekly e-mail tips for weight loss, and an e-mail social support system. The more intensive intervention programs included more e-mail and telephone prompts plus either automated feedback on progress (mid-level of intervention intensity), or weekly feedback from a human counselor (highest level of intensity). An ITT analysis at 6 months did not find a significant difference in mean weight loss between the groups, but did find a significant difference in the proportion of participants in each treatment group that achieved a 5 percent or greater weight loss: 27 percent in the lowest intensity group, 34 percent in the higher intensity group, and 52 percent in the highest intensity group. One trial (200) compared the same weight loss program delivered in three ways: delivered in person by a professional counselor; delivered via the Internet; and a combination hybrid intervention that included both in person and Internet

contacts. In an ITT analysis, the in-person intervention resulted in significantly more weight loss at 6 months compared to the Internet only or combined conditions (7.6 kg, 5.5 kg, or 5.7 kg, respectively).

One trial identified for this review as using electronic intervention methods (282) has not been discussed here because the intervention program was not described in enough detail to make comparisons to the other studies.

6.9 Efficacy/Effectiveness of Comprehensive, Telephone-Delivered Lifestyle Interventions in Achieving Weight Loss—Summary Table 4.4

Evidence Statement 4. In comprehensive lifestyle interventions that are delivered by telephone or face-to-face counseling, and which also include the use of either commercially prepared, prepackaged meals or an interactive Web-based program, the telephone and face-to-face-delivered interventions produced similar mean net weight losses of approximately 5 kg at 6 months and 24 months, compared with a usual care control group.

Strength of the Evidence: Low

Rationale: Three trials (201,203,316) have compared the efficacy of providing behavioral counseling onsite (in person) or by telephone. Two were rated good quality; one was rated fair. Rock et al. (201) assigned obese women to a control condition or one of two active interventions. Participants in both interventions received pre-packaged meals, as well as access to a Web site providing weight loss advice and a message board for communicating with interventionists and other participants. Participants in both interventions also were offered weekly counseling contacts with a trained interventionist throughout the two-year study. In one group, contacts

occurred in person (onsite), while in the other group, counseling was delivered by telephone. At 12 months, the two interventions achieved mean losses of 10.1 and 8.5 kg, respectively, with no significant differences between groups; both interventions were superior to the control group (-2.6 kg). A similar pattern of results was observed at 24 months.

Appel (203) randomly assigned participants to either a control condition in which they received only physician advice to lose weight (usual care) or to one of two active intervention conditions. Participants in both received the following interventions: physician advice to lose weight; encouragement to use a project weight-loss Web site that included learning modules, opportunities for self-monitoring weight, calorie intake, and exercise, and feedback on progress in these key behaviors; and e-mail prompts to check into the Web site every week. In the "in person" condition, participants were offered a series of onsite group and individual sessions conducted by a trained interventionist. In the "remote" condition, participants were offered individual counseling via telephone. The number of counselor contacts was the same in both conditions. At 24 months, participants in these two groups lost an average of 4.6 and 5.1 kg, respectively; these losses did not differ significantly but were superior to the control condition (-0.8 kg). A third study (316) examined the use of a telephone-based intervention to facilitate the maintenance of lost weight. This study is discussed in the section on weight-loss maintenance.

6.10 Efficacy/Effectiveness of Comprehensive Weight Loss Programs in Patients Within A Primary Care Practice Setting Compared With Usual Care—Summary Table 4.5

Evidence Statement 5. In studies to date, low- to moderate-intensity lifestyle interventions for weight loss provided to overweight or obese adults by primary care practices alone have not been shown to be effective.

Strength of the Evidence: High

Rationale: Studies of comprehensive lifestyle interventions in the primary care setting were included if the intervention was delivered within the context of the primary practice and used members of the primary care team to deliver the intervention. We identified four studies that met these criteria (205,283,309,327). Two were rated good quality; two were rated fair quality. Members of the primary care team could include physicians, nurse practitioners, physician assistants, nurses, or medical assistants. In all studies included in Summary Table 4.5, members of the primary care team responsible for intervention delivery were trained by the research team to provide the intervention. Participants included in these studies were broadly representative of obese patients within a general primary care practice, although, in some instances, they specifically included those with CVD risk factors or diabetes (283,327). The interventions tested were generally of low- or moderate-intensity, with treatment contacts occurring on average less than two encounters per month. Typically, intervention encounters were conducted either onsite (face-to-face) or by telephone or the two methods combined. Across several different practice settings and intervention strategies, researchers reported similar findings, with negligible to modest weight losses compared to usual care. At 12 months, weight losses were ≤1.1 kg greater

than control; at 24 months, weight losses were ≤1.2 kg greater than control. (An exception to this conclusion was observed in the study by (205), which included a third treatment arm that added either meal replacements or a weight loss medication [orlistat or sibutramine] to lifestyle counseling. Participants who received this intervention lost 2.7 kg more than control participants. However, the removal of sibutramine from the market limits the clinical significance of this finding.)

6.11 Efficacy/Effectiveness of Commercial-Based, Comprehensive Lifestyle Interventions in Achieving Weight Loss—Summary Table 4.6

Evidence Statement 6. Commercial-based, comprehensive weight loss interventions that are delivered in person have been shown to induce an average weight loss of 4.8 to 6.6 kg at 6 months in two trials when conventional foods are consumed and 6.6 to 10.1 kg at 12 months in two trials with provision of prepared food, losses that are greater than those produced by minimal-treatment control interventions.

Strength of the Evidence: Low

Rationale: Four RCTs were identified that compared a commercial-based weight loss programs with a minimal-intervention control group (201,295,319,328). All four were rated fair quality. Two were electronically delivered interventions, one was onsite; the other involved a mixture of delivery methods. Trials of commercial-based interventions were included if they assessed comprehensive weight loss programs delivered in a manner consistent with the usual business practice for that commercial program. Therefore, the studies reviewed replicated the usual program delivery provided to paying customers. However, the issue of payment raises the only notable difference between the studies included in the summary table and typical commercial

practice. In all instances, study volunteers received services and food for free as a part of the study protocol rather than paying for the program out of pocket.

All four studies identified included an onsite (face-to-face) counseling intervention to deliver the educational and behavioral components of the program (201,295,319,328). One of the four studies (295,328) also included a telephone counseling intervention to provide the same content as the face-to-face program. Two of the four studies (295,328) used commercial programs that employed trained peer counselors to deliver face-to-face counseling in group settings. These peer counselors are typically individuals who have demonstrated long-term, ongoing success in the program but may not have any specific professional degrees or certifications in behavior change, nutrition, physical fitness, or other health related field.

In all four studies, the intervention groups lost significantly more weight than the control groups. In the Rock (319) study, maximal weight loss was achieved at six months (-7.2 kg), and the weight change in the second six months of the study was a weight gain of 0.6 kg. In the longer study by Rock (201), maximum weight loss was not reached until month 12 (-10.1 and -8.5 kg for in person and telephone interventions, respectively). In the following year, participants regained approximately 2.3 to 2.7 kg. In the two studies that employed peer counseling to deliver the group-based intervention, weight loss at six months ranged from -4.8 to -6.6 kg (295,328). Treatment and follow-up of the originally randomized groups was continued in the Heshka study for a total of 2 years. The 6-month weight loss represented the maximum weight loss achieved. At 1 and 2 years, the weight loss was -4.3 and -2.9 kg, respectively.

Two of the four studies (201,319) provided pre-packaged foods to participants and achieved weight losses that were greater at 6 months (-7.2 to -9.2 kg) than the other two studies (295,328) of

similar intervention length that did not provide food (-4.8 to -6.2 kg). The differences persisted at 12 and 24 months. Only two studies (201,296) reported weight losses at 24 months. The study that provided food (201) reported approximately twice the amount of weight loss at 24 months (5.4 kg, net of control) compared to the study that did not (296) (2.7 kg, net of control). (The Panel notes that the present four trials do not provide an adequate assessment of the effects of prescribing pre-packaged foods vs. conventional foods. The lifestyle interventions provided in the four studies differed in several important ways, in addition to the prescription of pre-packaged vs. conventional foods.)

6.12 Efficacy/Effectiveness of Very Low-Calorie Diets, as Used as Part of a Comprehensive Lifestyle Intervention in Achieving Weight Loss—Table 4.7

***Evidence Statement 7A*.** Comprehensive, high-intensity, onsite lifestyle interventions that include a medically supervised very low-calorie diet (VLCD) (often defined as <800 kcal/day), as provided by complete meal replacement products, produce total weight loss of approximately 14.2 to 21 kg over 11 to 14 weeks, which is larger than that produced by no intervention or a usual care control group (i.e., advice and education only).

Strength of the Evidence: High

***Evidence Statement 7B*.** Following the cessation of a high-intensity lifestyle intervention with a medically supervised VLCD diet of 11 to 14 weeks, weight regain of 3.1 to 3.7 kg has been observed during the ensuing 21 to 38 weeks of non-intervention follow-up.

Strength of the Evidence: High

Evidence Statement 7C. The prescription of various types (resistance or aerobic training) and doses of moderate-intensity exercise training (e.g., brisk walking 135 to 250 minutes/week), delivered in conjunction with weight-loss maintenance therapy does not reduce the amount of weight regained after the cessation of the VLCD, as compared with weight loss maintenance therapy alone.

Strength of the Evidence: Low

Rationale: The three preceding evidence statements are based on findings from four RCTs that used very VLCD as part of the dietary component of the comprehensive interventions. Two were weight loss trials (185,187), and two were weight loss maintenance trials in which participants received the VLCD before randomization (185,187). All four were rated fair quality.

All four studies (184-187) provided VLCD, typically in the range of 420-525 kcal/day, for a period of time that was generally ≤14 weeks. In each instance, the VLCD was provided under medical supervision, and participants were supplied with the diet at no cost. The VLCD was followed by a period of transitioning back to regular foods with a gradual increase in caloric intake to reach a point at which weight maintenance was achieved. Two trials (184,186) were designed as comparisons of short-term weight loss, reporting results at the conclusion of the exclusive use of the VLCD, with follow-up reports of weight maintenance at 32 and 52 weeks. Weight loss ranged from 14.2 kg to 21.1 kg at the end of the VLCD (up to 14 weeks). During a period of non-intervention follow-up, approximately 21 to 38 weeks following completion of the VLCD, weight regain of 3.1 to 3.7 kg was observed.

Two of the four studies were designed to assess weight maintenance interventions after completing initial weight loss using a VLCD (185,187). After completing 6 to 8 weeks of VLCD followed by

2 to 4 weeks of LCD, participants were assigned to behavioral weight maintenance interventions with various exercise prescriptions to test the effects on weight maintenance. Both studies reported weight change at 6 to 9 months following randomization, and one study reported weight change at 33 months post randomization. In the short term, weight change ranged from a loss of 0.7 kg to a gain of 1.8 kg. Including specific exercise prescriptions in the weight maintenance intervention resulted in a range of weight change at 6 to 9 months of -2.7 kg to 0.3 kg net of the control intervention. At 33 months, participants regained weight on average, ranging from 5.9-9.7 kg. The range of weight change for the exercise interventions was 3.5 kg to 0.2 kg less than the control weight maintenance intervention (differences not statistically significant).

6.13 Efficacy/Effectiveness of Comprehensive Lifestyle Interventions in Maintaining Lost Weight—Summary Table 4.8

***Evidence Statement 8A*.** After initial weight loss, some weight regain can be expected, on average, with greater regain observed over longer periods of time. Continued provision of a comprehensive weight loss maintenance program (onsite or by telephone), for periods of up to 2.5 years following initial weight loss, reduces weight regain, as compared to the provision of minimal intervention (e.g., usual care). The optimal duration of weight loss maintenance programs has not been determined.

Strength of the Evidence: Moderate

Rationale: Eleven RCTs were identified that examined the maintenance of lost weight, following initial weight loss during a run-in period (185,187,206,277,284,285,294,306,316,317,323). Five were rated good quality; six were rated fair quality. In the first nine trials cited, participants were randomized to treatment conditions

after achieving initial weight loss, whereas in the last two they were randomized to conditions at the start of the run-in period, but the randomization was concealed until the maintenance phase began. Nine trials provided an onsite (i.e., face-to-face) intervention that often included regularly scheduled contacts and guidance on behavioral strategies for weight maintenance (185,187,206,277,285,306,316,317,323), and five trials included an electronic or telephone intervention arm (187,277,285,294,323). Five trials provided weight change outcomes at 3 to 6 months (185,277,294,306,323), eight trials included 6 to 12 month outcomes (187,206,277,284,285,306,316,323) and five trials provided weight change data at greater than 12 months (187,277,285,294,323). Participants in all weight loss maintenance interventions were instructed to consume a reduced-calorie diet (needed to maintain their lower body weight) and to engage in high levels of physical activity (typically ≥225 minutes per week of brisk walking or similar activity).

. The most compelling test of the efficacy of weight loss maintenance interventions is to randomly assign individuals who have achieved initial weight loss to either a minimal-treatment control condition or to an active maintenance intervention. Six trials with at least 1 year of post-randomization follow-up assessment have used this design (185,277,284,316,317,323). Four of these trials showed that the provision of continuing maintenance intervention, compared to a minimal treatment or no-treatment control, significantly reduced the amount of weight regain following initial weight loss (277,316,317,323). The nature of these continuing intervention contacts may be important. Two studies found that person-to-person counseling, delivered by a trained interventionist either face to face or by telephone, was associated with significantly less weight regain than automated interventions delivered via internet Web sites (277,323). Of the two of six trials with negative results, one compared no further treatment to an Internet-based

maintenance intervention (284), and the other compared no further treatment to two active maintenance interventions. One intervention focused on moderate intensity physical activity (walking) and the other focused on resistance training (185).

Four other trials compared two or more active interventions that were designed to promote weight loss maintenance. Leermakers (306) randomly assigned participants who had completed an initial 6-month weight loss program to either an exercise-focused maintenance program or a weight-focused weight maintenance program. At 1–year post-randomization, the weight-focused program resulted in significantly less weight regain than the exercise-focused program. West (206) compared two maintenance programs following an initial 6–month weight loss program and did not find a significant difference in weight loss maintenance between a motivation-focused intervention and a skill-focused program. Fogelholm (187) compared two different levels of recommended physical activity, 2 to 3 hours per week of walking vs. 4 to 6 hours per week, and did not find significant differences in weight loss maintenance at one–year post randomization. Dale (285) compared two maintenance programs among women who previously lost 5 percent of their initial body weight on their own in the previous 6 months. The two maintenance programs involved either a nurse support program (weekly contact as weigh-in or brief phone call) or an intensive support program (supervised exercise and professional individual counseling). Both interventions led to comparable results of an average weight loss of approximately 2 kg over 2 years of intervention. These weight loss outcomes are exceptions to the typical weight regain observed in the other included studies of weight loss maintenance interventions. It is notable that the Dale study provided many more participant contacts, even in the lower intensity intervention, than any of the other included weight loss maintenance interventions. One additional trial comparing weight loss maintenance interventions has not been discussed here because the

outcome data were not reported as change from randomization to final follow-up data collection (294).

Evidence Statement 8B. Approximately 40 to 60 percent of overweight/obese adults who participate in a high-intensity, long-term comprehensive lifestyle intervention maintain a loss of 5 percent or more of initial body weight at 2 or more years follow-up (post randomization).

Strength of the Evidence: Moderate

Rationale: Three large studies (presented previously in Summary Tables 4.2 and 4.8) have reported on the proportion of participants who achieved different categories of weight loss 2 years or more following the start of behavioral intervention (201,203,204) (204). (These studies are presented together in the final section of Summary Table 4.8. One was rated good quality; two were rated fair quality.) Each of these studies used various weight loss categories and follow-up intervals, but in each study trial a substantial proportion of participants achieved meaningful long-term weight loss (i.e., ≥5 percent of initial weight). Rock (201) reported that among participants who received a combination of behavioral counseling and prepared meals, 62 percent of those who received counseling in person and 56 percent of those who received counseling by telephone achieved a 5 percent or greater weight loss at a 2-year follow-up. Appel (203) reported that the proportion of participants maintaining at least a 5 percent reduction in body weight at a 2-year follow-up was 38 percent of those assigned to a telephone-based intervention and 41 percent of those assigned to an in person-delivered intervention. In the Look AHEAD study, 46 percent of participants in the intensive lifestyle intervention (ILI) achieved a loss of at least 5 percent of initial body weight at year 4 (204).

6.14 Characteristics of Lifestyle Intervention Delivery That May Affect Weight Loss: Intervention Intensity—Summary Table 4.9

Evidence Statement 9A Moderate intensity, onsite comprehensive lifestyle interventions, which provide an average of 1 to 2 treatment sessions per month typically produce mean weight losses of 2 to 4 kg in 6 to 12 months, losses which generally are greater than those produced by usual care (i.e., minimal intervention control group).

Strength of Evidence: High

Eight RCTs were identified that compared a moderate-intensity, onsite comprehensive lifestyle intervention with usual care or minimal treatment (i.e., characterized by the limited provision of advice or educational materials) (205,278,288,289,292,304,308,309,329). Six were rated good quality; two were rated fair quality. Moderate intensity was defined as providing 6 to 13 sessions during the first 6 months (i.e., approximately monthly to every-other-week contact). In all trials treatment was delivered by trained interventionists in group or individuals sessions and provided recommendations for consuming a lower calorie diet, engaging in regular physical activity, and using behavioral strategies to achieve these recommendations (as described previously for high-intensity interventions).

Two of eight moderate-intensity trials reported weight loss at 6 months, at which time the intervention group was superior to usual care (205,292). Four trials reported mean 12-month weight losses, which ranged from 2.4 to 4.2 kg (205,278,304,329). The difference at this time between intervention and usual care groups ranged from 1.1 to 3.4 kg; differences were statistically significant in two studies (278,304). Five of eight RCTs (205,288,308,309,329) reported mean weight losses at 24 to 36 months. In two studies reporting results at 24 months,

differences between intervention and control groups of approximately 0.2 and 1.2 kg were not statistically significant) (205,309). A third study, the Finnish Diabetes Prevention Study, reported weight loss outcomes at 24 and 36 months. At 24 months, the investigators observed a loss of 3.5 kg, with a significant net-of-control difference of 2.7 kg, and at 36 months the intervention group maintained the 3.5 kg loss, with a significant net-of-control difference of 2.6 kg. By contrast, two other studies reported 24-month weight losses of 14.0 and 15.0 kg, which were achieved through monthly intervention sessions the first year and every-other-month sessions in year 2 (288,289). The differences between intervention and control groups were 11.0 and 13.0 kg, respectively. The same investigative team conducted these two studies, using the same protocol. The details of the intervention for these two studies are only briefly described in the publication, thereby, preventing adequate understanding of the above average results achieved. (It is possible that participants in both studies had separate, monthly visits with a dietitian, exercise specialist, and psychologist, which would have increased the intensity of the intervention. The study, however, does not provide sufficient detail to resolve this question. Similar questions arose about the intensity of the intervention used in the study by Tuomilehto et al. (329). In summary, the preponderance of the evidence (i.e., 5 of 8 studies) indicates that moderate-intensity lifestyle interventions produce short- to long-term weight losses of up to 4 kg, although substantially larger losses have been reported in two studies (288,289).

Evidence Statement 9B. Low-intensity, onsite comprehensive lifestyle interventions~~,~~ which provide fewer than monthly treatment sessions, do not consistently produce weight loss when compared to usual care.

Strength of the Evidence: Moderate

Rationale: Two RCTs were identified that compared a low-intensity, onsite comprehensive lifestyle intervention (i.e., provided ≤5 sessions over the first year) with usual care or minimal treatment. One was rated good quality and the other fair quality. The two studies reported mean 12-month weight losses of approximately 0.1 percent to 1.9 percent of initial weight Christian, (327). The difference between intervention and usual care groups ranged from approximately 0.7 percent to 1 percent and was statistically significant in one study (ter Bogt 327).

Evidence Statement 9C. When weight loss with each intervention intensity (i.e., low, moderate, and high) is compared to usual care, high-intensity lifestyle interventions (>14 sessions in 6 months) typically produce greater net-of-control weight losses than low-to-moderate intensity interventions.

Strength of the Evidence: Moderate

Rationale: No RCTs of fair or good quality were identified that directly compared the effects of interventions of different intensity (i.e., low, moderate, or high intensity) on weight loss. Thus, in trying to assess the effects of intervention intensity on weight loss, the panel examined trials that provided a moderate-intensity intervention (i.e., 6 to 13 sessions in 6 months) compared with usual care (i.e., minimal intervention), as well as studies that evaluated low-intensity interventions (1 to 5 sessions in 6 months) compared with usual care. The mean net weight losses associated with these two treatment intensities were compared (indirectly) with the mean net weight loss produced by high-intensity, onsite interventions (14 or more sessions in 6 months), considered the gold standard in lifestyle management for obesity. As discussed in section 8.7 (and shown in Summary Table 4.2), net-of-control weight losses at 1 year in high-intensity interventions ranged from 4.3 to 7.9 kg, in favor of the intervention group (over usual care). As discussed in this

section, net-of-control losses at 1 year in moderate intensity interventions ranged from 1.1 to 3.0 kg, in favor of the intervention over usual care. Corresponding differences at 1 year in low-intensity interventions ranged from approximately 0.7 to 1.0 kg (values estimated from percentage change data). These comparisons suggest that high-intensity interventions produce greater net-of-control weight losses than do low- and moderate-intensity interventions.

6.15 Characteristics of Lifestyle Intervention Delivery That May Affect Weight Loss or Weight Loss Maintenance: Individual vs. Group Treatment—Summary Table 4.1

***Evidence Statement 10*.** There do not appear to be substantial differences in the size of the weight losses produced by individual- and group-based sessions in high-intensity, comprehensive lifestyle intervention delivered onsite by a trained interventionist.

Strength of the Evidence: Low

Rationale: No RCTs of fair or good quality were identified that compared the effectiveness of high-intensity, onsite comprehensive interventions that were delivered using individual vs. group treatment sessions. Nine of the 10 high-intensity, onsite interventions reviewed in Summary Table 4.1 were delivered predominantly in group sessions, as reviewed elsewhere in this report (section 8.7) (46,202,203,276,281,305,311,320-322). Six were rated good quality; four of fair quality. In contrast to group-based interventions, one major trial, the Diabetes Prevention Program (303), provided weight loss induction interventions exclusively in an individual counseling format, and achieved weight loss results that were similar to those achieved in group-based interventions. Although it would be helpful to conduct additional direct

comparisons of group and individual counseling, it appears that they result in similar weight losses.

6.16 Characteristics of Lifestyle Intervention Delivery That May Affect Weight Loss Or Weight Loss Maintenance: Onsite vs. Electronically Delivered Interventions—Summary Table 4.10

Evidence Statement 11. Weight losses observed in comprehensive lifestyle interventions, which are delivered onsite by a trained interventionist in initially weekly and then biweekly group or individual sessions, are generally greater than weight losses observed in comprehensive interventions that are delivered by Internet or e-mail and which include feedback from a trained interventionist.

Strength of the Evidence: Low

Rationale: Only one RCT rated of fair quality has directly compared the efficacy of a high-intensity, comprehensive lifestyle intervention delivered onsite (face-to-face) with the same program delivered by Internet (200). Twenty-four weekly group sessions, delivered onsite, produced a mean loss of 7.6 kg (at month 6), compared with a significantly smaller 5.5 kg for the same program delivered by Internet, using a chat room facilitated by a trained interventionist and electronic food and activity diaries. A third treatment arm, which combined one onsite meeting per month with three electronic contacts per month, produced a mean loss of 5.7 kg.

Ten onsite, high-intensity RCTs (20,46,199,202-204,274,276,281,286,303,305,311,320-322,331) were compared with nine electronically delivered trials (200,279,282,291,293,297,314,324,325), all of which examined the induction (not maintenance) of weight loss. These studies, which are drawn from Summary

Tables 4.1 and 4.3, respectively, are summarized in Summary Table 4.10. Of the onsite trials, six were rated good quality; four were of fair quality. Of the electronically delivered trials, four were rated good quality; five were rated fair quality. In all trials, an intervention group delivered by a trained interventionist was compared with a usual care, minimal intervention group, thus, allowing calculation of net-of-control differences in weight loss (i.e., intervention–usual care difference). Net of control differences were consistently greater in the onsite, high-intensity trials than in the electronically delivered interventions. Differences were consistent with those observed in the RCT by Harvey-Berino (200), which directly compared the method of intervention delivery.

6.17 Recommendations

Recommendation 4a. Advise overweight and obese individuals who would benefit from weight loss to participate for ≥6 months in a *comprehensive lifestyle program* that assists participants in adhering to a lower calorie diet and in increasing physical activity through the use of behavioral strategies.

(Grade A, Strong); ACC/AHA COR I, LOE A

Rationale: The objective with overweight and obese patients is to produce weight loss that is clinically meaningful. This is generally considered to be approximately a 5–10 percent loss of initial body weight, which is associated with reductions in key cardiometabolic risk factors (e.g., blood pressure, blood glucose control, risk of diabetes). Participation for 6 months in a comprehensive, high-intensity, onsite lifestyle intervention produces a mean weight loss of approximately 5 to 8 kg (and up to 10 kg in some studies), equal to about a 5 to 8 percent reduction in initial weight [Summary Table 4.2 (274,281,303,322)]. In comprehensive lifestyle programs, more than 50 percent of participants can be expected to achieve a loss of 5 percent or more of

initial weight [Summary Table 4.2- (46,202,274,303,331)]. Most individuals achieve their maximum weight loss in the first 6 months of a comprehensive intervention. The average weight loss does not change substantially from months 6 to 12, even when participants are provided continued, although less frequent (e.g., every-other-week) treatment sessions [Summary Table 4.2 (46,202,274,303,331)]. To achieve these weight losses, a comprehensive lifestyle program should include specific behavioral strategies for reducing calorie intake and increasing physical activity [Summary Table 4.1]. Long-term participation in a comprehensive lifestyle intervention is recommended to prevent or slow weight regain, which is common following the cessation of weight loss interventions (20,46).

Recommendation 4b: Prescribe on-site, high-intensity (i.e., ≥14 sessions in 6 months) comprehensive weight loss interventions provided in individual or group sessions by a trained interventionist.[ii]

(Grade A, Strong); ACC/AHA COR I, LOE A

Rationale: The studies reviewed show evidence of greater weight loss with higher frequency of contact. Intervention contact has typically been provided in group or individual, face-to-face sessions. Therefore, comprehensive lifestyle interventions that provide 14 or more face-to-face meetings over 6 months are preferred, because this intervention format consistently produces clinically meaningful weight loss [Summary Table 4.2 (20,46,202,203,274,281,303,311,320-322)]. However, some initial evidence suggests that telephone-based counseling interventions can be similarly successful with high frequency of contact [Summary Table 4.4 (201,203)]. High-intensity interventions are usually provided in research or medical centers but also may be offered in community or worksite settings, as well as commercial programs.

Another important feature of the studies reviewed (that included high-intensity comprehensive weight loss programs) is the use of trained interventionists. Interventionists can have different professional backgrounds (e.g., registered dietitians, psychologists, exercise specialists, health counselors) and, in some cases, may be trained laypersons.

If a high-intensity, onsite comprehensive program is not available to the patient, a similar intervention of moderate intensity (i.e., providing 6 to 13 sessions in 6 months) can be recommended as an alternative approach. Evidence suggests that the weight losses achieved (averaging 1 to 3.5 kg in 6 to 12 months) will be lower than those produced by high-intensity programs [Summary Table 4.9 (204,278,292,304,309)]. Low-intensity lifestyle interventions, as typified by quarterly counseling delivered by a primary care practitioner, are probably more appropriate for facilitating weight stability (i.e., preventing weight gain) than inducing clinically meaningful weight loss [Summary Table 4.9- (283,ter Bogt 327)].

Recommendation 4c: Electronically delivered weight loss programs (including by telephone) that include personalized feedback from a trained interventionist[iii] can be prescribed for weight loss but may result in smaller weight loss than face-to-face interventions.
(Grade B, Moderate); ACC/AHA COR IIa, LOE A

Rationale: Interventions delivered using electronic media, such as Web sites, text messaging (via telephone or the Internet), and similar methods, have great promise to reach large numbers of patients at potentially low cost. To date, relatively few controlled clinical trials of electronic media for weight loss have been published, but more can be expected soon. It remains to be seen which combination of intervention strategies and communication channels will be the most effective for helping patients lose weight and maintain their weight loss. Until additional

research is available, it is advisable to anticipate that smaller weight losses will be achieved with electronic-based programs, as compared with traditional face-to-face programs [Summary Table 4.10 (200,279,282,291,293,297,314,324,325)].

Recommendation 4d: Some commercial-based programs that provide a comprehensive lifestyle intervention can be prescribed as an option for weight loss, provided there is peer-reviewed published evidence of their safety and efficacy.
(Grade B, Moderate); ACC/AHA COR IIa, LOE A

Rationale: A range of commercial programs may be effective in producing weight loss. The intention of this recommendation is not to endorse a specific commercial program but instead is to guide practitioners in helping patients identify which types of programs may be effective. Characteristics of commercial programs that produce significant weight loss include providing all components of a comprehensive behavioral intervention program (including a calorie-restricted diet, a physical activity prescription, and behavioral counseling) with a high frequency of contact [Summary Table 4.6 (201,295,319,328)]. Because a wide range of commercial programs are available, published peer-reviewed research should be used to evaluate program components, as well as the safety and efficacy of the program.

Recommendation 4e: Use a very-low-calorie diet (defined as <800 kcal/day) only in limited circumstances and only when provided by trained practitioners in a medical care setting where medical monitoring and high-intensity lifestyle intervention can be provided. Medical supervision is required because of the rapid rate of weight loss and potential for health complications.
(Grade A, Strong); ACC/AHA COR IIa, LOE A

Rationale: There was no direct evidence from RCTs to change the previous conclusion reached by the NIH/NHLBI Obesity Expert Panel in 1998, which stated "VLCDs produce greater initial weight loss than LCDs. However, the long-term (>1 year) weight loss is not different from that of the LCD. Category A. Therefore, the recommendation using VLCDs is limited to short-term use and induction of rapid weight loss. To warrant implementation of this treatment strategy, the benefits of rapid, short-term weight loss should be greater than the risks associated with VLCDs. Beyond the short-term, the benefit of VLCDs over LCDs has not been demonstrated. The lack of a demonstrated long-term benefit, combined with higher medical risk and weight regain, suggests that there is no indication for long-term or widespread use of VLCDs [Summary Table 4.7 (184-187)]. When this strategy is medically indicated for short-term weight loss induction (e.g., pre-bariatric surgical weight reduction protocol), oversight by trained medical professionals is required to manage the medical risk of the VLCD.

Recommendation 4f: Advise overweight and obese individuals who have lost weight to participate long term (≥1 year) in a comprehensive weight loss maintenance program. *(Grade A, Strong); ACC/AHA COR I, LOE A*

Maintaining a reduced body weight, following initial weight loss, is a long-term process. Ongoing support and intervention are effective in slowing weight regain, which occurs in most patients following weight loss [Summary Table 4.8 (185,187,206,277,284,294,306,316,317,323)]. Rather than considering short-term weight loss in a comprehensive lifestyle intervention as the end goal, advise patients to seek a long-term weight loss maintenance intervention that includes behavioral counseling to sustain key behaviors associated with maintenance of a lower body weight, These includes increased physical activity and regular self-monitoring of dietary intake and body weight.

Recommendation 4g: For weight loss maintenance, prescribe face-to-face or telephone-delivered weight loss maintenance programs that provide regular contact (monthly or more frequently) with a trained interventionist[iv] who helps participants engage in high levels of physical activity (i.e., 200-300 minutes/week), monitor body weight regularly (i.e., weekly or more frequently), and consume a reduced-calorie diet (needed to maintain lower body weight). *(Grade A, Strong); ACC/AHA COR I, LOE A*

Rationale: A weight maintenance intervention helps participants focus on maintaining several key behaviors following initial weight loss. A skilled interventionist is a key component of the weight loss maintenance intervention, providing ongoing behavioral support for 1 year or more. A successful weight loss maintenance intervention would be expected to include a prescription for high levels of moderate-intensity physical activity, regular self-monitoring of body weight, and an appropriate calorie intake required to maintain the new lower body weight [Summary Table 4.8-(185,187,206,277,284,294,306,316,317,323)].

Weight maintenance interventions have been delivered using a variety of methods. Real-time communication with a trained interventionist, either face-to-face or via telephone, appears to lead to the best outcome (i.e., less weight regain) [Summary Table 4.8 (185,187,206,277,306,316,317,323)]. However, some studies have included Internet-based approaches, and this approach may be more accessible or acceptable to some patients. There is evidence for the effectiveness of this approach [Summary Table 4.8 (277,284,294,316,323)]. Given the limited number of options currently available, it is most important to identify a weight loss maintenance intervention that has the requisite components and that the patient is able to access consistently to achieve the best outcome.

6.18 Gaps in Evidence and Future Research Needs

1. Further research is needed with onsite interventions (and those delivered by other methods) to determine the optimal frequency (and duration) of contact needed to induce clinically significant weight loss (≥5 percent of initial weight). The literature suggests that high-intensity interventions (≥14 contacts in 6 months) are more effective than moderate-intensity interventions (6 to 13 contacts in this period) but no randomized RCTs have addressed this issue. Such RCTs are needed and could include efforts to match the intervention intensity to the needs of the specific patient. Study is also warranted of stepped-care interventions that provide overweight/obese individuals with some minimum number of contacts over 6 months, with more sessions provided only to persons who do not achieve clinically significant weight loss.

2. More research is needed on how to effectively translate and disseminate comprehensive, high-intensity lifestyle interventions, shown to be effective in efficacy studies based in academic research centers, into programs that can be delivered in community, work-site, and other settings (including commercial programs). This includes a determination of the personal characteristics, formal credentials, and training required for intervention counselors who deliver a comprehensive lifestyle intervention.

3. RCTs are needed to identify the most effective methods of delivering lifestyle interventions remotely (e.g., Internet, mobile phone, text messaging, telephone, DVDs, etc. or some combination of these) to achieve and maintain clinically significant weight loss (>5 percent). In addition, there is a need for head-to-head comparisons to evaluate relative effectiveness and

associated costs of delivery of onsite, remotely delivered, and hybrid lifestyle interventions for achieving weight loss and health improvements.

4. More research is needed to better understand how to promote additional weight loss beyond the first six months, at which time, weight loss plateaus in most individuals. Is the cessation in weight loss at this time, when many individuals still remain overweight or obese, due to a decline in adherence to behavioral weight loss interventions or is it related to physiologic changes that occur with prolonged energy deficit, or some combination of the two? Examination of these issues could identify methods to extend weight loss, with lifestyle intervention, beyond 6 months (and beyond the average loss of approximately 8 kg achieved at this time).

5. Methods of improving the maintenance of lost weight also require additional study. This includes determining whether overweight/obese individuals require continuous, long-term treatment (i.e., as provided by indefinite participation in a weight-loss maintenance program) or they can be successful with periodic bouts of intervention, in response to weight re-gain (or the desire for further weight loss). The use, following weight loss, of new technologies (e.g., mobile phones) and therapies (e.g., motivational interviewing or acceptance and commitment therapy) also should be examined to determine whether they improve the maintenance of lost weight. Studies are needed to assess the efficacy of long-term (2 to 5 years) weight loss maintenance interventions.

6. Further research is needed to identify the optimal role of PCPs (PCPs) in managing obesity using comprehensive lifestyle intervention. Options range from serving as trained interventionists, as supported by new regulations from the Centers for Medicare and Medicaid

Services, to referring patients to appropriate lifestyle intervention programs or practitioners and checking weight management progress at regular intervals. Economic analyses are needed of different models involving PCPs in the management of obesity.

7. Further study is needed on the effect of weight loss treatment on health care utilization and cost. Observational data suggest that weight loss for some groups of patients, such as older individuals with type 2 diabetes, would have a substantial effect on health and health care utilization.

8. Further research is needed on the effects of weight loss for some key populations, including older adults and ethnic minority groups. The overall safety of weight loss interventions for patients aged 65 and older remains controversial. Although older participants tend to respond well to comprehensive behavioral weight loss treatments, and they experience the same improvements in CVD risk factors as do middle-age participants, the effect of weight loss treatment on risk of CVD, longevity, and osteoporosis has not been extensively studied. More studies on the health consequences of weight loss treatment with this age group are needed. Additionally, individuals from ethnic minority populations in the United States typically have less mean weight loss when provided the same intervention as non-Hispanic whites. This difference has been observed over a number of different types of comprehensive lifestyle interventions (e.g., group, individual, electronic, etc.). Further research is needed to understand the most appropriate strategies and prescriptions for those who may systematically lose less weight in response to a standard, comprehensive behavioral intervention.

7. CRITICAL QUESTION 5

7.1 Statement of the Question

Critical question 5 (CQ5) has three parts:

7.1.1. Efficacy

What are the long-term effects of the following surgical procedures on weight loss, weight loss maintenance, cardiovascular (CV) risk factors, related comorbidities, and mortality?

1. LAGB
2. Laparascopic RYGB
3. Open RYGB
4. BPD with or without duodenal switch
5. Sleeve gastrectomy (SG)

What are the long-term effects of the surgical procedures (listed above) in patients with different body mass indexes (BMIs) and comorbidities?

1. BMI <35
2. BMI of 35 to < 40 with no comorbidities
3. BMI ≥35 with comorbidities, and
4. BMI ≥40 with no comorbidities

7.1.2. Predictors

What are the predictors associated with long-term effects of the following surgical procedures on weight loss, weight loss maintenance, CV risk factors, related comorbidities, and mortality?

1. Laparoscopic adjustable gastric banding
2. Laparascopic RYGB
3. Open RYGB
4. BPD with or without duodenal switch
5. Sleeve gastrectomy

What are the predictors associated with long-term effects of the surgical procedures (listed above) in patients with different BMIs and comorbidities?

1. BMI <35
2. BMI of 35 to < 40 with no comorbidities
3. BMI ≥35 with comorbidities, and
4. BMI ≥40 with no comorbidities.

7.1.3. Complications

What are the short-term (less than 30 days) and long-term (30 days or more) complications of the following bariatric surgical procedures? What are the predictors associated with complications?

1. Laparoscopic adjustable gastric banding
2. Laparascopic RYGB

3. Open RYGB
4. BPD with or without duodenal switch
5. Sleeve gastrectomy

What are the complications of the surgical procedures (listed above) in patients with different BMIs and comorbidities?

1. BMI <35
2. BMI of 35 to < 40 with no comorbidities
3. BMI ≥35 with comorbidities, and
4. BMI ≥40 with no comorbidities.

7.1.3.1. Subgroup Analyses

7.1.3.1.1. By Population Subgroups

- Age (especially age >65)
- Sex
- Socioeconomic status (SES) –no evidence anticipated
- Race/Ethnicity
- Baseline BMI <35; BMI of 35 to < 40 with no comorbidities; BMI >35 with comorbidities, BMI >40 with no comorbidities; by different comorbidities
- Presence or absence of comorbid conditions
  - Diabetes
  - Metabolic syndrome
  - Chronic kidney disease

  - Nonalcoholic steatohepatitis and liver disease
  - Cancer
  - Sleep apnea
  - Skeletal disability
  - Genetic syndromes (i.e., Prader-Willi)
  - Psychiatric disorders (depression, psychosis, mental retardation, addiction, borderline personality disorder)
  - Quality of life issues
  - Multiple (2+) risk factors (that do not constitute metabolic syndrome)
  - Diagnosed CHD/CVD
- Presence or Absence of CVD risk factors (diagnosed or treated)
  - Smoking status
  - Multiple (2+) risk factors (that do not constitute metabolic syndrome)
  - Baseline (not necessarily pre-treatment) LDL-C≥100 mg/dL
  - Triglycerides (TG) ≥200 mg/dL
  - HDL-C≤40 mg/dL
  - Hypertension
  - Elevated fasting insulin, fasting glucose, HbA1c
  - Previous CVD event
  - Elevated CRP
  - Diagnosed CVD/CHD (Acute coronary syndrome; coronary artery disease; congestive heart failure; history of myocardial infarction; angina with objective evidence of atherosclerotic CHD; history of coronary revascularization (angioplasty or bypass);

cerebrovascular disease; other forms of atherosclerotic CVD (e.g., peripheral artery disease (PAD))

7.1.3.2. By Amount of Weight loss

- Different cutpoints

7.1.3.3. By Weight loss Maintenance

- Different cutpoints

Note: Predictors will address patient factors, provider factors, and procedure (surgery) factors. Patient factors include: BMI, age, comorbidities, and functional status, and can include multiple risk factors assessed.

7.2 Selection of the Inclusion/Exclusion Criteria

Panel members developed eligibility criteria, based on a PICOTS approach, to use for screening potential studies for inclusion in the evidence review. Table 7.0 presents the details of the PICOTS approach for CQ 5. Studies considered included RCTs, non-RCTs, prospective cohort studies, retrospective cohort studies, case cohort studies, case control studies, nested case control studies, case-crossover studies, interrupted time series studies, before-after studies, time series studies, and case series. For the predictors and complications component of CQ5, observational studies were included if the sample size was ≥100 with 10 or more years of follow-up or studies on BPD procedures or SG procedures. Other observational studies were included if the sample size was ≥500. Due to time and resource constraints, the panel was not able to conduct all the subgroup analyses originally planned (e.g., race/ethnicity as predictors; non-alcoholic fatty liver disease or sleep apnea as outcome measures).

Table 7.0. Criteria for Selection of Publications for CQ5

	Inclusions	Exclusions
Population	• Adults	• Children • Animal studies
Intervention	• Laparoscopic adjustable gastric banding • Laparascopic RYGB • Open RYGB • BPD with or without duodenal switch • Sleeve gastrectomy Any of the above interventions AND pre or post operative intervention components (can be multi-component): • diet • physical activity • behavioral treatments	• Other bariatric surgical interventions not listed in inclusions
Comparator	*Efficacy Component:* • Any type of non-surgical alternate intervention differing from the main study intervention *Predictor and Complication Components:* • Any type of alternate intervention differing from the main study intervention *All Components:* • No care • Usual care • Observational studies may not have pre-specified comparison groups (For example, intervention and comparison groups, or exposed and unexposed groups, may emerge over time as patients are being followed for a cohort study.)	
Outcome	*Reduction in body weight as measured by:* • Weight (kg, lbs., percent) • Body fat measures: (BMI and BMI change) • Waist circumference • Waist-hip ratio • Percent body fat • Weight loss maintenance (weight change from end of treatment to follow-up)	

	Inclusions	Exclusions
	• Percent reduction of excess weight Self-reported weight outcomes are permitted For all but short term postoperative outcomes, study must report a body weight measure plus one or more of the following outcomes: *Long- and Short-Term Surgical Complications* • Intraoperative • Short-term postoperative (<30 days post op) • Long-term postoperative (≥30 days) *Quality of Life* • Function • Disability *CVD Events* • MI • Heart failure • Hospitalization for heart failure or stroke *CVD Risk Factors* • Systolic blood pressure or diastolic blood pressure • Total cholesterol, HDL-C, LDL-C, Non-HDL-C, TG • Fasting glucose, fasting plasma insulin, HbA1C • Smoking status • CRP *Morbidity* • CHD/CVD • Incidence and remission of diabetes • Incidence and remission of hypertension • Liver disease • Sleep apnea • Depression • Eating disorders • Chronic renal failure *Mortality* • CVD-related • All-cause *Physical activity*	

	Inclusions	Exclusions
Timing	*Efficacy and Predictor Components:* • Intervention period: for lifestyle components ≥3 months • Follow-up periods: – ≥6 months for lifestyle components – ≥2 years for surgery *No follow-up time criteria for complications components	• Intervention periods for lifestyle components of <3 months • Follow-up of <6 months for lifestyle components • Follow up periods of l< 2 years for surgery intervention *No follow-up time criteria for complications components
Setting	*Westernized countries:* • United States • Canada • European Union • Australia • New Zealand • Israel Any clinical or research setting	• Countries not applicable to western weight goals and diets
Study Design	*Efficacy Component* • RCTs, non-RCTs, prospective cohort studies, retrospective cohort studies, case cohort studies, case control studies, nested case control studies, case-crossover studies, interrupted time series studies	*Efficacy Component* • Before-after studies, time series studies, cross-sectional studies, case series, case reports
	Predictor Component RCTs, non-RCTs, prospective cohort studies, retrospective cohort studies, case cohort studies, case control studies, nested case control studies, case-crossover studies, interrupted time series studies, before-after studies	*Predictor Component* Time series studies, cross-sectional studies, case series, case reports
	Complications Component • RCTs, non-RCTs, prospective cohort studies, retrospective cohort studies, case cohort studies, case control studies, nested case control studies, case-crossover studies, interrupted time series studies, before-after studies, time series studies, case series *Sample Size Criteria for Predictor and Complications Components Only:* Sample size requirements only for observational studies: ≥100 for studies with 10 or more years of follow-up or studies on BPD or SG procedures; ≥500 for all other	*Complications Component* • Cross-sectional studies, case reports *All components:* • SRs)/MAs • Dropout rate ≥35 percent overall at 1 year

	Inclusions	Exclusions
	observational studies	
Language	• Abstract must be available in English	• Full text translation into English must be feasible
Publication Type	Published studies	• SRs/MA • Unpublished literature – Unpublished industry-sponsored trials – Other unpublished data • FDA Medical and Statistical reviews • Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Publication Time Frame	• Studies published in years 1998–2009; RCTs published in 2010 through 2012 were included if they included ≥100 participants per treatment arm and otherwise met inclusion criteria.	• Studies published before 1998

7.3 Introduction and Rationale for Question and the Inclusion/Exclusion Criteria

Extreme obesity, also known as Class III obesity, is prevalent in the U.S. population, with 8.1 percent of women and 4.4 percent of men having a BMI of 40 or above (18). Among some racial and ethnic minority populations, extreme obesity is even more common. For example, 17.8 percent of non-Hispanic African American women have a BMI ≥40 (18). Patients with extreme obesity have a high prevalence not only of complications such as CVD and type 2 diabetes, but also of non-alcoholic fatty liver disease, joint disease, sleep apnea and thromboembolic disease (332). Patients with extreme obesity also have a substantially elevated mortality risk (333).

Many, if not most, patients with extreme obesity have tried to lose weight numerous times. Some have lost substantial amounts of weight successfully, only to regain it. Although lifestyle intervention is the mainstay of all weight management treatment, there is increasing recognition of

the need for adjunctive treatments for patients with obesity who are at high medical risk and who are unable to achieve or maintain sufficient weight loss to improve their health. Bariatric surgery is one treatment option that has been increasingly used in patients with extreme obesity or with lesser degrees of obesity but with obesity-related comorbid conditions. Since the 1998 clinical guidelines on overweight and obesity in adults were published, there have been new bariatric procedures, devices, and surgical approaches introduced, as well as additional data on short-term and longer term benefits and risks. This section reviews evidence about the efficacy of bariatric surgery for weight loss and improvement in health and quality of life, which patient or procedural factors influence outcomes, and what short- and long-term complications can be expected. With these data, PCPs can better advise their patients about the risks and benefits of bariatric surgery compared with other treatment approaches.

Bariatric surgery is, by definition, invasive and has inherent short-term risks as well as adverse effects that may only become apparent during long-term follow-up. Incurring these risks may be acceptable if health benefits are sustained over time. Therefore, the expert panel members believed that evaluation of *efficacy* endpoints for weight loss and change in CVD risk factors and other health outcomes required studies with a minimum post-surgical follow-up of 2 years and inclusion of a nonsurgical comparator group. Studies evaluating *predictors* of weight change or medical outcomes, including patient factors (e.g., presence vs. absence of diabetes) or surgical factors (e.g., RYGB vs. BPD) required studies that directly compared these factors plus a minimum 2-year follow-up. Studies evaluating *complications* of bariatric surgery required at least a 30-day post-surgical follow-up. For observational studies with 10 or more years of follow-up or for studies on BPD or sleeve gastrectomy (SG) procedures, sample size ≥100 was required, and for all other observational studies sample size requirement was ≥500. This sample

size requirement was instituted because the most important complications are infrequent (e.g., perioperative mortality <1 percent), such that smaller studies could give inaccurate estimates of complication rates.

7.3.1. Bariatric Surgical Procedures

7.3.1.1. Classifications/Mechanisms of Action

In the past, bariatric surgical procedures have been classified as restrictive, in which a small gastric pouch is created, thereby limiting the amount of food that can be ingested, malabsorptive, or a combination of the two. It is now clear that, while elements of gastric constriction, which limits food intake and malabsorption, may be components of bariatric surgical procedures, the mechanisms of action are considerably more complex. Neuroendocrine signaling to appetite and satiety centers in the central nervous system from the gastric pouch and possibly the distal esophagus, as well as behavioral variations, all contribute to the efficacy of gastric restriction. Procedures that alter the gastrointestinal anatomy, including bypass or resection of variable portions of the stomach, alter the delivery of ingested nutrients to more distal sites in the small intestine for digestion and absorption. They also produce numerous neuroendocrine signals that have complex interactions with central nervous system receptors (334). The following is a brief review of the more commonly used procedures, past, present, and possibly future.

7.3.1.2. Procedures Used in the Past

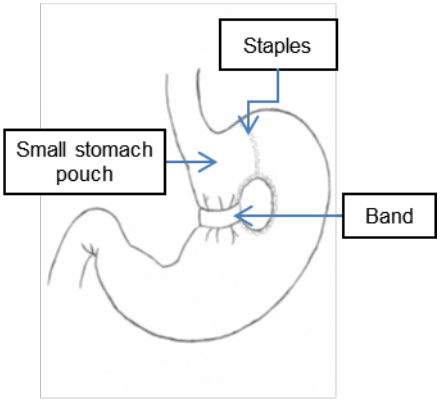
The first bariatric surgical procedure to gain popularity was the jejunoileal bypass. As much as 90 percent of the small intestinal absorptive surface was bypassed, such that ingested nutrients were delivered to the very distal ilium. This resulted in a definite degree of malabsorption,

especially of fat. Diminished nutrient intake, however, accounted for the predominant explanation for the major weight loss that occurred (335). Multiple complications secondary to micronutrient malabsorption, liver and renal dysfunction, and others led to abandonment of these procedures, despite the successful weight loss that was regularly achieved.

7.3.1.3. Vertical Banded Gastroplasty

This procedure was developed in response to the unacceptable metabolic complications that led to abandonment of the jejunoileal bypass. A stapling device was used to partition a small upper gastric pouch. To prevent dilation of the stomach at the "stoma" point of nutrient entry into the body of the stomach, the stomach wall was reinforced with a prosthetic band. This procedure was the predominant bariatric surgical procedure in the 1980s but has been largely abandoned due to insufficient durable weight loss and complications secondary to progressive narrowing at the point of the fixed gastric banding (336).

Figure 9. Vertical Banded Gastroplasty



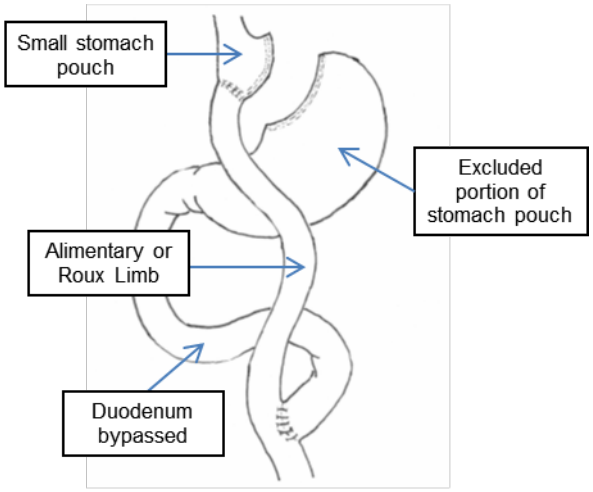
7.3.2. Currently Used Procedures

7.3.2.1. Roux-en-Y Gastric Bypass

The RYGB combines gastric restriction and neuroendocrine modulation of appetite and satiety signals. A gastric pouch is created by transecting the upper stomach. Intestinal continuity is reestablished by Roux-en-Y gastrojejunostomy. The size of the gastric pouch as well as the length of the jejunal limbs vary. Malabsorption of micronutrients (calcium, iron, vitamin B12) may occur, but malabsorption of macronutrients is minimal.

Gastric bypass as well as the other procedures described below can all be done using a minimally invasive or laparoscopic approach (337,338).

Figure 10. Roux-en-Y Gastric Bypass

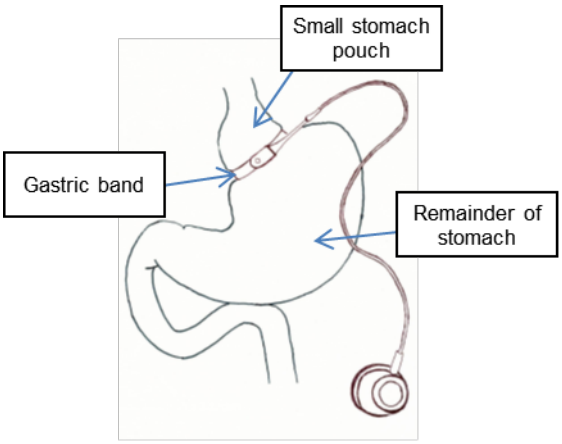


7.3.2.2. Laparoscopic Adjustable Gastric Banding

In this procedure, a gastric band or collar is placed above the upper stomach just below the gastroesophageal junction, creating a small gastric pouch as in vertical banded gastroplasty and

gastric bypass. The inner aspect of the band consists of a balloon, which can be adjusted by injecting or withdrawing saline through a subcutaneous port positioned on the anterior abdominal wall. Thus, the tightness of the band can be adjusted for optimal effect.

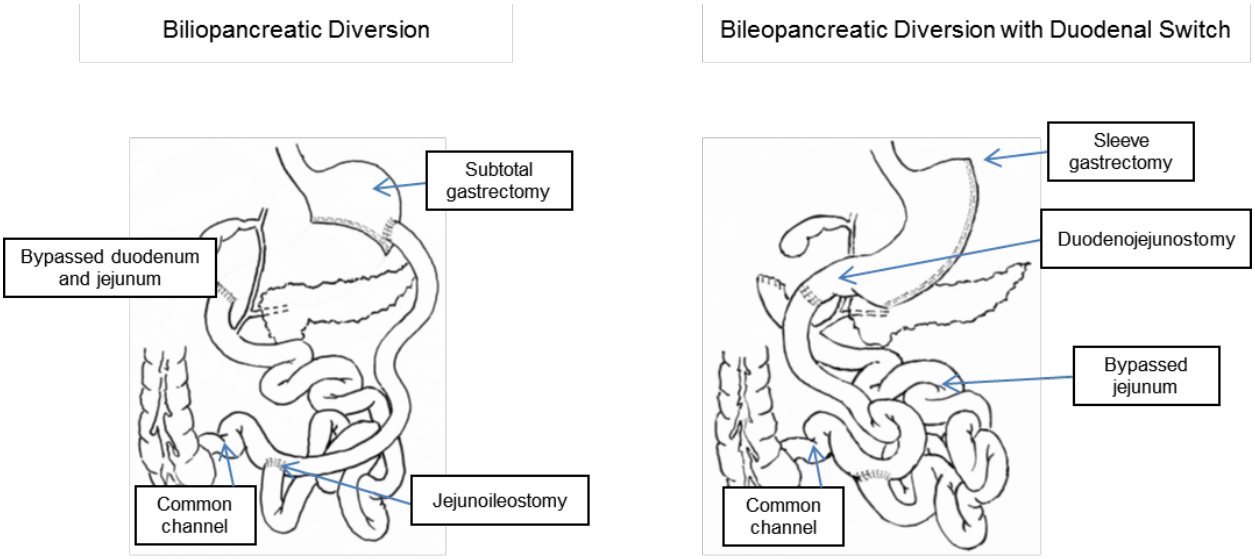
Figure 11. Laparoscopic Adjustable Gastric Banding



7.3.2.3. Biliopancreatic Diversion With or Without Duodenal Switch

The BPD was devised in Italy in the late 1970s. It combines a subtotal gastric resection, Roux-en-Y gastrojejunostomy, and distal intestinal anastomosis, such that the digestive enzymes contained in bile and pancreatic juice do not mix with ingested nutrients until the terminal ileum is reached, creating a degree of gastric restriction, malabsorption, and neuroendocrine signaling that combines to accomplish weight loss. A modification of this procedure known as the duodenal switch consists of a substantial gastric resection leaving a tubular stomach along the lesser curvature of the stomach. A bypass of the small intestine is created by anastomosis of the small intestine to the transected duodenum distal to the pylorus and, as with BPD, a distal mixing of digestive enzymes with ingested nutrients.

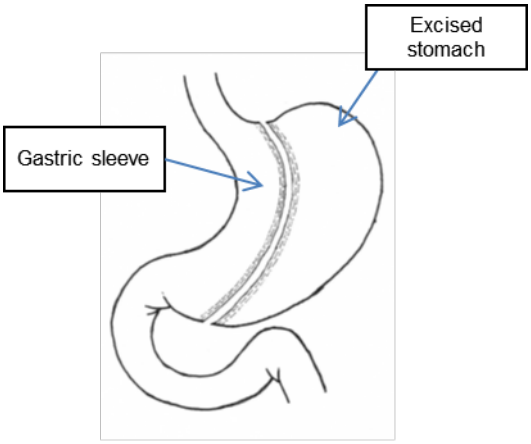
Figure 12. Biliopancreatic Diversion With or Without Duodenal Switch



7.3.2.4. Sleeve Gastrectomy

In response to problematic perioperative complications and mortality, particularly among the most severely obese patients, the BPD with or without duodenal switch procedure was done in two stages. The first stage consisted of the SG followed by weight loss, reduction of operative risk, and construct of the intestinal component of the procedure at second operation. Subsequently, SG became an independent procedure. This procedure has gained considerable popularity at the present time.

Figure 13. Sleeve Gastrectomy



7.3.3. Investigational Procedures

In an effort to develop interventions for obesity and related metabolic diseases that would represent lesser degrees of invasion, risk, and/or cost but maintain efficacy, a number of procedures or approaches are being evaluated at differing stages of development including gastric imbrication, neuromodulation, and gastrointestinal luminal (flexible) endoscopic interventions. These guidelines do not further discuss investigational procedures.

7.4 Methods for Critical Question 5

The literature search for CQ5 included an electronic search of the Central Repository for RCTs, controlled clinical trials, and observational studies published in the literature from January 1998 to December 2009. The Central Repository contains citations pulled from seven literature databases (PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts). The search produced 2317 citations, with 9 additional citations identified

from non-search sources, i.e., by the panel members or hand search of SRs/MA (obtained through the electronic search). The SRs/MA were only used for manual searches and were not part of the final evidence base. This manual cross-check was done to ensure that major studies were not missing from the evidence base. A similar manual cross-check of citations from the American Society for Metabolic & Bariatric Surgery position statement was performed in May 2012 (339). Eight of the 9 citations identified from non-search sources were published after December 31, 2009. Per NHLBI policy, certain lifestyle and obesity intervention studies published after the closing date could be allowed as exceptions. These studies must be RCTs in which each study arm contained at least 100 participants and were identified by experts' knowledgeable of the literature. Three of the 9 citations published after December 2009 met the criteria and were eligible for inclusion in the CQ 5 Evidence Base (340-342). In contrast, five of the 9 citations did not meet the criteria and were excluded from the Question 5 evidence base (343-347). The remaining citation, identified through non-search sources, was published before 2009 (348). This citation met the criteria and was eligible for inclusion. Thus, of the nine citations identified through non-search sources, four were screened and found eligible for inclusion; all these studies were subsequently quality rated as good studies.

Figure 14 below of the PRISMA diagram outlines the flow of information from the literature search through the various steps used in the systematic review process for CQ5.

A natural language processing filter was used to identify studies with sample sizes less than 100, 100 to 299, and/or a follow-up time of less than 6 months. The natural language processing filter was executed against titles and abstracts. Of the 2317 citations identified through the database search, 811 citations were automatically excluded using the natural language processing filter. Two reviewers independently screened the remaining titles and abstracts of the 1515

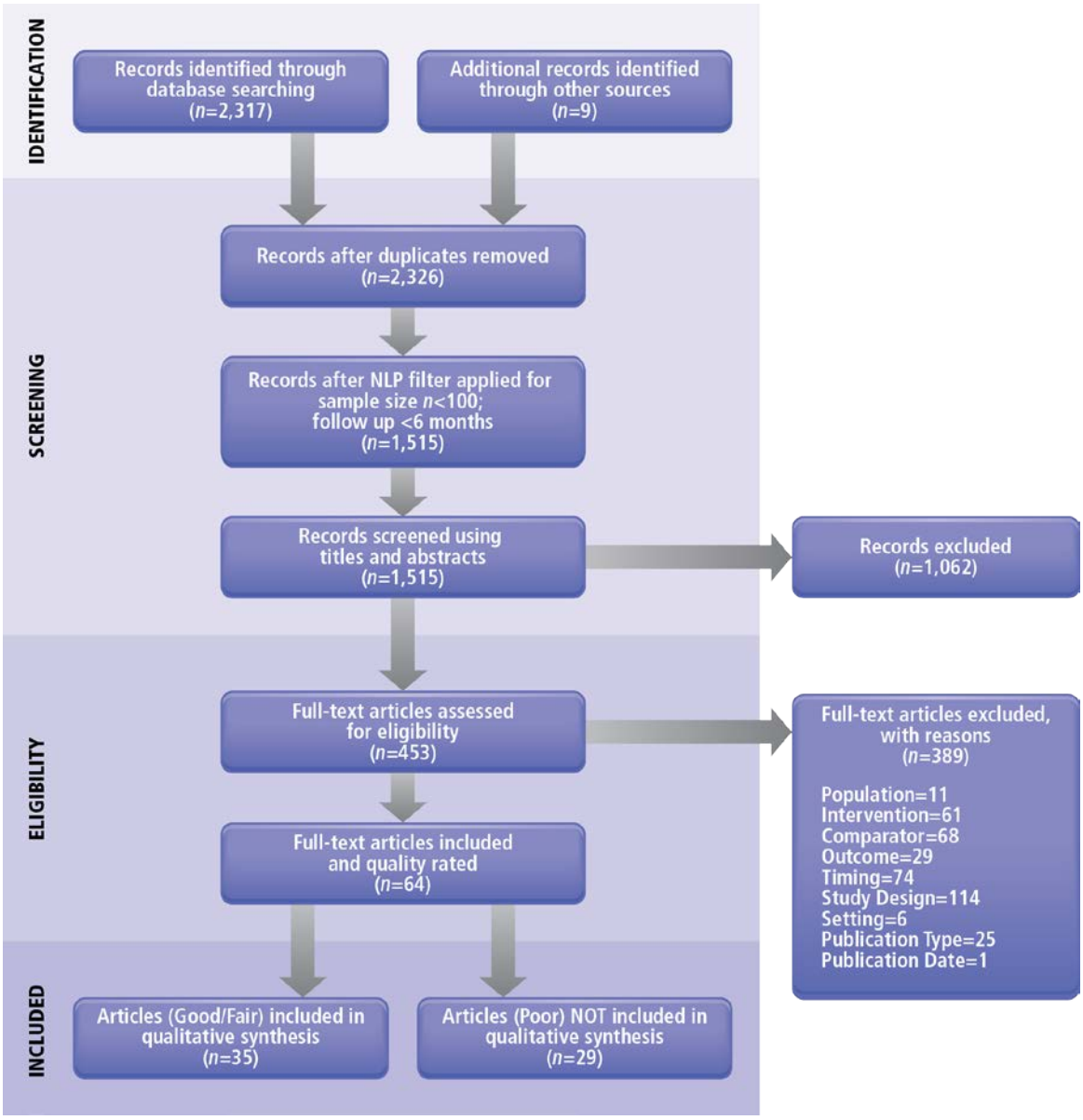
remaining citations against the I/E criteria for each of the three components (Efficacy, Predictors, and Complications). This resulted in 1062 publications being excluded (on one or more of the I/E criteria for each of the three components of this CQ) and 453 publications being retrieved for full-text review to further assess eligibility.

Sixty-four of the 453 full-text publications met the criteria and were included. The quality (internal validity) of these 64 publications was assessed using the 6 quality assessment tools that were developed (see Appendix 2). Of these, 29 publications were excluded because they were rated as poor quality (337,338,349-375); of these 18 studies were rated poor due to the intention-to-treat (ITT) and/or attrition rates. Rationales for all poor quality studies are included in Appendix 3. The remaining 22 studies (35 articles) that met the criteria for **at least** one of the three components were rated good or fair quality and included in the evidence base (340-343,348,376-405). Of these, eight articles did not provide additional or useful data beyond the data in the summary table; seven articles are listed in the summary table for the Efficacy component (348,384,392,393,398-400), and one article is listed in the summary table for the Complications component (382). The remaining articles were used to formulate the evidence statements and recommendations (with the exception of Agaba (377) and Weiner (405) for the Complications component, see CQ5: Statement of Question, 5c. Complications). For the Efficacy, Predictors, and Complications components, there were 5 studies (17 articles), 10 studies (12 articles) and 14 studies (15 articles) rated as good/fair, respectively. There were a total of eight articles that were used across more than one component (341,378,379,381,385,394,401,402).

Panel members reviewed the final studies on the include list, along with their quality ratings, and had the opportunity to raise questions. Some trials previously deemed to be of fair or good quality were downgraded to poor quality upon closer review of evidence tables. These trials used

completers analyses rather than ITT analysis and had overall attrition rates exceeding 10 percent. If the study reported only an analysis of completers and had attrition at <10 percent, it was allowed in the evidence base. The methodologists worked with the systematic review team to re-evaluate these trials and make a final decision. Evidence tables and summary tables consisted only of data from the original publications of eligible RCTs and observational studies; these tables formed the basis for panel deliberations.

Figure 14 PRISMA Diagram Showing Selection of Articles for Obesity Question 5



7.5 Evidence Statements and Summaries

In all, 22 studies (35 articles) satisfied the final inclusion criteria and were rated fair or good quality. Studies of complications included RCTs, cohort studies, before-after studies, and case series if they met methodologists' search and quality criteria.

7.5.1 Component 1: Efficacy Summary Table 5.1

Five studies (17 articles) met search and quality criteria for determining the efficacy of bariatric surgery for weight loss and impact on obesity-related comorbid conditions (341,348,381,384-387,392-394,396-402). The number of studies meeting inclusion criteria was limited, due to the requirement that surgical treatment be compared to a nonsurgical comparator group (341,381,385,386,394) with a minimum postsurgical follow-up of 2 years. Three of the studies were RCTs comparing surgical treatment against conventional medical treatment, lifestyle intervention, or medically supervised weight loss (341,381,394). One trial was a 3-year prospective cohort study with nonsurgical comparators (385). The largest and one with the longest follow-up, the Swedish Obese Subjects study, was a non-randomized prospective cohort study of patients who underwent vertical banded gastroplasty, gastric banding or gastric bypass; this was compared with a matched cohort who received standard clinical care (348,384,386,387,392,393,396-402). Patients in all but one study (394) had a mean BMI >35, but in the most recent included studies, patients with obesity-related comorbid conditions who had an initial BMI as low as 30 kg/m2 were enrolled (381,394). Comparator groups ranged from intensive lifestyle treatment that included very low-calorie diets, pharmacotherapy, and lifestyle counseling (394) to usual care by the primary care practitioner (386,387,396,397,401,402). From these trials, evidence statements may be made regarding the efficacy of bariatric surgery for weight loss; for reduction in CVD risk factors, including progression to or remission from type 2 diabetes; for impact on quality of life; and for impact on mortality.

Summary Table 5.1 presents summary data from the five included studies on efficacy. Some studies appear in more than one summary table because they address more than one framework of analysis (e.g. predictors or complications).

For the purposes of this document, all the weight loss data are reported as percent of total weight lost or calculated as the percent of BMI lost. It is common among surgical studies to report weight loss as the "excess weight loss" or EWL. This form of weight loss reporting is problematic, however, due to varying definitions of ideal body weight, which are frequently not provided in the manuscripts. In addition, the relationship between percent total weight loss and percent excess weight loss is not linear throughout a full range of BMI values (406).

Evidence Statement 1. In obese adults, bariatric surgery produces greater weight loss and maintenance of lost weight than that produced by usual care, conventional medical treatment, lifestyle intervention, or medically supervised weight loss, and weight loss efficacy varies depending on the type of procedure and initial body weight.

- Weight loss at two to three years following a variety of surgical procedures in adults with presurgical BMI ≥30 varies from a mean of 20 to 35 percent of initial weight and a mean difference from nonsurgical comparators of 14 to 37 percent depending on procedure.

  Strength of the Evidence: High

- Mean weight loss at 10 years following a variety of bariatric surgical procedures (predominantly vertical banded gastroplasty) is approximately 16 percent of initial weight, representing a mean weight regain of 7 percent.

  Strength of the Evidence: Low

Rationale: Five studies meeting criteria for inclusion (341,381,385,394,397) assessed weight loss at 2 to 3 years after surgery. Surgical procedures included LAGB (381,394), gastric bypass (385,397), and other procedures such as vertical banded gastroplasty (397) and BPD (341). Data are not presented on SG because no studies met inclusion criteria for efficacy outcomes. All included studies showed substantial weight loss following surgery, but varied with type of procedure (see *Predictors)* as well as presurgical BMI. Only one small study meeting inclusion criteria (394) restricted patient BMI to <35; all other included studies, even those that recruited patients with a BMI as low as 30 (381), had a mean BMI of >35. Thus, there are limited data on weight loss and maintenance outcomes 2 years or more post-surgery in patients with a BMI <35.

One included study (SOS) had 10-year follow-up data (401), and found regain of 7% between 2 and 10 years post-surgery. As previously noted, this study evaluated patients undergoing a variety of bariatric procedures, including vertical banded gastroplasty, nonadjustable or adjustable gastric banding, or gastric bypass. Only a minority underwent RYGB—the most common bariatric procedure currently performed and more efficacious for weight loss than procedures such as vertical banded gastroplasty.

Evidence Statement 2. In obese adults, bariatric surgery generally results in more favorable impact on obesity-related comorbid conditions than that produced by usual care, conventional medical treatment, lifestyle intervention, or medically supervised weight loss.

- At 2 to 3 years following a variety of bariatric surgical procedures in adults with BMI ≥30 who achieve a mean weight loss of 20–35 percent, fasting glucose and insulin are reduced, and incidence of type 2 diabetes is decreased, and there is a greater likelihood of diabetes remission* among those with type 2 diabetes at baseline.

Strength of the Evidence: High

- At 10 years, incidence and prevalence of type 2 diabetes are lower in those who have undergone surgery. However, among those in whom type 2 diabetes remits after surgery, diabetes may recur over time.

Strength of the Evidence: Low

Rationale: Over the short term (2 to 3 years), several RCTs and prospective cohort studies comparing usual care, lifestyle treatment, or medical therapy to bariatric surgical procedures, including LAGB, RYGB, and BPD (341,381,385,394,397,401) for type 2 diabetes have consistently found more improvement in fasting glucose and insulin levels in individuals who had bariatric surgery,. This improvement was seen in both those without diabetes and those with an established diagnoses of type 2 diabetes. Mean percent decrease in plasma glucose at 2 years ranged from 56 percent in patients with type 2 diabetes who underwent BPD (vs. 14 percent for medical management) (341) to 7 percent in mostly non-diabetic patients who underwent LAGB (compared with <1 percent with nonsurgical weight loss treatment) (394). Among those without type 2 diabetes at baseline, the SOS study reported a reduced incidence of diabetes after undergoing a variety of surgical procedures, with 1 percent of the surgical group vs. 8 percent of the control group developing diabetes at 2 years. Data are not presented on SG because no studies met inclusion criteria for efficacy outcomes. Some studies have also reported rates of remission from type 2 diabetes. The American Diabetes Association (ADA) consensus statement defines remission as complete (normal glycemic measures of at least 1-year duration with no active pharmacologic therapy or ongoing procedures) or partial (hyperglycemia below diagnostic thresholds for diabetes of at least 1-year duration with no active pharmacologic therapy or ongoing

procedures). Prolonged remission is further defined as complete remission of at least 5 years duration (407). However, the included studies have defined diabetes remission or recovery variably. Regardless of definition, surgical treatment groups as compared to nonsurgical controls have greater 2-year remission from type 2 diabetes defined variably as: fasting plasma glucose (FPG) of <100 mg/dL and a HbA1c of <6.5 percent without pharmacologic therapy (341); FPG <126 mg/dL and HbA1c <6.2 percent without use of oral hypoglycemic agents or insulin (381); or fasting blood glucose level of <6.7 mmol/L with no anti-diabetic medications (397). Among those with type 2 diabetes, remission of diabetes lasting at least two years is reported in 72-95% in the included studies, compared with 0 to 21 percent in non-surgical comparators.

One of the studies (381) enrolled patients with a recent (within 2 years) onset of diabetes. However, another study (341) enrolled patients with "uncontrolled" diabetes (defined as HbA1C of 7 or more) and longer duration of diabetes.

Ten-year data are from the SOS study (401). To be concordant with new ADA criteria (408), diabetes remission (recovery) was defined as fasting blood glucose level of <110 mg/dL (<6.1 mmol/L) or less, corresponding to a fasting plasma glucose level of <126 mg/dL (7.0 mmol/L) with no anti-diabetic medications. Using these criteria, although 72 percent of patients with diabetes were in remission at 2 years post-surgery, only 36 percent were in remission at 10 years (compared with 13 percent in the non-surgical comparator group). Thus, long-term diabetes remission may not be durable for all patients. There was still, however, a significantly lower rate of both incidence of new cases and remission of diabetes in the surgical group compared with controls at 10 years. Only a minority, recruited later in the study, underwent RYGB., which leads to greater weight loss than than other procedures such as vertical banded gastroplasty or gastric banding. Thus, long-term results from this study may show smaller effects than those attained

with RYGB or other procedures, such as BPD, that may have metabolic effects on glycemia greater than that expected by weight loss alone (See *Predictors* for impact of type of surgical procedure on glycemic outcomes.)

Only one small study meeting inclusion criteria (394) restricted patient BMI to <35; all other included studies, even those that recruited patients with a BMI as low as 30 (381) had a mean BMI of >35. Thus, there are limited data on outcomes 2 years or more post-surgery related to glycemic control and remission of diabetes in patients with BMI <35.

In summary, bariatric surgery in adults with type 2 diabetes is more likely than usual care, medical management, or lifestyle treatment to result in improvement or diabetes remission over 2 years. There are limited data on long-term (5 years or more) durability of remission of diabetes after bariatric surgery.

***Evidence Statement 2 (continued*).** In obese adults, bariatric surgery generally results in more favorable impact on obesity-related comorbid conditions than that produced by usual care, conventional medical treatment, lifestyle intervention, or medically supervised weight loss.

- At 2 to 3 years following a variety of bariatric surgical procedures in adults with BMI ≥30 who achieve mean weight loss of 20 to 35 percent, blood pressure or use of blood pressure medication is reduced compared with nonsurgical management. Blood pressure tends to increase over time, and at 10 years post surgery, there is no difference in mean systolic blood pressure or the incidence of new cases of hypertension in those who underwent bariatric surgery compared to those who did not undergo surgery.

  Strength of the Evidence: Low

- Among obese adults with baseline hypertension, a greater percentage are in remission* at two to three years and ten years following bariatric surgery compared with nonsurgical management.

Strength of the Evidence: Low

Rationale: Some (394,397,401) but not all (341) studies showed a decrease in systolic blood pressure and/or diastolic blood pressure at 2 to 3 years or a reduction in antihypertensive medication use (381) when compared with a non-surgical group receiving standard care or lifestyle intervention. Blood pressure changes were calculated from percentiles or by subtraction from baseline when not presented in the paper as change values. Mean blood pressure reductions ranged from 6 to 26 mm Hg systolic and 1 to 14 mm Hg diastolic (vs. 0 to 21 mm Hg systolic and 0 to 9 mm Hg diastolic in non-surgical comparators. For example, in the SOS trial (397,401), mean BP fell from 144/90 at baseline to 137/84 at 2 years in the surgical group vs. 139/86 to 139/85 in controls (p-value between groups <001).

Two studies (385,397) reported higher likelihood of recovery from hypertension (397) and/or lower incidence or prevalence of hypertension in the surgical group vs. comparator group (385,397) at 2 to 3 years. In addition, the SOS study (401) reported a slightly lower diastolic blood pressure and greater rate of recovery from hypertension at 10 years, although incidence of new cases of hypertension and change in systolic blood pressure were not different between groups. Sjostrom (397) defined recovery as systolic blood pressure <160 and <95 and no antihypertensive medications at 2 years, revised to systolic blood pressure <140 or diastolic blood pressure <90 and no antihypertensive medication for the 10-year data (401). There are no standardized definitions for remission or recovery from hypertension, although the Framingham

Heart Study (409) defined remission as normotension (blood pressure below both 140 mmHg systolic and 90 mmHg diastolic) in a previously hypertensive individual without receiving antihypertensive medication, while relapse was defined as return to blood pressure medication use and/or blood pressure of at least 140/90 mmHg or death due to CVD.

Evidence Statement 2 (continued). In obese adults, bariatric surgery generally results in more favorable impact on obesity-related comorbid conditions than that produced by usual care, conventional medical treatment, lifestyle intervention, or medically supervised weight loss.

- At 2 to 3 years and 10 years following a variety of bariatric surgical procedures in adults with BMI ≥30 who achieve mean weight loss of 20 to 35 percent, serum TG levels are lower, HDL-C levels are higher, total cholesterol to HDL-C ratio is lower, and changes in TC or LDL-C levels are inconsistent, compared with nonsurgical management.

  Strength of the Evidence: Low

Rationale: Some (385,397) but not all (381,394) studies showed reductions in TC or LDL-C at 2 to 3 years after bariatric surgery compared with non-surgical management. HDL-C (381,394,397) was higher and TG lower (381,394,397) after bariatric surgery, with the SOS (397) finding a decreased incidence of low HDL-C (defined as HDL-C of <0.9 mmol/L) and hypertriglyceridemia (defined as TG ≥2.8 mmol/L) but no difference in incidence of hypercholesterolemia (defined as TC ≥6.2 mmol/L). One study (341) showed improvement from baseline in LDL-C (-65 percent) and TG (-57 percent) compared with conventional medical therapy (-21 percent AND -18 percent respectively) only among those who had undergone RYGB but not BPD. However, there was a higher HDL-C (+30 percent) compared with medical therapy (+6 percent) only in those who underwent RYGB. Mingrone (341) also found that significantly

more surgical patients "normalized" TC, TG, and HDL-C levels compared with those who received medical treatment. In those studies reporting the measure (381,394), TC to HDL-C ratio was lower at 2 years in those who underwent bariatric surgery. Ten-year data from the SOS study (401) found those who had undergone bariatric surgery had higher HDL-C and lower TG compared with matched controls receiving usual care. TC was slightly higher in the surgical group; there was no difference in incidence new cases of or recovery from hypercholesterolemia (defined as TC ≥ 201 mg/dL, 5.2 mmol/L) between groups.

Evidence Statement 2 (continued). In obese adults, bariatric surgery generally results in more favorable impact on obesity-related comorbid conditions than that produced by usual care, conventional medical treatment, lifestyle intervention, or medically supervised weight loss.

- Most measures of health-related quality of life (HRQOL) are improved at 2 and 10 years following bariatric surgery.

Strength of the Evidence: Moderate

Rationale: Three papers, representing two studies found that most measures of HRQOL in those who underwent a variety of bariatric surgical procedures improved compared with nonsurgical management controls at 2 (386,394) and 10 (387) years. O'Brien (394) found greater improvements in patients who underwent bariatric surgery compared with a nonsurgical control group in 5 of 8 physical and mental health domains of the well-validated Medical Outcomes Study 36-item short-form general health survey (SF-36), including physical function, physical role, general health, energy, and emotional role, but not in pain or mental health. The SOS measured HRQOL in multiple domains: subjective health measured by the current health scale of the general health rating index; mental well-being using the mood adjective checklist and the hospital

anxiety and depression scale; social interaction measured by the sickness impact profile, a study-specific module developed to assess obesity-related problems in everyday life; and self-assessment of eating behavior through the three factor eating questionnaire, including general health and all measures of psychosocial dysfunction. At 2 years, there were greater improvements in all measures of HRQOL in the surgical group, although there was no absolute difference between the surgical and control groups in anxiety. Amount of weight loss was correlated with improvement in HRQOL measures, and weight regain tended to be accompanied by decreased HRQOL (386). However, at 10 years, there was still a significantly better outcome in the surgical group on most measures of HRQOL, with greater improvements in current health perceptions, social interaction, obesity-related problems, and depression, but not overall mood or anxiety (387).

Evidence Statement 2 (continued). In obese adults, bariatric surgery generally results in more favorable impact on obesity-related comorbid conditions than that produced by usual care, conventional medical treatment, lifestyle intervention, or medically supervised weight loss.

- Total mortality is decreased compared with nonsurgical management at mean follow-up of 11 years after undergoing a variety of bariatric surgical procedures (predominantly vertical banded gastroplasty) in patients with mean BMI >40 who achieve a mean long-term weight loss of 16 percent.

  Strength of the Evidence: Low

Rationale: The SOS study found a reduced HR (0.76) CI (0.59 to 0.99) in subjects who underwent bariatric surgery compared with the nonsurgical comparator group (402). This was a prospective cohort study with comparators matched on a variety of biomedical, psychosocial, and

demographic factors; however, lack of randomization is a limitation. As previously noted, this study evaluated patients undergoing a variety of bariatric procedures, including vertical banded gastroplasty, nonadjustable or adjustable gastric banding, or gastric bypass. Only a minority, recruited later in the study, underwent RYGB, the most common bariatric procedure currently performed and considered more efficacious for weight loss than procedures such as vertical banded gastroplasty. Mean weight loss at 10 years ranged from 14 percent with banding to 25 percent with gastric bypass (402). In addition, bariatric surgical approaches, including increasing use of laparoscopic surgery and other medical and surgical advances, have reduced early morbidity and mortality from bariatric surgery (389). Thus, the above referenced study may represent a conservative estimate of the impact of bariatric surgery on mortality. As the SOS was not a randomized trial, it is also possible that those who underwent surgery differed in unmeasured ways from those who did not, or that current surgical approaches have different short- or -long term complications that may impact mortality. Thus, both the directionality and magnitude of the impact of bariatric surgery on total and cause-specific mortality requires additional study.

***Evidence Statement 3*.** There are insufficient data on the efficacy of bariatric surgical procedures for weight loss and maintenance or CVD risk factors two or more years post-surgery in patients with a BMI <35.

Rationale: In the current evidence review, only one small study meeting inclusion criteria (394) restricted patient BMI to ≤35; all other included studies, even those that recruited patients with a BMI as low as 30 (381) had a mean BMI of >35. Although the FDA has approved the LAGB for patients with a BMI of 30 to <35 with comorbid conditions, (410), the primary endpoint for the pivotal approval study for this indication was 12-month weight loss (411).

Thus, there are limited data on outcomes at two years or more post-surgery related to weight loss and maintenance, adverse effects, glycemic control, dyslipidemia, or blood pressure control in patients with BMI <35.

7.5.2. Component 2: Predictors—Patient Characteristics Summary Table 5.2

7.5.2.1. Predictors

The predictors component of CQ5 addresses aspects of bariatric surgery specific to different operative procedures as well as other potential predictors of outcome such as patient characteristics or provider aspects of bariatric surgery. The search criteria, as with the efficacy component, required a comparator group but not necessarily a non-surgical comparator, as well as outcomes regarding specific bariatric operative procedures. A total of 10 studies (12 articles) met these criteria and were rated as good or fair quality and are included in the summary table (340,341,378,379,381,385,391,394,395,401,402,404). The literature search included studies that address patient factors such as BMI, age, gender, or the presence of associated comorbid conditions. Several published studies have indicated patient factors may influence outcomes after bariatric surgery. One of the studies included in the predictors component addresses the outcomes following BPD among patients with or without preoperative type 2 diabetes (391). No studies met search criteria addressing provider factors such as surgeon or center experience, center designation, or protocols. The following comparative studies are included as outcome predictors: LAGB vs. no surgery (381,394); modified RYGB vs. no surgery (385); RYGB vs. LAGB (378,404); RYGB vs. LSG (340). open RYGB ; laparoscopic vs. open RYGB (395); RYGB with or without an added gastric band (379); and various procedures (the SOS trial described above (401,402)). Four of these studies (five articles) are also included in the evidence base for efficacy

(381,385,394,401,402). As for efficacy, weight loss is reported as percent loss of total baseline weight. Mean percent total weight loss was calculated when mean weight loss in pounds or kilograms or mean BMI change from baseline was reported. Comorbidity remission was as designated by the study authors.

Evidence Statement 4. Weight loss following bariatric surgery, expressed as percentage of total body weight loss, varies by procedure.

In direct comparative studies at 2 to 3 years post-surgery:

- Weight loss following gastric bypass exceeds LAGB

  Strength of the Evidence: Moderate

- Weight loss following BPD, gastric bypass, and SG are similar.

  Strength of the Evidence: Low

Included studies reporting the weight loss following LAGB, RYGB, BPD and LSG in direct comparative studies show short-term weight loss following gastric bypass exceeds LAGB. Weight loss is similar among RYGB, BPD and SG in the limited number of studies that met inclusion criteria. Two- to three-year weight loss following LAGB is reported by four studies and is somewhat variable at 15 to 23 percent. Weight loss for RYGB is robust with data from studies that is somewhat more consistent: 2- to 3-year mean weight loss of 30 to 38 percent. Two studies include a direct comparison between LAGB and RYGB (378,404); both report superior weight loss following RYGB (30 percent vs. 18 percent; 37 percent vs. 32 percent, $p<0.05$). The weight loss following gastric banding vs. RYGB comparison from the SOS is not reported in the

evidence statements, as the gastric banding procedures were done prior to the availability of the adjustable gastric band.

Two included studies report weight loss at 2 to 3 years following BPD at 34 to 38 percent (341,391). No study reporting on the duodenal switch modification of the BPD is included in the evidence base. Weight loss 3-years post-LSG was 34 percent in the single included study. Thus, weight loss at 2 to 3 years following RYGB, BPD and LSG is similar.

Weight loss ranges discussed above differ slightly from those in evidence statement 1, due to different studies being included in the evidence base for efficacy vs. predictors.

Evidence Statement 4 (continued). Weight loss following bariatric surgery, expressed as percentage of total body weight loss, varies by procedure

In direct comparative studies at 5 to 10 years postsurgery:

- Weight loss following gastric bypass exceeds LAGB

Strength of the Evidence: Low

Long-term weight loss at 5 or more years is reported in 3 included studies (378,391,401,402). Following rapid weight loss for 12 to 24 months after bariatric surgery, weight commonly stabilized or some regain of weight occurs. At 5 years postsurgery, Angrisani (378) reported 18 percent weight loss for LAGB and 30 percent for RYGB, while Marinari reported 37 percent for BPD . The SOS (401,402) reported 10-year weight loss of 13 percent for gastric banding (fixed and adjustable) and 25 percent for gastric bypass. No report of weight loss beyond 3 years is included in the present evidence base regarding LSG.

Several published studies have indicated patient factors may influence outcomes after bariatric surgery. One of the studies included in the predictors component addresses the outcomes following BPD among patients with or without preoperative type 2 diabetes (391). The presence of diabetes did not impact weight loss up to 5 years following BPD.

Evidence Statement 5. The remission of obesity-related comorbidities varies by procedure.

- Type 2 diabetes remission or improved glycemic control occurs with increasing frequency according to procedure as follows: LAGB, gastric bypass, and BPD.

Strength of the Evidence: Low

The induction of remission of type 2 diabetes is described and discussed in the efficacy component of these guidelines. None of the included studies used the recently published criteria defining diabetes remission (407), such that it is necessary to accept the authors' designation of diabetes remission. As for efficacy, diabetes remission is variably defined in these studies. Predictors of diabetes remission may be patient factors or specific bariatric surgical procedures. The included studies do not provide evidence regarding patient predictors of diabetes remission such as duration or severity of diabetes, BMI, or other factors. The number of included studies reporting diabetes remission by procedure is LAGB (2) (381,404); RYGB (4) (340,341,385,404); LSG (1) (340); and BPD (2) (341,391). The remission rates reported are: LAGB 57 to 73 percent, RYGB 75 to 86 percent, LSG 80 percent, and BPD 95 to 100 percent at 2 or more years postoperative. These data must be interpreted with caution due to the generally small numbers of diabetic subjects in each trial, variable patient populations ranging from a diagnosis of diabetes for less than 2 years (381) to poorly controlled diabetes (341), and the lack of a standard definition of diabetes remission.

Evidence Statement 5 (continued). The remission of obesity-related comorbidities varies by procedure.

- Reduction in the prevalence of hypertension is more frequent following gastric bypass than LAGB.

  Strength of the Evidence: Low

- The prevalence of dyslipidemia is lower following gastric bypass compared to LAGB.

  Strength of the Evidence: Low

The response of hypertension and dyslipidemia to bariatric surgery is discussed in the efficacy narrative. The included evidence regarding the effects of specific bariatric surgical procedures is limited, supporting the above qualitative statements but insufficient to be more specific regarding the magnitude of the effect size. The interpretation of the reported effects on dyslipidemia is further limited by a lack of clear definition of dyslipidemia (404) or variable responses of the specific lipid components (341). There was insufficient evidence to assess the impact of differential response of hypertension or dyslipidemia following BPD or SG.

7.5.3. Component 3: Complications Summary Table 5.3

7.5.3.1. Complications

The benefits of weight loss among obese adults, especially those with obesity related comorbid disease, are well described in these guidelines. Bariatric surgery produces greater weight loss and maintenance of weight loss than that produced by usual care or medically supervised weight loss. The potential benefit of weight loss for severely obese adults must, however, consider the risk of

complications in the short- or long-term. The panel determined that examination of the evidence specific to complications of bariatric surgery required expansion of the search criteria beyond those used for the efficacy and predictors of bariatric surgery. Due to the relatively low incidence of complications such as perioperative mortality (less than 1 percent), substantial sample sizes are required to accurately establish the frequency of complications and analyze associated factors. The complication evidence base therefore included those studies from the efficacy and predictors searches that included complication data (341,378) as well as those studies that met the expanded search criteria (342,343,376,380,382,383,388,389,403). The study by Agaba (377) also met the I/E criteria, thus is listed as an included study, but was not used by the panel due to concerns about the accuracy of the data reported in this study. These expanded criteria added retrospective cohort studies, before and after studies, and case series, among others. A comparator group was not required. Additional criteria for observational studies were a sample size ≥100 for studies with 10 or more years of follow-up or studies on BPD or SG procedures; ≥500 for all other observational studies. These variable search requirements were based on the limitations of the number of subjects typically reported for BPD or SG. In addition, the number of subjects reported in the studies identified in the efficacy and predictors searches were usually less than 100 with the exception of the SOS, which did not report detailed complication data by procedure. RCTs published after the search date December 31,2009 were also included if complication data was reported, and the study otherwise met criteria for inclusion (342). Conclusions regarding comparative aspects of complications following different procedures, populations, or studies require interpretation, as the population of patients undergoing specific procedures or reported in specific studies may vary. In addition, there are no standardized criteria for classifying postoperative complications. Several studies have identified predictive factors for complications.

These factors may be patient-derived, provider variables or procedure-specific (344,389,412). No provider factors such as surgeon or hospital case volume were identified as associated with complications among the included studies. The Complications Summary Table is based on 14 studies. Complications following LAGB are reported in 6 of the 14 included studies, following gastric bypass in 5 of 14, BPD in 3 of 14 and SG in 2 of 14.

7.5.3.2. Laparoscopic adjustable gastric banding

Evidence Statement 6. Perioperative (≤30 days) and longer term (>30 days) complications following bariatric surgery vary by procedure and patient-derived risk factors. When performed by an experienced surgeon, perioperative complications following laparoscopic adjustable gastric bypass are infrequent and do not tend to be life-threatening: major adverse outcomes (1.0 percent) such as deep venous thrombosis (DVT) and reoperations, and minor complications (3 percent) such as wound infection.

Strength of the Evidence: Moderate

The 30-day complication data following LAGB is derived primarily from the Longitudinal Assessment of Bariatric Surgery (LABS), a National Institutes of Health (NIH)-funded multicenter research consortium. This study and four others reported no LAGB perioperative mortality (378,380,383,389,403). The incidence of serious complications reported by LABS was 1 percent consisting of reoperation (0.8 percent) and deep venous thrombosis (0.3 percent) (389). Steffen reported severe complications among 824 patients: gas embolism with secondary brain injury and esophageal perforation. Minor perioperative complications included atelectasis or pneumonia (1.5 percent) and minor wound problems (1.2 percent).

- Longer term complications continue to occur over time and may require operative correction: misplacement of band ~3 to 4 percent, erosion of gastric wall ~1 percent, and port complication 5 to 11 percent.

- Longer term LAGB failure leading to removal of the band with or without conversion to another bariatric procedure varies from 2 to 34 percent. Inadequate weight loss is the most often reported basis for removal of band.

Strength of the Evidence: Moderate

Longer term complications following LAGB, the frequency of which varies considerably among the included studies, may be considered in three groups.

Complications requiring intra-abdominal surgery for correction include misplacement of the band on the stomach (gastric slip, approximately 3 to 4 percent) and erosion of the gastric wall by the band (approximately 1 percent) (383,403). Technical complications with the subcutaneous port used for the band adjustment that require operative correction are more frequent and variable (5 to 11 percent) but are relatively minor outpatient procedures done under local anesthesia. The wide range of reported band removal in different procedures is due primarily to variable institutional or surgeon determination that the band has failed to accomplish the desired weight loss, such that further adjustments and diet and physical activity instruction is unlikely to produce further weight loss.

7.5.3.3. Roux-en-Y Gastric Bypass

Evidence Statement 6 (continued). Perioperative (≤30 days) and longer term (>30 days) complications following bariatric surgery vary by procedure and patient-derived risk factors.

When performed by an experienced surgeon, perioperative complications following laparoscopic gastric bypass:

- Consist of a major adverse outcome in approximately 4 to 5 percent, including mortality (0.2 percent), DVT and/or pulmonary embolism (PE) (0.4 percent), and a requirement for reoperation (3 to 5 percent); and any complication, major or minor (2 to 18 percent).

Strength of the Evidence: Moderate

Prior reports (413) described complication rates that were considerably higher than those currently included here.

In the present evidence base, smaller studies (n <100) reported no mortality following RYGB (341,342,378,379). Lopez-Jimenez also reported no mortality among 559 subjects.(390) The LABS consortium reported a 0.2 percent mortality among the 2975 subjects. The incidence of reported complications varies with definitions. Following RYGB, the LABS consortium reported a 4.8 percent incidence of complications of a composite consisting of mortality, DVT, reoperation, or continued hospitalization on day 30. Other investigators reported similar complication rates. Although micronutrient deficiencies have been reported with RYGB (414), the included studies, which primarily reported short-term complications, did not provide data on rates of micronutrient or other nutritional deficiencies.

Evidence Statement 6 (continued). Perioperative (≤30 day) and longer term (>30 days) complications following bariatric surgery vary by procedure and patient-derived risk factors. When performed by an experienced surgeon, perioperative complications following laparoscopic gastric bypass:

- Are less frequent for the laparoscopic approach than for open incision.

Strength of the Evidence: Moderate

When performed by an experienced surgeon, perioperative complications following open gastric bypass:

- Consist of a major adverse outcome in approximately 8 percent, including mortality (2 percent), DVT/PE (1 percent), and reoperation (5 percent).

Strength of the Evidence: Low

Several explanations for the improved safety of RYGB over the past 10 years have been proposed. Multiple studies have reported the transition to the laparoscopic methodology from the traditional open incision to be an important contributor to improved outcome. In the present evidence base, only the LABS consortium (389), an observational trial, reported comparative outcomes. In this study, the reported mortality for open RYGB (2.1 percent) was higher than for laparoscopic RYGB (0.2 percent). The composite endpoint indicating a serious complication occurred in 7.8 percent of the open and 4.8 percent of the laparoscopic RYGB subjects. These two populations are not entirely comparable; presently, open gastric bypass is limited to patients who have a contraindication for the laparoscopic methodology. The risk profile for the open patients was consistently greater than for laparoscopic ones.

Evidence Statement 6 (continued). Perioperative (≤30-day) and longer term (>30 days) complications following bariatric surgery vary by procedure and patient-derived risk factors.

When performed by an experienced surgeon, perioperative complications following gastric bypass (laparoscopic or open):

- Are associated with extremely high BMI, inability to walk 200 feet, history of DVT/PE, and history of obstructive sleep apnea.

Strength of the Evidence: Low

Several studies (415-418) have performed correlation analyses of potential risk factors with complication outcomes following RYGB (laparoscopic or open). The present evidence base is limited to the LABS consortium analysis. This consortium found extremes of BMI, inability to walk 200 feet without an assist device, a history of DVT/PE, and a history of obstructive sleep apnea to be associated with the composite measure of adverse short-term outcomes. There is insufficient evidence to support an evidence statement regarding the mid-term and long-term complications of RYGB.

7.5.3.4. Biliopancreatic Diversion

Evidence Statement 6 (continued). Perioperative (≤30-day) and longer term (>30 days) complications following bariatric surgery vary by procedure and patient-derived risk factors.

The mortality rate for BPD was reported by two of the three included studies. When performed by an experienced surgeon, perioperative complications following BPD:

- Occur in 2 to 8 percent of cases and include mortality (<1 percent); DVT/PE (0.4 percent). The frequency of anastomotic leak, hemorrhage, and wound complication is variable.

Strength of the Evidence: Low

Mortality of 0.9 percent among 343 subjects (388) and zero mortality among 20 subjects (341) were reported. Variable complication rates from 2.2 to 7.6 percent were reported by Adami (376) (n=734) and 7.6 by Larrad-Jimenez (388) (n=343). The lack of studies with direct comparisons and the variable definitions among studies, however, precludes drawing any conclusions regarding the relative perioperative safety of BPD as opposed to RYGB.

7.5.3.5. Biliopancreatic Diversion Longer Term Complications

Evidence Statement 6 (continued). Perioperative (≤30-day) and longer term (>30 days) complications following bariatric surgery vary by procedure and patient-derived risk factors. When performed by an experienced surgeon, perioperative complications following BPD:

- 1- to 3-year complications include anemia (13 to 20 percent); deficiency of protein (0.3 to 3.0 percent), iron (17 percent), and zinc (6 percent), and neuropathy (0.4 percent). Deficiency of vitamin D and elevated parathyroid hormone may exceed 40 percent.

- When performed by open incision, include ventral hernia as high as 72 percent.

Strength of the Evidence: Low

Presumably as the result of the malabsorptive component of the BPD procedure, longer term complications following BPD have been reported to be problematic. One study reported 1- to 3-year data (376), while two studies reported 2-year data (341,388). The incidence of anemia was reported to be 11 to 20 percent, protein deficiency 0.3 to 10 percent, and neuropathy 0.4 percent. A single study (388) reported deficiencies of iron (17 percent), zinc (6 percent), magnesium (0.3 percent), and vitamin D (43 percent). Although these deficiencies can be restored with replacement therapy, operative revision to diminish the extent of malabsorption has been required

in some cases. The incidence of postoperative ventral hernia following open BPD is reported by a single study in the included evidence base (388). A clinical ventral hernia occurred in 44 percent; an additional 28 percent were found to have a subclinical ventral hernia.

7.5.3.6. Laparoscopic Sleeve Gastrectomy

Evidence Statement 6 (continued). Perioperative (≤30-day) and longer term (>30 days) complications following bariatric surgery vary by procedure and patient-derived risk factors. When performed by an experienced surgeon, perioperative complications following laparoscopic SG:

- There is insufficient evidence to establish the incidence of perioperative and longer term complications.

Despite the increasing popularity of this procedure with multiple associated publications, the present evidence from studies that met inclusion criteria was judged insufficient to establish incidence of perioperative and longer term complications following SG.

7.5.4. Summary

Bariatric surgical procedures have established efficacy for up to 2 years in producing mean weight losses of 20 percent or more and ameliorating obesity-related medical conditions including type 2 diabetes, hypertension, and dyslipidemia. Long-term (5 years or more) data are more limited, but suggest continued benefits for most risk factors despite some weight regain over time. The impact of bariatric surgery on health seems to be most strong for diabetes, with decreased incidence and increased likelihood of remission at both 2 and 10 years post-surgery. Data are less robust for hypertension or TC. Most measures of HRQOL, especially related to physical

functioning, improve with bariatric surgery, although some of these improvements wane with weight regain. Type of procedure has an impact on both degree of weight loss as well as reduction in comorbidities. In general, procedures such as gastric bypass and BPD produce greater weight loss and risk factor reduction as well as greater likelihood of remission from diabetes than less invasive procedures such as LAGB. However, these procedures also have a higher likelihood of short-term complications and adverse effects. Limited data suggest that bariatric surgery may be associated with reductions in total mortality, although further data are needed to determine both the strength of this association in larger samples as well as directionality by cause of death.

7.6 Recommendations

To provide clinicians and patients with practical guidance based on reviewed evidence, the following recommendations regarding bariatric surgery in adults ≥18 years are offered. The recommendations take into account both the demonstrated benefits of bariatric surgery as well as surgical complications and risks of various procedures.

Evidence-based recommendations for the efficacy of bariatric surgery were limited by the small number of bariatric surgical studies meeting inclusion criteria, including nonsurgical comparators plus follow-up of 2 years or more (341,348,381,384-387,392-394,396-402). In addition, in this rapidly changing field, newer and less invasive procedures are being introduced, often with limited clinical trials data. The patient populations in whom bariatric surgical procedures are performed are also being expanded, including patients with BMI in the mildly obese or even overweight range with associated comorbidities. Because of limited data, some recommendations for bariatric surgical patient or procedure selection are therefore based on expert opinion.

Recommendation 5a. Advise adults with a BMI ≥40 kg/m2 or BMI ≥35 kg/m2 with obesity-related comorbid conditions who are motivated to lose weight and who have not responded to behavioral treatment with or without pharmacotherapy with sufficient weight loss to achieve targeted health outcome goals that bariatric surgery may be an appropriate option to improve health and offer referral to an experienced bariatric surgeon for consultation and evaluation.

(Grade A, Strong); ACC/AHA COR IIa, LOE A

Rationale: Well-controlled studies comparing various bariatric surgical procedures to usual care, conventional medical treatment, lifestyle intervention, or medically supervised weight loss in obese adults have consistently found superior weight loss for up to 10 years, with 2 to 3 year weight loss in the bariatric surgical group of 20 to 35 percent (341,381,385,394,397). Although some regain is likely, mean weight loss at 10 years is still significantly greater than in nonsurgical controls (401). Short-term weight loss varies with procedure, with the LAGB having the least weight loss, and more extensive procedures, such as RYGB or BPD, producing larger weight losses (350,404). Data are limited on patient or procedural factors impacting long-term weight loss.

Consistent data from controlled studies show that bariatric surgery has a favorable impact on glycemic control, including serum or plasma glucose, insulin, and HbA1c, as well as reductions in diabetes incidence and increases in remission (341,381,385,394,397,401). These data are most striking in patients with type 2 diabetes, in whom short-term remission may occur in up to 95% at 2 years, depending on the procedure. The extent to which longer duration of diabetes impacts initial remission due to bariatric surgery is not clear. With follow-up out to 10 years, recurrence of type 2 diabetes may occur in about half of patients (401), although more data are needed to

ascertain recurrence rates with surgical procedures in use today. Patient factors (age, race/ethnicity, duration of diabetes) or procedural factors that impact long-term recurrence of diabetes remain to be elucidated. A continued benefit for bariatric surgery in prevention of development of diabetes for up to 15 years (hazard ratio 0.17) was recently reported from the Swedish study (419).

The evidence for impact of bariatric surgical procedures on blood pressure, including the development of or remission from hypertension, is less robust than for glycemic control (341,381,385,394,397,401). At 2 to 3 years, some but not all studies show reductions in blood pressure or use of blood pressure medication, remission from hypertension, or lower incidence or prevalence of hypertension in those undergoing bariatric surgery compared with nonsurgical controls. Blood pressure tends to increase over time, and although there are limited long-term data, one study showed greater remission from hypertension at 10 years but no difference in incidence of new cases of hypertension or in systolic blood pressure compared with nonsurgical controls (401).

There is evidence of a favorable impact of bariatric surgical procedures on some components of dyslipidemia at both 2 to 3 and 10 years, including higher HDL-C and lower TG (341,381,385,394,397,401). Data on TC and LDL-C are mixed, although in the few studies in which it was evaluated LDL-TC ratio improved with bariatric surgery.

In addition, this recommendation is supported by a more recent analysis from the SOS, which found benefit of bariatric surgery on incidence of CVD among patients with and without diabetes (420,421).

Bariatric surgical procedures appear to have a favorable impact on most components of HRQOL for up to 10 years (381,386,387,394). The degree of improvement appears to correlate with amount of weight loss and is attenuated with regain.

One prospective cohort study, the SOS study (402), found a lower total mortality in those who underwent bariatric surgery compared with controls at 10 years. Most patients in this study underwent vertical banded gastroplasty, which is less efficacious for weight loss and reduction in medical comorbidities than procedures such as gastric bypass (336).

Advances in bariatric surgical approaches, including increasing use of laparoscopic surgery, and improvements in perioperative care have decreased early morbidity and mortality from bariatric surgery; thus, the SOS findings may represent a conservative estimate of the impact of bariatric surgery on mortality. However, more data are needed on both the magnitude and directionality of total and cause-specific mortality.

Because bariatric surgery leads to improvements in both weight-related outcomes and many obesity-related comorbid conditions, the benefit-to-risk ratio may be favorable in appropriately selected patients at high risk for obesity-related morbidity and mortality. In the absence of RCTs to identify the optimal duration and weight loss outcomes of nonsurgical treatment prior to recommending bariatric surgery, the decision to proceed to surgery should be based on multiple factors: patient motivation, treatment adherence, operative risk, and optimization of comorbid conditions, among others. Bariatric surgery should be considered an adjunct to lifestyle treatment: behavioral treatment, appropriate dietary modification, and physical activity.

Recommendation 5b. For individuals with a BMI <35 kg/m2, there is insufficient evidence to recommend for or against undergoing bariatric surgical procedures.

(Grade N, No Recommendation For or Against)

Included studies suggest that patients with a BMI of 30 to 35 achieve more weight loss and greater improvements in CVD risk factors and quality of life than controls undergoing nonsurgical management for up to two years (381,394). However, in the current evidence review, only one small study meeting inclusion criteria (394) restricted patient BMI to ≤ 35; all other included studies, even those that recruited patients with a BMI as low as 30 (381) had a mean BMI of >35. The limited data on the impact of bariatric surgical procedures in patients with a BMI <35 on weight loss and maintenance, adverse effects, glycemic control, dyslipidemia, or blood pressure control 2 or more years post-surgery preclude recommendations for or against bariatric surgery in this population. A more recent meta-analysis of bariatric surgery in adults with a BMI <35 and diabetes or impaired glucose tolerance concuded that evidence was insufficient to reach conclustions about appropriate use of bariatric surgery in this population pening additional data on long-term outcomes and complications (422).

Recommendation 5c. Advise patients that choice of a specific bariatric surgical procedure may be affected by patient factors, including age, severity of obesity/BMI, obesity-related comorbid conditions, other operative risk factors, risk of short- and long-term complications, behavioral and psychosocial factors, and patient tolerance for risk as well as provider factors (surgeon and facility).

(Grade E, Expert Opinion); ACC/AHA COR IIb, LOE C

The evidence review evaluated bariatric surgical procedures currently in common use, including the RYGB, LAGB, SG, and BPD. Bariatric surgery is an evolving field, and new procedures and surgical techniques will continue to be implemented over time. In addition, less invasive

experimental procedures to reduce weight or improve metabolic abnormalities are also in development. As experience with newer procedures and techniques grows, early results may not be in line with longer term outcomes. Complication rates or weight loss outcomes may improve as preoperative, perioperative, and postoperative management is refined. Enhancements in patient selection may result in a better match between risk of the procedures and potential health benefits. Alternatively, a newer surgical technique or approach that appears promising initially may have unanticipated adverse effects or result in less optimal outcomes over the long term. Thus, looking at current outcomes data on predictive factors for bariatric surgical procedures provides a snapshot in time in which the only certainty is change.

Different bariatric surgical procedures are likely to have differential effects on metabolic abnormalities and CVD risk factors. For example, data suggestive of greater impact of RYGB compared with LAGB on prevention of diabetes as well as glycemic control in patients with type 2 diabetes may influence choice of procedures in this population, although more data are needed on long-term durability of diabetes remission. Recent data suggest that factors such as baseline hyperinsulinemia or dysglyceia may be more important than initial BMI in determining health benefits from bariatric surgery (423), although additional research is needed, particularly in populations with BMI <35. Behavioral predictors of short- and long-term bariatric surgical outcomes are also limited and insufficient to determine choice of procedure at present. Emerging data, such as a potential association of RYGB with postoperative problem alcohol use (424,425) and a possible increased risk of suicide or accidental death (426), emphasize the rapidly evolving knowledge in this field and the need for flexibility as our knowledge base increases.

Short- and long-term adverse effects of bariatric surgery are also important considerations when choosing to undergo surgery as well as which procedure will offer the most favorable benefit to

risk ratio. More extensive procedures also entail greater risk, including perioperative morbidity and mortality, albeit with the potential for increased weight loss and resolution of comorbidities.

There were insufficient data in the literature reviewed to determine the impact of factors such as surgeon or hospital volume on outcomes. However, most of the studies reviewed were conducted in high-volume academic medical centers with experienced bariatric surgeons. It is reasonable to consider factors such as surgeon and hospital bariatric surgical volume and experience, as well as experience with managing the surgical approach being considered, when choosing a surgeon or hospital.

In summary, determining which procedure will provide the greatest likelihood of a favorable outcome is an individual decision for each patient and provider. Patient factors, including underlying medical conditions; initial BMI; behavioral and psychosocial factors; social support; and tolerance for risk; the experience of both the surgeon and hospital; availability of pre- and postoperative care; and procedural differences in short- and long-term benefits and adverse outcomes are all reasonable to consider when choosing whether to undergo bariatric surgery, which procedure to undergo, and where and by whom the surgery should be performed.

7.7 Gaps in Evidence and Future Research Needs

For patients with obesity who have obesity-related comorbid conditions or who are at high risk for their development, bariatric surgery offers the possibility of meaningful health benefits, albeit with significant risks. The potential for prevention or remission of diabetes, better control of CVD risk factors, improvement in quality of life and possibly decreased mortality, underscores the need for research that can better characterize those patients who are most likely to benefit from and least likely to suffer adverse consequences from bariatric surgical procedures. There is a need to

understand which surgical procedures are best applied to different populations, based on factors such as presence and duration of comorbid conditions, age, sex, race/ethnicity, degree and duration of obesity, underlying genetic etiologies, and psychosocial or behavioral characteristics. Obtaining these data will require large and well-designed experimental, quasi-experimental, and observational studies. The panel identified the following priority questions for research focus:

1. What are the preoperative, perioperative, and postoperative patient and procedure characteristics that best predict successful prevention or remission of Type 2 diabetes both short-term and long-term?

2. What are the complications and adverse effects of various bariatric surgical procedures, both short- and long-term? Which patient or practitioner factors predict such complications?

3. What is the long-term impact of bariatric surgical procedures on CVD, all-cause, and cause specific mortality, compared with nonsurgical treatment of obesity or its comorbidities? Does this vary by type of procedure or by underlying comorbid condition (e.g., type 2 diabetes, prior CVD)?

4. Which health effects result from surgically induced metabolic alterations rather than or in addition to weight loss?

5. What is the long-term impact of bariatric surgical procedures on healthcare utilization and costs?

6. What is the impact of bariatric surgical procedures on non-CVD or diabetes outcomes, including but not limited to musculoskeletal disease, pulmonary disease, liver disease, cancers,

reproductive outcomes (including pregnancy), sleep disorders, and psychosocial outcomes such as substance use disorders or depression?

7. What is the impact of preoperative patient factors, including but not limited to insulin resistance, genetic abnormalities and psychosocial and behavioral variables such as binge eating, in predicting short and longer-term outcomes? Do any of these factors moderate the relationship between weight loss and resolution of comorbidities?

8. What is the long-term impact of bariatric surgical procedures on weight loss and maintenance, CVD risk factors and incidence, type 2 diabetes incidence or remission, other obesity-related morbidity, and mortality in patients with a BMI <35?

The panel members also recognize that the evidence that formed the basis for these recommendations came primarily from studies conducted within academic medical centers. There is a need for studies evaluating the impact of bariatric surgery in non-university hospital and clinical settings, which may be more reflective of real-world medical practices.

APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (RELEVANT)—2013 ACCF/AHA GUIDELINE FOR THE MANAGEMENT OF OVERWEIGHT AND OBESITY IN ADULTS

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/ Principal	Personal Research	Expert Witness
Michael D. Jensen *(Co-Chair)*	Mayo Clinic Endocrine Research Unit—Professor of Medicine, Endocrinology, Metabolism, Diabetes, Nutrition, and Internal Medicine Division	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 •Eisai •Novo Nordisk •Vivus	**2013** None	**2013** None	**2013** None	**2013** None
Donna H. Ryan *(Co-Chair)*	Pennington Biomedical Research Center—Associate Executive Director for Clinical Research	**2008-2012** •Alere Wellbeing •Amylin •Arena Pharmaceuticals •Eisai •Novo Nordisk •Nutrisystem •Orexigen •Takeda •Vivus	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 •Arena Pharmaceuticals •Eisai •Novo Nordisk •Takeda •Vivus	**2013** None	**2013** •Scientific Intake	**2013** None	**2013** None
Caroline M. Apovian	Boston Medical Center— Professor of Medicine and Pediatrics; Center for Nutrition and Weight Management—Director	**2008-2012** •Amylin •Arena Pharmaceuticals •Johnson &Johnson •Merck •Nutrisystem •Orexigen •Sanofi-aventis •Zafgen	**2008-2012** None	**2008-2012** None	**2008-2012** •Amylin •Dr. Robert C. and Veronica Atkins Foundation •Eli Lilly •MetaProteomics •Orexegin •Pfizer •Sanofi-aventis	**2008-2012** None
		2013 •Abbott Nutrition	**2013** None	**2013** None	**2013** •Amylin† •Aspire Bariatrics†	**2013** None

		• Allergan • Amylin • Arena Pharmaceuticals • GI Dynamics • Johnson &Johnson • Merck • Novo Nordisk • NutriSystem • Orexigen Therapeutics • Pfizer • Sanofi-Aventis • Zafgen			• Dr. Robert C. and Veronica Atkins Foundation† • Eli Lilly† • GI Dynamics† • GlaxoSmithKline • MetaProteomics • Orexigen Therapeutics† • Pfizer† • Sanofi-aventis	
Jamy D. Ard	Wake Forest University—Assistant Professor of Epidemiology and Prevention; Weight Management Center—Co-Director	**2008-2012** • Arena Pharmaceuticals • Nestle Healthcare Nutrition • OPTIFAST Division • Vivus	**2008-2012** None	**2008-2012** None	**2008-2012** • OPTIFAST—Medical Director	**2008-2012** None
		2013 • Eisai • Nestle Healthcare Nutrition • OPTIFAST Division • Vivus	**2013** None	**2013** None	**2013** None	**2013** None
Anthony G. Comuzzie	Southwest Foundation for Biomedical Research—Scientist, Department of Genetics	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** None	**2013** None
Karen A. Donato	NHLBI—Acting Director, Division for the Application of Research Discoveries	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** None	**2013** None
Frank B. Hu	Harvard University School of Public Health—Professor, Nutrition and Epidemiology	**2008-2012** • Amgen • Novo Nordisk • Nutrition Impact • Unilever	**2008-2012** None	**2008-2012** None	**2008-2012** • Merck	**2008-2012** None
		2013 • Bunge	**2013** None	**2013** None	**2013** • Merck	**2013** None
Van S. Hubbard *(Ex-officio)*	NIDDK—Director, NIH Division of Nutrition Research Coordination	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** None	**2013** None

John M. Jakicic	University of Pittsburgh—Professor and Chair, Physical Activity and Weight Management Research Center	**2008-2012** • Alere Wellbeing • Jenny Craig • Nestle Nutrition	**2008-2012** None	**2008-2012** None	**2008-2012** • BodyMedia—PI	**2008-2012** None
		2013 • Calorie Control Council	**2013** None	**2013** None	**2013** • BodyMedia—PI	**2013** None
Robert F. Kushner	Northwestern University Feinberg School of Medicine—Professor, Division of General Internal Medicine	**2008-2012** • Abbott • Amylin • Novo Nordisk • Orexigen • Retrofit • Sanofi-aventis • Zafgen	**2008-2012** None	**2008-2012** None	**2008-2012** • Novo Nordisk • Weight Watchers	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** • Aspire Bariatrics	**2013** None
Catherine Loria *(Ex-officio)*	NHLBI —Nutritional Epidemiologist	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** None	**2013** None
Barbara E. Millen	Boston Nutrition Foundation—Chairman; Millennium Prevention—President	**2008-2012** None	**2008-2012** None	**2008-2012** • Boston Nutrition Foundation * • Millennium Prevention *	**2008-2012** None	**2008-2012** None
		2013 None	**2013** None	**2013** • Boston Nutrition Foundation * • Millennium Prevention *	**2013:** None	**2013:** None
Cathy A. Nonas	NYC Dept of Health and Mental Hygiene—Senior Advisor, Bureau for Chronic Disease Prevention and Tobacco Control	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** None	**2013** None
F. Xavier Pi-Sunyer	Columbia University—Professor of Medicine, College of Physicians and Surgeons	**2008-2012** • Amylin • AstraZeneca • Eisai • Eli Lilly • McNeil • Novo Nordisk • Weight	**2008-2012** None	**2008-2012** None	**2008-2012** • Arena Pharmaceuticals • Novo Nordisk • Orexigen • Roche • Vivus	**2008-2012** None

		Watchers • Zafgen				
		2013 • AstraZeneca • Eisai • McNeil • Novo Nordisk • Vivus • Weight Watchers • Zafgen	**2013** None	**2013** None	**2013** • Novo Nordisk	**2013** None
June Stevens	University of North Carolina at Chapel Hill—Chair, Department of Nutrition; Department of Epidemiology Schools of Public Health and Medicine—Professor	**2008-2012** • CMeducation Resources	**2008-2012** None	**2008-2012** None	**2008-2012** • Dannon • PepsiCo, Gatorade • Sanofi-aventis • Wyeth Nutrition	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** • PepsiCo, Gatorade • Sanofi-aventis • Wyeth Nutrition	**2013** None
Victor J. Stevens	Kaiser Permanente Center for Health Research—Assistant Director, Epidemiology and Disease Prevention	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** None	**2013** None
Thomas A. Wadden	Perelman School of Medicine at the University of Pennsylvania—Professor of Psychology in Psychiatry; Center for Weight and Eating Disorders—Director	**2008-2012** • Alere Wellbeing • BMIQ • Novo Nordisk • Orexigen • Vivus	**2008-2012** None	**2008-2012** None	**2008-2012** • Novo Nordisk • Nutrisystem • Weight Watchers	**2008-2012** None
		2013 • Novo Nordisk • Orexigen	**2013** None	**2013** None	**2013** None	**2013** None
Bruce M. Wolfe	Oregon Health and Science University—Professor of Surgery	**2008-2012** • Crospon • EnteroMedics	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 • EnteroMedics	**2013** None	**2013** None	**2013** None	**2013** None
Susan Z. Yanovski *(Ex-officio)*	NIDDK—Co-Director, Office of Obesity Research, Division of Digestive Diseases and Nutrition	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None	**2008-2012** None
		2013 None	**2013** None	**2013** None	**2013** None	**2013** None

This table reflects the relevant healthcare-related relationships of authors with industry and other entities provided by the panels during the document development process (2008-2012). Both compensated and uncompensated relationships are reported. These relationships were reviewed and updated in conjunction with all meetings and conference calls of the Expert Panel during the document development process. Authors with relevant relationships during the document development process recused themselves from voting on recommendations relevant to their relationships. In the spirit of full transparency, the ACC and AHA asked Expert Panel members to provide updates and approve the final version of this table, which includes current relevant relationships (2013).

To review the NHLBI and ACC/AHA's current comprehensive policies for managing relationships with industry and other

entities, please refer to http://www.nhlbi.nih.gov/guidelines/cvd_adult/coi-rwi_policy.htm and http://www.cardiosource.org/Science-And-Quality/Practice-Guidelines-and-Quality-Standards/Relationships-With-Industry-Policy.aspx.

Per ACC/AHA policy:
A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$10,000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

*Significant relationship.
†No financial benefit.

NHLBI indicates National Heart, Lung, and Blood Institute; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases; and PI, principal investigator.

APPENDIX 2: DETAILED METHODS APPLYING TO ALL CRITICAL QUESTIONS

Description of How Panel Members Were Selected

The NHLBI initiated a public call for nominations for panel membership to ensure adequate representation of key specialties and stakeholders and appropriate expertise among expert panel and work group members. A nomination form was posted on the NHLBI website for several weeks and was also distributed to a Guidelines Leadership Group, which had given advice to the NHLBI on its guideline efforts. Information from nomination forms, including contact information and areas of clinical and research expertise, was entered into a database.

After closing the call for nominations, the NHLBI staff reviewed the database and selected a potential chair and co-chair for each expert panel and work group. The potential chairs and co-chairs provided to the NHLBI Conflict of Interest (COI) disclosures and a copy of their curriculum vitae. The NHLBI Ethics Office reviewed the COI disclosures and cleared or rejected individuals being considered as chairs and co-chairs. Then, the selected chairs were formed into a Guidelines Executive Committee.

The NHLBI received 440 nominations for potential panel members with appropriate expertise for the task. Panel selection focused on creating a diverse and balanced composition of members. Panel members were selected based on their expertise in the specific topic area (e.g., high blood pressure, high blood cholesterol, and obesity) as well as in specific disciplines: primary care, nursing, pharmacology, nutrition, exercise, behavioral science, epidemiology, clinical trials, research methodology, evidence-based medicine, guideline development, guideline implementation, systems of care, and informatics. The panels also include, as voting ex officio

members, senior scientific staff from the NHLBI and other NIH Institutes who are recognized experts in the topics being considered.

Description of How Panels Developed and Prioritized Critical Questions

After panels were convened, members were invited to submit topic areas or questions for systematic review. Members were asked to identify topics of the greatest relevance and impact for the target audience of the guideline: PCPs.

Over several months, panel members submitted proposed questions and topic areas. The number of critical questions (CQs) was scoped and then prioritized based on resource constraints. After group discussion, panel members ranked priority CQs through collaborative dialogue and voting. The rationale for each priority CQ is addressed in the main report.

With support from the methodologist and systematic review team, panel members formulated priority CQs. They also developed inclusion and exclusion criteria (I/E criteria) to ensure that criteria were clear and precise and could be applied consistently across literature identified in the search. Using I/E criteria, the PICOTS format (patient population, intervention/exposure, comparison group, outcome, timing, and setting) were defined and formatted. PICOTS is a framework for a structured research question and includes the following components in the CQ statement or in the question's I/E criteria:

P person, population

I intervention, exposure

C comparator

O outcome

T timing

S setting

I/E criteria define the parameters for selecting literature for a particular CQ. Panel members submitted final CQs and criteria to the literature search team to develop a search strategy. To gather the body of evidence for each CQ, they used two approaches: 1) to conduct a de novo literature search and review of all individual studies that met a CQ's I/E criteria. This approach was used for most critical questions; 2) to focus the literature search on existing SRs and MAs, which summarized a broad range of the scientific literature. Several CQs across panels and work groups used this approach, which was developed in response to resource limitations for the project overall. Additional information on SRs and MA is provided in the following section.

Literature Search Infrastructure, Search Strategy Development, and Validation

The literature search was performed using an integrated suite of search engines that explored a central repository of citations and full text journal articles. The central repository, search engines, search results, and web-based modules for literature screening and data abstraction were integrated within a technology platform called the Virtual Collaborative Workspace (VCW). The VCW was custom-developed for the NHLBI guidelines initiative.

The central repository consisted of 1.9 million citations and 71,000 full text articles related to cardiovascular disease (CVD) risk reduction. Citations were acquired from PubMed, Embase, Cinahl, Cochrane, PsycInfo, Wilson Science, and Biological Abstracts databases. Literature searches were conducted using a collection of search engines including: TeraText, Content Analyst, and Collexis, and Lucene. These engines were used for executing search strategies; Lucene was used in correlating the search with screening results.

For every CQ, a literature search and screening were conducted according to the understanding of the question and the I/E criteria that provided specific characteristics of studies relevant to the question. Criteria were framed in the PICOTS format. Using Boolean and conceptual queries, the question and PICOTS components were translated into a search strategy.

A Boolean query encodes I/E rules. It grants access to the maximum quantity of citations, which are then analyzed by text analytics tools and ranked to produce a selection for literature screening. Two independent reviewers conducted the screening in the VCW's web-based module. Boolean queries select citations by matching words in titles and abstracts, as well as Medical Subject Headings (MeSH) and subheadings. The number of citations resulting from Boolean queries has ranged from a few hundred to several thousand depending on the question. The text analytics tools suite included:

- A natural language processing module for automated extraction of data elements to support the application of I/E criteria. Data elements that were frequently extracted and used were study size and intervention follow-up period.

- Content Analyst for automatically expanding vocabulary of queries, conceptual retrieval, and conceptual clustering. The conceptual query engine employed in Content Analyst leverages

word frequency features and co-occurrence in similar contexts to index, select and rank results. The indexing uses the Singular Value Decomposition (SVD) algebraic method.

- TeraText for ranking search results and a variety of fast operations on the inverted index.

Search strategy development was intertwined with the results of literature screening, which provided feedback on search quality and context. Screened literature was categorized into two subsets: relevant or not relevant to the question. Next, results were analyzed to determine the characteristics of relevant versus not relevant citations. Additional keywords and MeSH terms were used to expand or contract the scope of the query as driven by characteristics of relevant citations. If a revised search strategy produced more citations than the original strategy, the new batch of citations was added for literature review. The search strategy refinement/literature review cycle was repeated until all citations covered by the most recent Boolean query had been screened.

Each search strategy was developed and implemented in the VCW. The methodologist and panel members reviewed the search strategy, which was available for viewing and printing at any time by panel members and staff collaborating on the systematic review. The search strategy was available for execution and supplying literature updates until the literature search and screening cut-off date.

An independent methodology team validated the search strategies for a sample of questions. As part of this validation process, the methodology team developed and executed a separate search strategy and screened a random sample of citations against I/E criteria. Then, these results were compared to the search and screening results developed by the systematic review team. Based on the validation process, the searches were considered appropriate. In addition, studies identified in

SRs and MA were cross-checked against a CQ's list of studies included in the evidence base to ensure completeness of the search strategy.

Process for Literature Review

Using results of the search strategy, criteria were applied to screen literature for inclusion or exclusion in the evidence base for the CQ. I/E criteria address the parameters in the PICOTS framework and determine what types of studies are eligible and appropriate to answer the CQ. When appropriate, the panel members added (with guidance from the methodology team) I/E criteria, such as sample size restrictions, to fit the context of the CQ. To enhance the quality of the abstracted literature, these criteria were applied uniformly (by the systematic review and methodology teams) within a given question.

Pilot Literature Screening Mode

In the Pilot Literature Screening Mode, two reviewers independently screened the first 50 titles/abstracts in the search strategy results by applying I/E criteria. Reviewers voted to include or exclude the publication for full text review. To ensure I/E criteria were applied consistently, they compared their results. Discrepancies in votes were discussed, and clarification on criteria was sought from the panel when appropriate. For example, if criteria were not specific enough to be clearly applied to include or exclude a citation, they sought guidance to more explicitly word criteria.

During this phase, reviewers provided feedback to the literature search team about the relevance of search strategy results; the team used this feedback to further refine and optimize the search.

Phase 1: Title and Abstract Screening Phase

After completing the Pilot Mode phase, two reviewers independently screened search results at the title and abstract level by applying I/E criteria. Reviewers voted to include or exclude the publication for full text review.

When at least one reviewer voted to include a publication based on the title and abstract review, the publication advanced to Phase 2, Full Text Screening. When both reviewers voted to exclude a publication, then it was excluded and not reviewed further. These citations are maintained in the VCW and marked as "excluded at title/abstract phase."

Phase 2: Full Text Screening Phase

In Phase 2, two reviewers independently applied I/E criteria to the full text article and voted "include," "exclude," or "undecided." The reviewer specified the rationale for exclusion (i.e., population, intervention, etc.) in this phase.

Articles in which both reviewers voted "include" were moved to the Include List. Similarly, articles in which both reviewers voted to exclude were moved to the Exclude List. These citations were maintained in the VCW and identified as "excluded at the full article phase," and the rationale for exclusion was noted. Only articles with discrepant votes (i.e., one include and one undecided, one include and one exclude, and one exclude and one undecided.) advanced to Phase 3.

Phase 3: Resolution and Consultation Phase

In this phase, reviewers discussed their discrepant votes for include, exclude, or undecided and cited the relevant criteria for their decision. The two reviewers attempted to achieve consensus through collaborative discussion. If the reviewers could not reach consensus, they consulted the methodologist. If they were still unable to reach a consensus, they consulted the panel; however, the methodologist had the final decision. The final disposition of the article (include or exclude) was recorded in the VCW along with comments from the adjudication process.

Similar to search strategies being posted and available for viewing on the VCW, all citations screened for a CQ were maintained in the VCW with their reviewer voting status and collected comments.

Description of Methods for Quality Assessment of Individual Studies

Articles meeting the criteria after the three-phase review of the literature review process were then rated for quality. Each study design used a separate quality rating tools.

Design of the Quality Assessment Tools

Six quality assessment tools, developed by the NHLBI and the methodology team, were used to evaluate the quality of individual studies. The tools were based on quality assessment methods, concepts, and other tools, including those developed by researchers in Evidence-Based Practice Centers, The Cochrane Collaborative, the U.S. Preventive Services Task Force, the National Health Service Centre for Reviews and Dissemination, consulting epidemiologists, and others

working in evidence-based medicine. The methodology team and the NHLBI staff adapted these tools to assess the quality of the studies.

These tools were designed to help reviewers focus on concepts key to evaluating the internal validity of a study. The tools were not designed to provide a list of factors comprising a numeric score; instead, they were specific to individual types of study designs. They are described in more detail below.

The tools include items reviewers needed to evaluate studies: potential flaws in study methods or implementation: sources of bias (e.g., patient selection, performance, attrition, detection), confounding, study power, the strength of causality in the association between interventions and outcomes, and other factors. Reviewers selected "yes," "no," or "cannot determine (CD)/not reported (NR)/not applicable (NA)" in response to each item on the tool. For each item where "no" was checked, reviewers considered the potential risk of bias that may have been introduced by that flaw in the study design or implementation. CD and NR were also noted as representing potential flaws.

A detailed guidance document, developed by the methodology team and NHLBI, accompanies each of the six quality assessment tools. These documents, specific to each tool, provide more descriptions and examples on how to apply the items, as well as justifications for including the item. For some items, examples were provided to clarify the intent of the question and the appropriate rater response. The six quality assessment tools are depicted in Exhibits A–1 to A–6 .

Significance of the Quality Ratings of Good, Fair, or Poor

Using the quality assessment tools, reviewers rated each study as "good," "fair," or "poor" quality. In turn, they used the ratings on different items in the tool to assess the risk of bias in the study due to flaws in study design or implementation.

In general terms, a good study has the least risk of bias, so results are considered valid. A fair study is susceptible to some bias deemed not sufficient to invalidate its results. The fair quality category is likely to be broad, so studies with this rating will vary in their strengths and weaknesses.

A poor rating indicates significant risk of bias. Studies rated poor were excluded from the body of evidence to be considered for each CQ, except when there was no other evidence available. Then poor quality studies could be considered.

Training for the Application of Quality Assessment Tools

The methodology team conducted a series of training sessions on using four of the quality assessment tools. Initial training consisted of 2–day, in-person training sessions. Reviewers trained in the quality rating were Masters or PhD level staff with a background in public health or health sciences. Sessions included training in the following areas: identifying the correct study designs, the theory behind evidence-based research and quality assessment, explanations and rationales for the items in each tool, and methods for achieving overall judgments regarding quality ratings of good, fair, or poor. Participants practiced evaluating multiple articles, both with the instructors and during group work. They also practiced referring to related articles on study methods. Following in-person training sessions, the methodology team assigned several articles

with pertinent study designs to test the abilities of each reviewer. The methodology team asked reviewers to individually identify the correct study design, complete the appropriate quality assessment tool, and submit it to the team for grading against a methodologist-developed key. Next, the reviewers participated in a second round of training sessions, conducted via telephone, to review results and resolve any remaining misinterpretations. Depending on evaluation results, sometimes the methodology team convened a third round of exercises and training sessions.

The quality assessment tools for the before-after and case series studies were used only for Obesity Panel's CQ 5 on bariatric surgery interventions. This CQ included those types of study designs and related issues specific to this surgical intervention. As a result, a formal training program on these assessment tools was not conducted; instead, reviewers for CQ5 received individual training.

Quality Assessment Process

The systematic review team or methodology team rated each article that met CQ's inclusion criteria. Two reviewers independently rated the quality of each article, using the appropriate tool. If ratings differed, the reviewers discussed the article to reach consensus. If they were unable to reach consensus, a methodologist judged the quality.

Two methodologists independently rated SRs and MA. If ratings differed, reviewers discussed the article to try to reach consensus. If they were unable to reach consensus, a third methodologist judged the quality.

After they received the initial rating, panel members could appeal the rating of a particular study or publication. However, the methodology team, not the panel members, made the final decision on quality ratings for objectivity.

Quality Assessment Tool for Controlled Intervention Studies

Exhibit A–1 shows the quality assessment tool for controlled intervention studies along with guidance for that tool (see below). The methodology team and NHLBI developed this tool based in part on criteria from the Agency for Healthcare Research and Quality's (AHRQ) Evidence-based Practice Centers (EPCs), the U.S. Preventive Services Task Force, and the National Health Service Centre for Reviews and Dissemination.

This tool addresses 14 elements of quality assessment: randomization and allocation concealment, similarity of compared groups at baseline, use of intention-to-treat (ITT) analysis (i.e., analysis of all randomized patients even if some were lost to follow-up), adequacy of blinding, overall percentage of subjects lost to follow-up, differential rates of loss to follow-up between the intervention and control groups, and other factors.

Guidance for Assessing the Quality of Controlled Intervention Studies

The following questions correspond to those listed in the companion guidance document for quality assessment of controlled intervention studies.

Exhibit A–1. Quality Assessment of Controlled Intervention Studies

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?			
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?			
3. Was the treatment allocation concealed (so that assignments could not be predicted)?			
4. Were study participants and providers blinded to treatment group assignment?			

Criteria	Yes	No	Other (CD, NR, NA)*
5. Were the people assessing the outcomes blinded to the participants' group assignments?			
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?			
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?			
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?			
9. Was there high adherence to the intervention protocols for each treatment group?			
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?			
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?			
12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?			
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?			
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an ITT analysis?			
Quality Rating (Good, Fair, Poor) (see guidance)			
Rater #1 initials:	**Rater #2 initials:**		
Additional Comments (If POOR, please state why):			

*CD: cannot determine; NA: not applicable; NR: not reported

Question 1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?

A study does not satisfy quality criteria as randomized simply because the authors call it randomized; however, it is a first step in determining if a study is randomized.

Questions 2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?

Randomization is adequate if it occurred according to the play of chance (e.g., computer generated sequence in more recent studies, or random number table in older studies).

Randomization is inadequate if there is a pre-set plan (e.g., alternation where every other subject is assigned to treatment arm or another method of allocation is used, such as time or day of hospital admission or clinic visit, zip code, phone number, etc.). In fact, this is not randomization at all—it is another method of assignment to groups. If assignment is not by the play of chance, the answer to this question is "NO."

There may be some tricky scenarios that will need to be read carefully and considered for the role of chance in assignment. For example, this may be the case with group-randomized trials (GRTs), which evaluate interventions at the group level. Sites are randomized to receive treatment or no treatment, so all individuals at the site are thereby assigned to a treatment group. GRTs can be truly randomized, but often are "quasi-experimental" studies with comparison groups rather than true control groups.

Question 3. Was the treatment allocation concealed (so that assignments could not be predicted)?

Allocation concealment: This means that one does not know in advance, or cannot guess accurately, to what group the next person eligible for randomization will be assigned. Allocation concealment methods include sequentially numbered opaque sealed envelopes, numbered or

coded containers, central randomization by a coordinating center, computer generated randomization that is not revealed ahead of time, and others.

Questions 4. Were study participants and health care practitioners blinded to treatment group assignment? and Question 5. Were the individuals assessing the outcomes blinded to the participants' group assignments?

Blinding means that one does not know to which group – intervention or control – the participant is assigned. It is sometimes called "masking." The reviewer assessed whether individuals completing the following tasks were blinded to the treatment assignment: assessing the primary outcome(s) for the study (e.g., taking the measurements, examining medical records to determine type of event as in an adjudication committee, etc.); receiving the intervention (e.g., the patient or volunteer participant); and providing the intervention (e.g., the physician, nurse, or behavioral interventionist).

Generally placebo-controlled medication studies are blinded to patient, provider, and outcome assessors; behavioral or lifestyle studies may be blinded only to outcome assessors. Sometimes the individual providing the intervention is the same person performing the outcome assessment. This was noted when it occurred.

Question 6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?

This question relates to whether the intervention and control groups have similar characteristics on average. The point of randomized trials is to compare the effects of an intervention between similar groups. When reviewers abstracted baseline characteristics, they noted when there was a

significant difference between groups. Baseline characteristics for intervention groups are usually presented in a table in the article (often Table 1).

Groups can differ at baseline without raising red flags if: (1) the differences would not be expected to have any bearing on the interventions and outcomes; or (2) the differences are not statistically significant. When concerned about baseline difference in groups, reviewers recorded them in the comments section and considered them in their overall determination of the study quality.

Questions 7. Was the overall drop-out rate from the study at endpoint 20 percent or lower of the number allocated to treatment? and Question 8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?

Dropouts in a clinical trial are individuals for whom there are no endpoint measurements, often because they dropped out of the study and were lost to follow-up.

Generally, an acceptable overall dropout rate is considered 20 percent or less of participants who were randomized/allocated into each group. An acceptable differential dropout rate is an absolute difference between groups of 15 percentage points at most (calculated by subtracting the dropout rate of one group minus the drop-out rate of the other group). However, these are general rates. Higher overall dropout rates may be acceptable. In a systematic review on comparative efficacy of antidepressants, a cap of 20 percent for overall dropout is reasonable. On the other hand, in a study on joint space narrowing for targeted immune modulators (TIMs), the cap could be higher and still be considered an overall acceptable dropout rate. Studies comparing TIMs for this outcome will be of longer duration, meaning dropouts are more likely. The panels for the NHLBI SRs may set different levels of dropout caps.

Conversely, differential dropout rates are not flexible; there should be a 15 percent cap. If there is a differential drop-out rate of 15 percent or higher between arms, then there is a serious potential for bias. This constitutes a fatal flaw, resulting in a poor quality rating for the study.

Question 9. Was there high adherence to the intervention protocols for each treatment group?

Examples of study situations in which protocol adherence is questionable or was not met include the following:

- Group 1 was assigned to 10 mg/day of Drug A, but did most of the individuals in this group take 10 mg/day of drug A?
- A study evaluated the difference between a 30-lb. weight loss and a 10-lb. weight loss on specific clinical outcomes (e.g., heart attacks), in which the 30-lb. weight loss group did not achieve its intended weight loss target.
- Did a large percentage of participants assigned to one group "cross over" and receive the intervention provided to the other group?
- One group that was assigned to receive a particular drug at a particular dose had a large percentage of participants who did not end up taking the drug or the dose as designed in the protocol.

Question 10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?

Changes that occur in the study outcomes being assessed should be attributable to the interventions being compared in the study. When study participants receive interventions that are not part of the study protocol and could affect the outcomes being assessed, and they receive these interventions differentially, there is cause for concern. These interventions could bias results. This scenario depicts how bias can occur. In a study comparing two different dietary interventions on serum cholesterol, one group had a significantly higher percentage of participants taking statin drugs than the others groups. In this situation, it would be impossible to know if a difference in outcome was due to the dietary intervention or the drugs.

Question 11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?

Knowing the accuracy and reliability of tools or methods is essential. For example, were they validated, or are they objective? This is important as it indicates the confidence you can have in the reported outcomes. Perhaps even more important is ascertaining that outcomes were assessed in the same manner within and between groups. One example of differing methods is self-report of dietary salt intake vs. urine testing for sodium content (a more reliable and valid assessment method). Another example is using blood pressures measurements taken by practitioners who use their usual methods vs. using blood pressure measurements done by individuals trained in a standard approach. Such an approach may include using the same instrument each time and taking an individual's blood pressure multiple times. In each of these cases, the answer to this assessment question would be "NO" for the former scenario and "YES" for the latter one. In addition, a study in which an intervention group was seen more frequently than the control group, enabling more opportunities to report clinical events, would not be considered reliable and valid.

Question 12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80 percent power?

Generally, a study's methods section addresses the sample size needed to detect differences in primary outcomes. The current standard is at least 80 percent power to detect a clinically relevant difference in an outcome using a two-sided alpha of 0.05. Often, however, older studies will not report on power.

Question 13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?

Investigators should prespecify outcomes reported in a study for hypothesis testing—the reason for conducting a randomized controlled trial (RCT). Without prespecified outcomes, the study may be reporting ad hoc analyses; simply looking for differences supporting desired findings. Investigators also should prespecify subgroups being examined. Most RCTs conduct numerous post hoc analyses as a way of exploring findings and generating additional hypotheses. The intent of this question is to give more weight to reports that are not simply exploratory in nature.

Question 14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?

Intention-to-treat (ITT) means everybody who was randomized is analyzed according to the original group to which they are assigned. This is an extremely important concept because conducting an ITT analysis preserves the whole reason for doing a randomized trial; that is, to compare groups that differ only in the intervention being tested. When the ITT philosophy is not followed, groups being compared may no longer be the same. In this situation, the study would

likely be rated "poor." However, if an investigator used another type of analysis that could be viewed as valid, this would be explained in the "other" box on the quality assessment form.

Some researchers use a completers analysis (an analysis of only the participants who completed the intervention and the study), which introduces significant potential for bias. Characteristics of participants who do not complete the study are unlikely to differ from those who do complete the study. The likely impact of participants withdrawing from a study treatment must be considered carefully. ITT analysis provides a more conservative (potentially less biased) estimate of effectiveness.

General Guidance for Determining the Overall Quality Rating of Controlled Intervention Trials

The questions on the assessment tool were designed to help reviewers focus on the key concepts for evaluating a study's internal validity, instead of being used as a list from which to add up items to judge a study's quality.

Internal validity is the extent to which the results (effects) reported in a study can truly be attributed to the intervention being evaluated; not to flaws in the design or conduct of the study. Such flaws can increase the risk of bias. Critical appraisal involves considering the risk of potential for allocation bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other. Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues addressed in the questions above. High potential for risk of bias translates to a poor quality rating. Low potential for risk of bias translates to a good quality rating. (Again, the greater the risk of bias, the lower the quality rating of the study.)

If a study has a "fatal flaw," then risk of bias is significant, and the study is of poor quality. Among the fatal flaws in RCTs are high drop-out rates, high differential drop-out rates, no ITT analysis, and an unsuitable statistical analysis (e.g., completers-only analysis).

Generally, when evaluating a study, one will not see a "fatal flaw," however, one will find some risk of bias. During training, reviewers were instructed to look for the potential for bias in studies by focusing on the concepts underlying the questions in the tool. For any box checked "NO," reviewers were told to ask: What is the potential for bias as a result? That is, does this factor cause one to doubt the results that were reported in the study?

The NHLBI staff provided reviewers with background reading on critical appraisal, while emphasizing the best approach to use: to examine the questions in the tool in determining the potential for bias in a study. The staff emphasized that each study has specific nuances; therefore, reviewers should familiarize themselves with the key concepts.

In addition, the NHLBI staff gave reviewers examples of studies that fall into each of the categories: good, fair, and poor. At the same time, the staff again emphasized the need to assess each study on its own.

Quality Assessment Tool for Systematic Reviews and Meta-Analyses

Exhibit A–2 shows the quality assessment tool for SRs and MA along with the guidance document for that tool (see below). The methodology team and NHLBI developed this tool based in part on criteria from AHRQ's EPCs and the Cochrane Collaborative.

This tool addresses 8 elements of quality assessment: use of prespecified eligibility criteria, use of a comprehensive and systematic literature search process, dual review for abstracts and full text

of articles, quality assessment of individual studies, assessment of publication bias, and other factors.

Guidance for Quality Assessment of Systematic Reviews and Meta-Analyses

A SR is a study that attempts to answer a question by synthesizing the results of primary studies, while using strategies to limit bias and random error (427). These strategies include a comprehensive search of all potentially relevant articles and the use of explicit, reproducible criteria in the selection of articles included in the review. Research designs and study characteristics are appraised, data are synthesized, and results are interpreted using a predefined systematic approach that adheres to evidence-based methodological principles.

SRs can be qualitative or quantitative. A qualitative systematic review summarizes the results of the primary studies but does not combine the results statistically. A quantitative systematic review, or *meta-analysis*, is a type of SR that employs statistical techniques to combine the results of the different studies into a single pooled estimate of effect, often given as an odds ratio.

Exhibit A–2. Quality Assessment of Systematic Reviews and Meta-Analyses

Criteria	Yes	No	Other (CD, NR, NA)*
1. Is the review based on a focused question that is adequately formulated and described?			
2. Were eligibility criteria for included and excluded studies predefined and specified?			
3. Did the literature search strategy use a comprehensive, systematic approach?			
4. Were titles, abstracts, and full-text articles dually and independently reviewed for inclusion and exclusion to minimize bias?			
5. Was the quality of each included study rated independently by two or more reviewers, using a standard method to appraise its internal validity?			

Criteria	Yes	No	Other (CD, NR, NA)*
6. Were the included studies listed along with important characteristics and results of each study?			
7. Was publication bias assessed?			
8. Was heterogeneity assessed? (This question applies only to MAs.)			
Quality Rating (Good, Fair, or Poor):			
Reviewer #1 initials:	**Reviewer #2 initials:**		
Comments:			

*CD: cannot determine; NA: not applicable; NR: not reported

The following questions correspond to those listed in the companion document for quality assessment of SRs and MA.

Question 1. Is the review based on a focused question that is adequately formulated and described?

An example of a clearly stated and well-formulated question is one that uses the PICO format, with all components clearly described.

Question 2. Were eligibility criteria for included and excluded studies predefined and specified?

Eligibility criteria help clarify why studies were included or excluded.

Question 3. Did the literature search strategy use a comprehensive, systematic approach?

The search strategy should employ a comprehensive, systematic approach in order to capture all of the evidence possible that pertains to the question of interest. At a minimum, a comprehensive review has the following attributes:

- Electronic searches were conducted using multiple scientific literature databases, such as MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, PsychLit, and others as appropriate for the subject matter.

- Manual searches of references found in articles and textbooks, which supplement the electronic searches.

Additional search strategies that may be used to improve the yield include:

- Studies published in other countries.

- Studies published in languages other than English.

- Identification by experts in the field of studies and articles that may have been missed.

- Search of grey literature, including technical reports and other papers from government agencies or scientific groups or committees; presentations and posters from scientific meetings, conference proceedings, unpublished manuscripts; and others. Searching the grey literature is important (whenever feasible) because sometimes only positive studies with significant findings are published in the peer-reviewed literature. This can bias the results of a review.

In their reviews, researchers described the literature search strategy clearly, and ascertained it could be reproducible by others with similar results.

Question 4. Were titles, abstracts, and full-text articles dually and independently reviewed for inclusion and exclusion to minimize bias?

Titles, abstracts, and full-text articles (when indicated) should be reviewed by two independent reviewers to determine which studies to include and exclude in the review. Reviewers resolved disagreements through discussion and consensus or with third parties. They clearly stated the review process, including methods for settling disagreements.

Question 5. Was the quality of each included study rated independently by two or more reviewers, using a standard method to appraise its internal validity?

Each included study should be appraised for internal validity (study quality assessment) using a standardized approach for rating the quality of the individual studies. Ideally, at least two independent reviewers appraised each study for internal validity. However, there is not one commonly accepted, standardized tool for rating the quality of studies. So, in the research papers, reviewers looked for an assessment of the quality of each study and a clear description of the process used.

Question 6. Were the included studies listed along with important characteristics and results of each study?

All included studies were listed in the review, along with descriptions of their key characteristics. This was presented either in narrative or table format.

Question 7. Was publication bias assessed?

Publication bias is a term used when studies with positive results have a higher likelihood of being published or being published rapidly, being published in higher impact journals, in English, and more than once, or being cited by others (428,The Cochrane Collaboration Open Learning Material 429). Publication bias can be linked to favorable or unfavorable treatment of research findings due to investigators, editors, industry, commercial interests, or peer reviewers. To minimize potential for publication bias, researchers can conduct a comprehensive literature search that includes the strategies discussed in question 3.

A funnel plot, a scatter plot of component studies in a MA, is a commonly used graphical method for detecting publication bias. With no significant publication bias, the graph looks like a symmetrical inverted funnel.

Reviewers assessed and clearly described the likelihood of publication bias.

Question 8. Was heterogeneity assessed? (This question applies only to MA.)

Heterogeneity is used to describe important differences in studies included in a MA that may make it inappropriate to combine the studies (430). Heterogeneity can be clinical (e.g., important differences between study participants, baseline disease severity, and interventions); methodological (e.g., important differences in the design and conduct of the study); or statistical (e.g., important differences in the quantitative results or reported effects).

Researchers usually assess clinical or methodological heterogeneity qualitatively by determining whether it makes sense to combine studies. For example:

- Should a study that evaluates the effects of an intervention on CVD risk with elderly male smokers with hypertension be combined with a study that evaluates healthy adults ages 18–40? (Clinical Heterogeneity)

- Should a study that uses a randomized controlled trial design be combined with a study that uses a case-control study design? (Methodological Heterogeneity)

Statistical heterogeneity describes the degree of variation in the effect estimates from a set of studies; it is assessed quantitatively. The two most common methods used to assess statistical heterogeneity are the Q test (also known as the χ^2 or chi-square test) or I^2 test.

Reviewers examined studies to determine if an assessment for heterogeneity was conducted and clearly described. If the studies are found to be heterogeneous, the investigators should explore and explain the causes of the heterogeneity, and determine what influence, if any, the study differences had on overall study results.

Quality Assessment Tool for Cohort and Cross-Sectional Studies

Exhibit A–3 shows the quality assessment tool for cohort and cross-sectional studies along with the guidance document for that tool (see below). The methodology team and the NHLBI developed this tool based in part on criteria from AHRQ's EPCs, the U.S. Preventive Services Task Force, consultation with epidemiologists, and other sources.

This tool addresses 13 elements of quality assessment: clarity of the research question or research objective; definition, selection, composition, and participation of the study population; definition and assessment of exposure and outcome variables; measurement of exposures prior to outcome assessment; study time frame and follow-up; study analysis and power; and other factors.

Guidance for Assessing the Quality of Cohort and Cross-Sectional Studies

The following questions correspond to those listed in the companion guidance document for quality assessment of cohort and cross-sectional studies. The narrative accompanying each question guides the reviewers in assessing the question.

Exhibit A–3. Quality Assessment of Observational Cohort and Cross-Sectional Studies

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
4. Was a sample size justification, power description, or variance and effect estimates provided?			
5. For the analyses in this paper, were the exposure(s) of interest			

Criteria	Yes	No	Other (CD, NR, NA)*
measured prior to the outcome(s) being measured?			
6. Was the time frame sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
7. For exposures than can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
8. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
9. Was the exposure(s) assessed more than once over time?			
10. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
11. Were the outcome assessors blinded to the exposure status of participants?			
12. Was loss to follow-up after baseline 20% or less?			
13. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			
Quality Rating (Good, Fair, or Poor):			
Reviewer #1 initials:	**Reviewer #2 initials:**		
Comments:			

*CD: cannot determine; NR: not reported; NA: not applicable

Question 1. Was the research question or objective in this paper clearly stated?

To answer this question, reviewers asked: Did the authors describe their research goal? Is the goal easy to understand? This issue is important for all types of scientific papers. Higher quality scientific research explicitly defines a research question.

Question 2. Was the study population clearly specified and defined?

Reviewers asked: Did the authors describe the group of people from which the study participants were selected or recruited, using demographics, location, and time period? If the authors conducted this study again, would they know whom to recruit, from where, and from what time period?

Below are two examples of how populations can be described:

1. Men over 40 years old with type 2 diabetes, who began seeking medical care at Phoenix Good Samaritan Hospital, between January 1, 1990 and December 31, 1994. The population clearly describes "who" (men over 40 years old with type 2 diabetes); "where" (Phoenix Good Samaritan Hospital); and "when" (between January 1, 1990 and December 31, 1994).

2. Women who were in the nursing profession, ages 34 to 59 in 1980; had no known CHD, stroke, cancer, hypercholesterolemia, or diabetes; were recruited from the 11 most populous states; and were identified from contact information obtained from state nursing boards.

When needed, reviewers examined prior papers on methods to assess this question. They usually found the papers in the reference list.

Question 3. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were I/E criteria for being in the study prespecified and applied uniformly to all participants?

The two parts of question 3 relate to the description of the study population.

Most cohort studies begin with selection of the cohort; participants in this cohort are then measured or evaluated for their exposure status. Sometimes, cohort studies recruit or select exposed participants from a different time or place than that of unexposed participants, especially retrospective cohort studies. In these retrospective studies data are obtained from the past (retrospectively), but the analysis examines exposures prior to outcomes). The following question addresses the similarity of populations: Are diabetic men with clinical depression at higher risk for CVD than those without clinical depression? In the study, the researcher selects diabetic men with depression from a mental health clinic and diabetic men without depression from an internal medicine or endocrinology clinic. Because this study recruits groups from different clinic populations, the answer to question 3 would be "NO". However, the selection of women nurses described in the question 2 were based on the same I/E criteria, so in that case the answer to question 3 would be "YES".

Question 4. Was a sample size justification, power description, or variance and effect estimates provided?

Specifically, question 4 asks: Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Did they note or discuss the statistical power of the study? This question addresses whether the study had enough participants to detect an association if one truly existed.

Reviewers examined methods sections of articles for an explanation of the sample size needed to detect a hypothesized difference in outcomes. Reviewers examined discussion sections of articles for information on statistical power (i.e., the study had an 85 percent power to detect a 20 percent increase in the rate of an outcome of interest, with a 2-sided alpha of 0.05). Instead of

sample size calculations, sometimes an article gives estimates of variance and/or estimates of effect size. In all these cases, the answer to question 3 would be "YES."

However, observational cohort studies often do not report power or sample sizes because the analyses are exploratory in nature. In this case, the answer to question 3 would be "NO." A lack of a report on power or sample size is not a "fatal flaw." Instead it may indicate the researcher did not focus on whether the study was sufficiently sized to answer a prespecified question; it may have been an exploratory, hypothesis-generating study.

Question 5. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?

This question is important to determine if an exposure causes an outcome; the exposure must precede the outcome.

In some prospective cohort studies, investigators identify the cohort, then determine the exposure status of members of the cohort (large epidemiological studies like the Framingham Study use this approach). Yet, for other cohort studies, investigators select the cohort based on its exposure status, as in the example above of diabetic men with depression (the exposure being depression). Other examples include a cohort identified by its exposure to fluoridated drinking water and compared to a cohort living in an area without fluoridated water, or a cohort of military personnel exposed to combat in the Gulf War compared to a cohort of military personnel not deployed in a combat zone.

With either types of cohort studies, the investigator follows the cohort forward in time (i.e., prospectively) to assess the outcomes that occurred in the exposed compared to non-exposed

members of the cohort. In other words, the investigator begins the study in the present by examining groups that were exposed or not exposed to some biological or behavioral factor, intervention, or other factor, then follows them forward in time to examine outcomes. If a cohort study is conducted properly, the answer to question 5 should be "YES," since the investigators determined the exposure status of members of the cohort at the beginning of the study, before the outcomes occurred.

For retrospective cohort studies, the same principal applies. The difference is that rather than identifying a cohort in the present and following it forward in time, investigators go back in time (i.e., retrospectively) and select a cohort based on its past exposure status. Then, they follow them forward to assess the outcomes that occurred in the exposed and non-exposed cohort members. In retrospective cohort studies, the exposure and outcomes may have already occurred (it depends on how long they follow the cohort); consequently, investigators need to ensure that the exposure preceded the outcome.

Sometimes in cross-sectional studies (or cross-sectional analyses of cohort–study data) investigators measure exposures and outcomes during the same time frame. As a result, cross-sectional analyses provide weaker evidence than regular cohort studies regarding a potential causal relationship between exposures and outcomes. For cross-sectional analyses, the answer to question 5 would be "NO."

Question 6. Was the time frame sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?

The intent of question 6 is to determine whether a study allowed enough time for a sufficient number of outcomes to occur or be observed, or enough time for an exposure to have a biological

effect on an outcome. For example, if clinical depression has a biological effect on increasing risk of CVD, such an effect may take years. Similarly, if higher dietary sodium increases blood pressure, a short time frame may be sufficient to assess its association with blood pressure; yet, a longer time frame would be needed to examine its association with heart attacks.

Investigators must consider timeframe to conduct a meaningful analysis of the relationship between exposures and outcomes. Often, they must conduct a study for at least several years, especially when examining health outcomes. However, the timeframe depends on the research question and outcomes being examined.

Cross-sectional analyses allow no time to see an effect, since the exposures and outcomes are assessed at the same time. So with this type of analysis, the answer to question 6 would be "NO."

Question 7. For exposures than can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?

In other words, for exposures that can be defined as a range (e.g., drug dosage, amount of physical activity, amount of sodium consumed), did the investigators assess multiple categories of that exposure? For example, the categories of exposure to medicines may include "taking medicines," "not taking medicines," or "taking a low, medium, or high dose of medicine." Categories for the exposure of dietary sodium may include "higher than average U.S. consumption," "lower than recommended consumption," and "in between higher and lower consumptions." Sometimes, investigators do not measure discrete categories of exposure; instead, they measure exposures as continuous variables (e.g., mg/day of dietary sodium or blood pressure values).

In any case, studying different levels of exposure, when possible, enables investigators to assess trends or dose-response relationships between exposures and outcomes, e.g., the higher the exposure, the greater the rate of the health outcome. Trends or dose-response relationships lend credibility to the hypothesis of causality between exposure and outcome.

Yet, for some exposures question 7 may not be applicable, e.g., when the exposure is a dichotomous variable like living in a rural setting versus an urban setting, or being vaccinated or not being vaccinated with a one-time vaccine. If there are only two possible exposures (yes/no) then reviewers would have answered this question "NA." This answer should not negatively affect the quality rating.

Question 8. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

How question 8 is answered can influence confidence in reported exposures. When investigators measure exposures with less accuracy or validity, it is difficult to observe an association between exposure and outcome, even if one exists. As important is whether they assessed exposures in the same manner within and between groups; if not, bias may result.

The following two examples illustrate how differing exposure measures can affect confidence in associations between exposure and outcome. The first addresses measurement of dietary salt intake. A study that prospectively uses a standardized dietary log and tests participants' urine for sodium content is more valid and reliable than one that retrospectively reviews self-reports of dietary salt intake. In this example, the reviewer would answer "YES" to question 8 with the first method and "NO" for the second one. The second example addresses blood pressure measurement. A study that uses blood pressure measurements from a practice have the following

standards in place—uses trained blood pressure assessors, standardized equipment (e.g., the same BP device which has been tested and calibrated), and a standardized protocol (e.g., patient is seated for 5 minutes with feet flat on the floor, BP is taken twice in each arm, and all four measurements are averaged)—is more reliable and valid than a study that uses measurements from a practice that does not have such standards in place. Again, the reviewer would answer "YES" to question 8 with the first method and "NO" for the second one.

This final example illustrates the importance of assessing exposures consistently across all groups. In a study comparing individuals with high blood pressure (exposed cohort) with those with normal blood pressure (non-exposed group), an investigator may note a higher incidence of CVD in those with high blood pressure, concluding that high blood pressure leads to more CVD events. Although this increase may be true, it also may be due to these individuals seeing their health care practitioners more frequently. With more frequent visits, there are increased opportunities for detecting and documenting changes in health outcomes, including CVD-related events. Thus, the increased number of visits can bias study results and lead to inaccurate conclusions.

Question 9. Was the exposure(s) assessed more than once over time?

Multiple measurements with the same result increase confidence that investigators correctly classified the exposure status. Also multiple measurements enable them to observe changes in exposure over time. The example on individuals who had a high dietary intake illustrates changes that can occur over time. Some, may have had a high dietary sodium throughout the follow-up period. Others may have had a high intake initially and then reduced their intake, while still others may have had a low intake throughout the study. Once again, this example may not be

applicable in all cases. In many older studies, exposure was measured only at baseline. However, multiple exposure measurements do result in a stronger study design.

Question 10. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

Answers to this question can influence confidence in reported exposures. These answers also can help determine whether the outcomes were assessed in the same manner within and between groups.

Even with a measure as objective as death, differences can exist in the accuracy and reliability of how investigators assess death. For example, did they base outcomes on an autopsy report, death certificate, death registry, or report from a family member? A study on the relationship between dietary fat intake and blood level cholesterol in which fasting blood samples used to measure cholesterol were all sent to the same laboratory illustrates outcomes that would be considered objective, accurate, and reliable. However, outcomes in studies in which research participants self-reported they had a heart attack or self-reported how much they weighed would be considered questionable.

Similar to the example in question 9, results may be biased if one group (e.g., people with high blood pressure) is seen more frequently than another group (people with normal blood pressure); more frequent encounters with the health care system increase the chances of outcomes being detected and documented.

Question 11. Were the outcome assessors blinded to the exposure status of participants?

Blinding or masking means that outcome assessors did not know whether participants were exposed or unexposed. To answer this question, the reviewer examined article for evidence that the person(s) assessing the study outcome(s), (outcome assessor) was masked to the exposure status of the research participants. An outcome assessor, for example, may examine medical records to determine outcomes that occurred in the exposed and comparison groups. Sometimes, the person measuring the exposure is the same person conducting the outcome assessment. In this case, the assessor would most likely not be blinded to exposure status. A reviewer would note such a finding in the comments section.

In assessing this criterion, the reviewers determined whether it was likely that the outcome assessors knew the exposure status of the study participants. If not, then blinding was adequate. The following example depicts how adequate blinding of the outcome assessors can be done. Investigators created a separate committee whose members were not involved in the care of the patient and had no information about the study participants' exposure status. Following a study protocol, committee members reviewed copies of participants' medical records, which had been stripped of any potential exposure information or personally identifiable information, for prespecified outcomes. .

If blinding was not possible, which is sometimes the case, the reviewers marked question 11 "NA" and explained the potential for bias.

Question 12. Was loss to follow-up after baseline 20 percent or less?

Higher overall follow-up rates are always desirable to lower follow-up rates. Though higher rates are expected in studies of short duration, whereas lower rates are often seen in studies of longer duration. Usually an acceptable overall follow-up rate is considered 80 percent or more of participants whose exposures were measured at baseline. However, this rate is just considered a general guideline. For example, a 6–month cohort study examining the relationship between dietary sodium intake and blood pressure level may have over a 90 percent follow-up; whereas, a 20–year cohort study examining the effects of sodium intake on stroke may have only a 65 percent follow-up rate.

Question 13. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

Investigators often use logistic regression or other regression methods to account for the influence of variables not of interest. This is a key issue in cohort studies: statistical analyses need to control for potential confounders, in contrast to RCTs in which the randomization process controls for potential confounders. In their analysis, investigators need to control for all key factors that may be associated with both the exposure of interest and the outcome and are not of interest to the research question.

For instance, a study of the relationship between cardiorespiratory fitness and CVD events, should control for age, blood pressure, blood cholesterol, and body weight. All these factors are associated with both low fitness and CVD events. Well-done cohort studies control for multiple potential confounders.

General Guidance for Determining the Overall Quality Rating of Cohort and Cross-Sectional Studies

The questions in the assessment tool were designed to help reviewers focus on key concepts for evaluating a study's internal validity, instead of being used as a list from which to add up items to judge a study's quality.

Internal validity for cohort studies is the extent to which the results reported in a study can truly be attributed to the exposure being evaluated, rather than to flaws in the design or conduct of a study. Such flaws can increase the risk of bias.

Critical appraisal involves considering risks: potential for selection bias, information bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other). Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues addressed in the questions above. High risk of bias translates to a poor quality rating, while low risk of bias translates to a good quality rating. Again, the greater the risk of bias, the lower the quality rating of the study.

The more a study design addresses issues affecting a causal relationship between the exposure and outcome, the higher quality the study. Issues include exposures occurring prior to outcomes, evaluation of a dose-response gradient, accuracy of measurement of exposure and outcome, sufficient time frame to see an effect, and appropriate control for confounding.

Generally, in evaluating a study, one will not see a "fatal flaw," but will find some risk of bias. To assess potential for bias, reviewers focused on concepts underlying the questions in the quality assessment tool. For any box checked "NO," reviewers asked: What is the potential for bias as a

result? That is, did this factor cause them to doubt the study results or doubt the ability of the study to accurately assess an association between exposure and outcome?

In summary, the NHLBI staff stressed that the best approach was to examine the questions in the tool and assess the potential for bias in a study, as well as become familiar with the key concepts. Examples of studies rated good, fair, and poor are useful, nevertheless each study had to be assessed on its own.

Quality Assessment Tool for Case-Control Studies

Exhibit A–4 shows the quality assessment tool for case-control studies along with the guidance document for that tool (see below). The methodology team and the NHLBI developed this tool based in part on criteria from AHRQ's EPCs, consultation with epidemiologists, and other factors.

This tool includes 12 items for assessment of study quality: clarity of the research objective or research question; definition, selection, composition, and participation of the study population; definition and assessment of case or control status; exposure, and outcome variables; use of concurrent controls; confirmation that the exposure occurred prior to the outcome; statistical power; and other factors.

Guidance for Assessing the Quality of Case-Control Studies

The following questions correspond to those listed in the companion guidance document for case-controlled studies. The narrative accompanying each question guides the reviewing in assessing the question.

Exhibit A–4. Quality Assessment of Case-Control Studies

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated and appropriate?			
2. Was the study population clearly specified and defined?			
3. Did the authors include a sample size justification?			
4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same time frame)?			
5. Were the definitions, inclusion and exclusion criteria, and algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?			
6. Were the cases clearly defined and differentiated from controls?			
7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?			
8. Was there use of concurrent controls?			
9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?			
10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?			
11. Were the assessors of exposure/risk blinded to the case or control status of participants?			
12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?			

Criteria	Yes	No	Other (CD, NR, NA)*
Quality Rating (Good, Fair, or Poor):			
Reviewer #1 initials:	**Reviewer #2 initials:**		
Comments:			

*CD: cannot determine; NR: not reported; NA: not applicable

Question 1. Was the research question or objective in this paper clearly stated and appropriate?

Did the authors describe their goal in conducting this research? Is it easy to understand what they were looking to find? This issue is important for any scientific paper of any type. High quality scientific research explicitly defines a research question.

Question 2. Was the study population clearly specified and defined?

In other words, did the authors describe the group of people from which the cases and controls were selected or recruited, while using demographics, location, and time period? If the investigators conducted this study again, would they know exactly who to recruit, from where, and from what time period?

Investigators identify case-control study populations b location, time period, and inclusion criteria for cases (people with the disease or problem) and controls (people without the disease or health problem). For example, the population for a study of lung cancer and chemical exposure would be all incident cases of lung cancer diagnosed in patients aged 35 to 79 years, from January 1, 2003 to December 31, 2007, in 6 regions of northern France, as well as lung cancer-free controls recruited from the same population during that time. The population is clearly described as: 1) who (men and women ages 35-79 with [cases] and without [controls] incident lung cancer); 2)

where (6 regions of northern France); and 3) when (between January 1, 2003 and December 31, 2007).

Other studies may use disease registries or data from cohort studies to identify cases. In these cases, the populations are individuals who live in the area covered by the disease registry or included in a cohort study (i.e., nested case-control or case-cohort). For instance, a study of the relationship between vitamin D intake and myocardial infarction might use patients identified via the GRACE registry, a database of heart attack patients.

NHLBI staff encouraged reviewers to examine prior papers on methods (listed in reference list) to make this assessment, if necessary.

Question 3. Did the authors include a sample size justification?

In other words, did the authors discuss their reasons for selecting or recruiting the number of people included? Did they discuss the statistical power of the study? This question addresses whether there was a sufficient sample size to identify an association if one did exist.

An article's methods section usually contains information on sample size and the size needed to detect differences in exposures and on statistical power.

Question 4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same time frame)?

To determine whether cases and controls were recruited from the same population, one can ask hypothetically, "If a control was to develop the outcome of interest (the condition that was used to select cases), would that person have been eligible to become a case?" Case-control studies begin

with the selection of the cases (those with the outcome of interest) and controls (those in whom the outcome is absent). Cases and controls are then evaluated and categorized by their exposure status. For the lung cancer example in question 2, cases and controls were recruited from hospitals in a given region. One may reasonably assume that controls in the catchment area for the hospitals, or those already in the hospitals for a different reason, would attend those hospitals if they became a case; therefore, the controls are drawn from the same population as the cases. If the controls were recruited or selected from a different region or time period, then the cases and controls were recruited from different populations.

The following example further explores selection of controls. In a study, eligible cases were men and women, ages 18–39, who were diagnosed with atherosclerosis at hospitals in Perth, Australia, between July 1, 2000 and December 31, 2007. Appropriate controls for these cases might be sampled using voter registration information for men and women ages 18–39, living in Perth (population-based controls); they also could be sampled from patients without atherosclerosis at the same hospitals (hospital-based controls). As long as the controls are individuals who would have been eligible to be included in the study as cases (if they had been diagnosed with atherosclerosis), then the controls were selected appropriately from the same source population as cases.

In a prospective case-control study, investigators may enroll individuals as cases at the time they are found to have the outcome of interest; the number of cases usually increases as time progresses. At this same time, they may recruit or select controls from the population without the outcome of interest. One way to identify or recruit cases is through a surveillance system. In turn, investigators can select controls from the population covered by that system. This is an example of population-based controls. Investigators also may identify and select cases from a cohort study

population and identify controls from outcome-free individuals in the same cohort study. This is known as a nested case-control study.

Question 5. Were the definitions, I/E criteria, and algorithms or processes used to identify or select cases and controls valid, reliable, and implemented?

To answer this question, reviewers determined if the investigators developed I/E criteria prior to recruitment or selection of the study population and if they used the same underlying criteria for all groups. The investigators should have used the same selection criteria, except for study participants who had the disease/condition, which would be different for cases and controls by definition. Therefore, the investigators use the same age (or age range), gender, race, and other characteristics to select cases and controls. Information on this topic is usually found in a paper's section on the description of the study population.

Question 6. Were the cases clearly defined and differentiated from controls?

For this question, reviewers looked for descriptions of the validity of case and control definitions and processes or tools used to identify study participants as such. They determine if the tools or methods were accurate, reliable, and objective. For example, cases might be identified as "adult patients admitted to a VA hospital from Jan 1, 2000 to Dec 31, 2009, with an ICD-9 discharge diagnosis code of acute myocardial infarction and at least one of the two confirmatory findings in their medical records: at least 2mm of ST elevation changes in two or more ECG leads and an elevated troponin level. Investigators might also use ICD-9 or CPT codes to identify patients. All cases should be identified using the same methods. Unless the distinction between cases and controls is accurate and reliable, investigators cannot use study results to draw valid conclusions.

Question 7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?

When it is possible to identify the source population fairly explicitly (e.g., in a nested case control study, or in a registry-based study), then random sampling of controls is preferred. When investigators used consecutive sampling, which is frequently done for cases in prospective studies, then study participants are not considered randomly selected. In this case, the reviewers would answer "NO" to question 7. However, this would not be considered a fatal flaw.

If investigators included all eligible cases and controls as study participants, then reviewers marked "NA" in the tool.

Question 8. Was there use of concurrent controls?

A concurrent control is a control selected at the time another person became a case, usually on the same day. This means that one or more controls are recruited or selected from the population without the outcome of interest at the time a case is diagnosed. Investigators can use this method in both prospective case-control studies and retrospective case-control studies. For instance, if hospital records indicate that Person A was diagnosed with adenocarcinoma of the colon on June 22, 2002, then investigators would select one or more controls from the population of patients *without* adenocarcinoma of the colon on that same day. This assumes they conducted the study retrospectively, using data from hospital records. The investigator could have also conducted this study using patient records from a cohort study, in which case it would be a nested case-control study.

Investigators can use concurrent controls in the presence or absence of matching and vice versa. A study that uses matching does not necessarily mean that concurrent controls were used.

Question 9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?

Investigators first determine case or control status (based on presence or absence of outcome of interest), and then assess exposure history of the case or control; therefore, reviewers ascertained that the exposure preceded the outcome. For example, if the investigators used tissue samples to determine exposure, did they collect them from patients prior to their diagnosis? If hospital records were used, did investigators verify that the date patients were exposed (e.g., received medication for atherosclerosis) occurred prior to the date they became a case (e.g., was diagnosed with type II diabetes)? For an association between an exposure and an outcome to be considered causal, the exposure *must* have occurred prior to the outcome.

Question 10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?

The answer to this question influences confidence in the reported exposures. As important is whether the investigators assessed exposures in the same manner within and between groups.

For instance, a retrospective self-report of dietary salt intake is not as valid and reliable as prospectively using a standardized dietary log plus testing participants' urine for sodium content. Similarly, blood pressure results from practices that use an established protocol for measuring blood pressure would be considered more valid and reliable than results from practices that did not use standard protocols. A protocol may include using trained blood pressure assessors,

standardized equipment (e.g., the same BP device which has been tested and calibrated), and a standardized procedure (e.g., patient is seated for 5 minutes with feet flat on the floor, BP is taken twice in each arm, and all four measurements are averaged).

Question 11. Were the assessors of exposure/risk blinded to the case or control status of participants?

Blinding or masking means that outcome assessors did not know whether participants were exposed or unexposed. To answer this question, reviewers examined articles for evidence that the outcome assessor (s), was masked to the exposure status of the research participants. An outcome assessor, for example, may examine medical records to determine the outcomes that occurred in the exposed and comparison groups. Sometimes, the person measuring the exposure is the same person conducting the outcome assessment. In this case, the outcome assessor would most likely not be blinded to exposure status. A reviewer would note such a finding in the comments section of the assessment tool.

One way to ensure good blinding of exposure assessment is to have a separate committee, whose members have no information about the study participants' status as cases or control, review research participants' records. To help answer the question above, reviewers determined if it was likely that the outcome assessor knew whether the study participant was a case or control. If it was unlikely, then the reviewers marked "NO" to question 11. Outcome assessor who used medical records to assess exposure should not have been directly involved in the study participants' care, since they probably would have known about their patients' conditions. If the medical records contained information on the patient's condition that identified him/her as a case

(which is likely), that information would have had to be removed before the exposure assessors reviewed the records.

If blinding was not possible, which is sometimes happens, the reviewers marked "NA" in the assessment tool and explained the potential for bias.

Question 12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?

Investigators often use logistic regression or other regression methods to account for the influence of variables not of interest. This is a key issue in case-controlled studies; statistical analyses need to control for potential confounders, in contrast to RCTs in which the randomization process controls for potential confounders. In the analysis, investigators need to control for all key factors that may be associated with both the exposure of interest and the outcome and are not of interest to the research question.

A study of the relationship between smoking and CVD events illustrates this point. Such a study needs to control for age, gender, and body weight; all are associated with smoking and CVD events. Well-done case-control studies control for multiple potential confounders.

Matching is a technique used to improve study efficiency and control for known confounders. For example, in the study of smoking and CVD events, an investigator might identify cases that have had a heart attack or stroke and then select controls of similar age, gender, and body weight to the cases. For case-control studies, it is important that if matching was performed during the

selection or recruitment process, the variables used as matching criteria (e.g., age, gender, race) *be controlled for in the analysis*.

General Guidance for Determining the Overall Quality Rating of Case-Controlled Studies

The NHLBI designed the questions in the assessment tool to help reviewers focus on the key concepts for evaluating a study's internal validity, not to use as a list from which to add up items to judge a study's quality.

Internal validity for case-control studies is the extent to which the associations between disease and exposure reported in the study can truly be attributed to the exposure being evaluated rather than to flaws in the design or conduct of the study. In other words, what is ability of the study to draw associative conclusions about the effects of the exposures on outcomes? Any such flaws can increase the risk of bias.

In critical appraising a study, the following factors need to be considered: risk of potential for selection bias, information bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other). Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues addressed in the question above. High risk of bias translates to a poor quality rating; low risk of bias translates to a good quality rating. Again, the greater the risk of bias, the lower the quality rating of the study.

If a study has a "fatal flaw," then risk of bias is significant; therefore, the study is deemed to be of poor quality. An example of a fatal flaw in case-control studies is a lack of a consistent standard process used to identify cases and controls.

Generally, when reviewers evaluated a study, they did not see a "fatal flaw," but instead found some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, reviewers examined the potential for bias in the study. For any box checked "NO," reviewers asked, "What is the potential risk of bias resulting from this flaw in study design or execution?" That is, did this factor lead to doubt about the results reported in the study?

By examining questions in the assessment tool, reviewers were best able to assess the potential for bias in a study. Specific rules were not useful, as each study had specific nuances. Also being familiar with the key concepts, helped reviewers assess the studies. Examples of studies rated good, fair, and poor were useful, yet each study had to be assessed on its own.

Quality Assessment Tool for Before-After Studies

Exhibit A–5 shows the quality assessment tool for before-after (pre-post) studies along with the guidance document for that tool (see below). The methodology team and the NHLBI developed this tool based in part on criteria from AHRQ's EPCs, other papers addressing quality assessment of similar studies, and other factors.

This tool includes 12 items for assessment of study quality: clarity of the research objective or research question; definition, selection, composition, and participation of the study population; definition and assessment of intervention and outcome variables; adequacy of blinding; statistical methods; and other factors.

Guidance for Assessing the Quality of Before-After (Pre-Post) Studies with No Control Group

The following questions correspond to those listed in the companion guidance document for before-after) pre-post) studies with no control group. The narrative below each question is intended to help the reviewers answer the question.

Exhibit A–5. Tool To Assess the Quality of Before-After (Pre-Post) Studies With No Control Group

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?			
2. Were eligibility/selection criteria for the study population prespecified and clearly described?			
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?			
4. Were all eligible participants that met the prespecified entry criteria enrolled?			
5. Was the sample size sufficiently large to provide confidence in the findings?			
6. Was the test/service/intervention clearly described and delivered consistently across the study population?			
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?			
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?			
9. Was the loss to follow-up after baseline 20 percent or less? Were those lost to follow-up accounted for in the analysis?			
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p-values for the pre-to-post changes?			
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?			
12. If the intervention was conducted at a group level (e.g., a whole			

Criteria	Yes	No	Other (CD, NR, NA)*
hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?			
Quality Rating (Good, Fair, or Poor):			
Reviewer #1 initials:	**Reviewer #2 initials:**		
Comments:			

*CD: cannot determine; NA: not applicable; NR: not reported

Question 1. Was the study question or objective clearly stated?

Did the authors describe their goal in conducting this research? Is it easy to understand what they were looking to find? This issue is important for any scientific paper of any type. Higher quality scientific research explicitly defines a research question.

Question 2. Were eligibility/selection criteria for the study population prespecified and clearly described?

In other words, if the investigators were to conduct this study again, would they know whom to recruit, from where, and from what time period?

Here is a sample description of a study population: men over age 40 with type 2 diabetes, who began seeking medical care at Phoenix Good Samaritan Hospital, between January 1, 2005 and December 31, 2007. The population is clearly described as: 1) who (men over age 40 years with type 2 diabetes); 2) where (Phoenix Good Samaritan Hospital); and 3) when (between January 1, 2005 and December 31, 2007). Another sample description is women who were in the nursing profession, who were ages34 to 59 in 1995, had no known coronary disease, stroke, cancer,

hypercholesterolemia, or diabetes, and were recruited from the 11 most populous states, with contact information obtained from state nursing boards.

To assess this question, reviewers examined prior papers on study methods (listed in reference list), when necessary.

Question 3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?

The participants in the study should be generally representative of the population in which the intervention will be broadly applied. Studies on small demographic subgroups may raise concerns about how the interventions will affect broader populations of interest. For instance, interventions on very young or very old individuals may affect middle-aged adults differently. Similarly, researchers may not be able to extrapolate study results from patients with severe chronic diseases to healthy populations.

Question 4. Were all eligible participants that met the prespecified entry criteria enrolled?

To further explore this question, reviewers may need to ask: Did the investigators develop the I/E criteria prior to recruiting or selecting study participants? Were the same underlying I/E criteria used for all research participants? Were all subjects who met the I/E criteria enrolled in the study?

Question 5. Was the sample size sufficiently large to provide confidence in the findings?

Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Did they note or discuss the statistical power of the study? This question addresses whether there was a sufficient sample size to detect an association, if one did exist.

An article's methods section may provide information on the sample size needed to detect a hypothesized difference in outcomes and a discussion on statistical power (such as, the study had 85 percent power to detect a 20 percent increase in the rate of an outcome of interest, with a 2-sided alpha of 0.05). Sometimes estimates of variance and/or estimates of effect size are given, instead of sample size calculations. In any case, if the reviewers determined that the power was sufficient to detect the effects of interest, then they would answer "YES" to question 5.

Question 6. Was the test/service/intervention clearly described and delivered consistently across the study population?

Another pertinent question regarding interventions is: Did the research participants have a high level of adherence to the requirements of the intervention? For example, if the investigators assigned a group to 10 mg/day of Drug A, did most participants in this group take the specific dosage of the drug? Or, did a large percentage of participants end up not taking the specific dose of Drug A indicated in the study protocol.

Reviewers ascertained that changes in study outcomes could be attributed to study interventions. If participants received interventions that were not part of the study protocol and could affect the outcomes being assessed, the results could be biased.

Question 7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?

Were the outcomes defined in detail? Were the tools or methods for measuring outcomes accurate and reliable – for example, have they been validated or are they objective? This question is important because the answer influences confidence in the validity of study results.

Even with a measure as objective as death, differences can exist in the accuracy and reliability of how investigators assess death. For example, did they base outcomes on an autopsy report, death certificate, death registry, or report from a family member?

An example of a valid study is one whose objective is to determine if dietary fat intake affects blood cholesterol level (cholesterol level being the outcome) and in which the cholesterol level is measured from fasting blood samples that are all sent to the same laboratory.

A reviewer would not consider a study that used self-reports from research participants on whether they had a heart attack, or their weight (assuming body weight was the outcome of interest), to be valid.

Question 8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?

Blinding or masking means that the outcome assessors did not know whether the participants received the intervention or were exposed to the factor under study. To answer the question above, the reviewers examined articles for evidence that the person(s) assessing the outcome(s) was masked to the participants' intervention or exposure status. An outcome assessor, for example, may examine medical records to determine the outcomes that occurred in the exposed and comparison groups. Sometimes, the person applying the intervention or measuring the exposure is the same person conducting the outcome assessment. In this case, the outcome

assessor would not likely be blinded to the intervention or exposure status. A reviewer would note such a finding in the comments section of the assessment tool.

In assessing this criterion, the reviewers determined whether it was likely that the person(s) conducting the outcome assessment knew the exposure status of the study participants. If not, then blinding was adequate. Here is an example of how adequate blinding of the outcome assessors can be done. Investigators created a separate committee, whose members were not involved in the care of the patient and had no information about the study participants' exposure status. Using a study protocol, committee members reviewed copies of participants' medical records, which had been stripped of any potential exposure information or personally identifiable information, for prespecified outcomes.

Question 9. Was the loss to follow-up after baseline 20 percent or less? Were those lost to follow-up accounted for in the analysis?

Higher overall follow-up rates are always desirable to lower follow-up rates. Though higher rates are expected in studies of short duration, whereas lower overall follow-up rates are often seen in studies of longer duration. Usually an acceptable overall follow-up rate is considered 80 percent or more of participants whose interventions or exposures were measured at baseline. However, this is a general guideline.

In accounting for those lost to follow-up, in the analysis, investigators may have imputed values of the outcome for those lost to follow-up or used other methods. For example, they may carry forward the baseline value or the last observed value of the outcome measure and use these as imputed values for the final outcome measure for research participants lost to follow-up.

Question 10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p-values for the pre-to-post changes?

Were formal statistical tests used to assess the significance of the changes in the outcome measures between the before and after time periods? The reported study results should present values for statistical tests, such as p-values, to document the statistical significance (or lack thereof) for the changes in the outcome measures.

Question 11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?

Were the outcome measures for each person measured more than once during the course of the before and after study periods? Multiple measurements with the same result increase confidence that the outcomes were accurately measured.

Question 12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?

Group level interventions are usually not relevant for clinical interventions such as bariatric surgery, in which the interventions are applied at the individual patient level. In those cases, the questions were coded as “NA” in the assessment tool.

General Guidance for Determining the Overall Quality Rating of Before-After Studies

The questions in the quality assessment tool were designed to help reviewers focus on the key concepts for evaluating the internal validity of a study, not to use as a list from which to add up items to judge a study's quality.

Internal validity is the extent to which the outcome results reported in the study can truly be attributed to the intervention or exposure being evaluated, and not to biases, measurement errors, or other confounding factors, resulting from flaws in the design or conduct of the study. In other words, what is the ability of the study to draw associative conclusions about the effects of the interventions or exposures on outcomes?

In critical appraising a study, the following factors need to be considered: risk of potential for selection bias, information bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other). Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues throughout the questions above. High risk of bias translates to a rating of poor quality; low risk of bias translates to a rating of good quality. Again, the greater the risk of bias, the lower the quality rating of the study.

In addition, the more attention in the study design to issues that can help determine if there is a causal relationship between the exposure and outcome, the higher quality the study. These include exposures occurring prior to outcomes, evaluation of a dose-response gradient, accuracy of measurement of both exposure and outcome, and sufficient time frame to see an effect.

Generally, when reviewers evaluated a study, they did not see a "fatal flaw," but instead found some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, reviewers examined the potential for bias in the study. For any box checked "NO" reviewers asked, "What is the potential risk of bias resulting from this flaw in study design or execution?" That is, did this factor lead to doubt about the results reported in the study or doubt the ability of the study to accurately assess an association between the intervention or exposure and the outcome?

By examining questions in the assessment tool, reviewers were best able to assess the potential for bias in a study. Specific rules were not useful, as each study had specific nuances. Also being familiar with the key concepts, helped reviewers assess the studies. Examples of studies rated good, fair, and poor were useful, yet each study had to be assessed on its own.

Quality Assessment Tool for Case Series Studies

Exhibit A–6 shows the quality assessment tool for case series studies. The methodology team and the NHLBI developed this tool based in part on criteria from AHRQ's EPCs, other papers addressing quality assessment of similar studies, and other factors.

This tool includes 9 items for assessment of study quality: clarity of the research objective or research question; definition, selection, composition, and participation of the study population, definition and assessment of intervention and outcome variables, statistical methods, and other factors.

Exhibit A–6. Quality Assessment of Case Series Studies

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?			
2. Was the study population clearly and fully described, including a case definition?			
3. Were the cases consecutive?			
4. Were the subjects comparable?			
5. Was the intervention clearly described?			
6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?			
7. Was the length of follow-up adequate?			
8. Were the statistical methods well-described?			
9. Were the results well-described?			
Quality Rating (Good, Fair, or Poor):			
Reviewer #1 initials:	**Reviewer #2 initials:**		
Comments:			

*CD: cannot determine; NA: not applicable; NR: not reported

Data Abstraction and Review Process

Articles rated good or fair during the quality rating process were abstracted into the VCW using a web-based data entry form. Requirements for abstraction were specified in an Evidence Table template that the methodologist developed for each critical question. The Evidence Table template included data elements relevant to the critical question such as study characteristics, interventions, population demographics, and outcomes.

The abstractor carefully read the article and entered the required information into the web-based tool. Once abstraction was complete, an independent quality control review was conducted.

During this review, data was checked for accuracy, completeness, and the use of standard formatting.

Development of Evidence Tables and Summary Tables

Evidence Tables

For each CQ, methodologists worked with the expert panel/work group members to identify the key data elements needed to answer the question. Using the PICOTS criteria as the foundation, expert panel/work group members determined what information was needed from each study to be able to understand the design, sample and baseline characteristics to interpret the outcomes of interest. A template for a standard evidence table was created and then populated with data from several example studies for the expert panel/work group to review. This was done to ensure that all appropriate study characteristics were being considered. Once a final template was agreed upon, evidence tables were generated by pulling the appropriate data elements from the master abstraction database for those studies that met the inclusion criteria for the CQ.

Only studies rated good and fair were included in the evidence tables.

Templates varied by each individual CQ but generally provided the following information:

- Study Characteristics: author, year, study name, country and setting, funding, study design, research objective, year study began, overall study N, quality rating
- Criteria and Endpoints: I/E criteria, primary outcome, secondary outcome, composite outcome definitions

- Study Design Details: treatment groups, descriptions of interventions, duration of treatment, duration of follow-up, run-in, wash-out, sample size

- Baseline Population Characteristics: demographics, biomarkers, other measures relevant to the outcomes

- Results: outcomes of interest for the CQ with between group *p* values or CIs for risk ratios, adverse events, attrition, adherence

Studies are presented in alphabetical order by study name (if none, the first author's last name). Some expert panels combined all the articles for a study and presented it as a single entry, but for those that did not, the articles were presented in chronological order within the group for the same study.

Summary Tables

To enable a more targeted focus on the specific aspects of a CQ, methodologists developed summary tables, or abbreviated evidence tables, in concert with the panels or workgroups. A summary table might be designed to address a general population or a specific subpopulation, such as individuals with diabetes, women, or the elderly, but it only presents concise data elements. All available data in the evidence tables were reviewed for a consistent format to present the specific outcome of interest. For example, some lifestyle interventions have lengthy descriptions in the evidence tables, but only key features were concisely stated in the summary tables. Within an outcome, the time periods were clearly identified and the order of the different measures were consistently applied. For example, weight loss is always listed in order of percentage change in body weight, followed by kilogram change, and lastly by proportion of subjects losing a certain

percent of their body weight. Templates varied by each aspect of the CQ being addressed but generally provide the following information:

- Study Characteristics: study name, author/year, design, overall study *N*, quality rating
- Sample Characteristics: relevant inclusion criteria
- Study Design Details: intervention doses and duration
- Results: change in outcomes by time periods, attrition, adherence

Each panel/work group determined its own ordering of studies to present the evidence within each summary table. For some, trials were listed in chronological order, for others it was by the type or characteristics of the intervention.

Process for the Development of Evidence Statements, Recommendations, and Panel Voting

Using the summary tables (and evidence tables as needed), panel members collaboratively wrote the evidence statements with input from methodology staff and oversight of the process by the NHLBI staff. Evidence statements aimed to summarize key messages from the evidence that could be provided to PCPs and other stakeholders. In some cases, the evidence was too limited or inconclusive, so no evidence statement was developed, or a statement of insufficient evidence was made.

Methodology staff provided panels with overarching guidance on how to grade the level of evidence (high, moderate, low), and the panels used this guidance to grade each evidence statement. This guidance is documented in the following section.

Panel members having relationships with industry (RWI) or other possible conflicts of interest (COI) were allowed to participate in discussions leading up to voting as long as they declared their relationships, but they recused themselves from voting on any issue relating to their RWI or potential COI. Voting occurred by a panel chair asking each member to signify his or her vote. The NHLBI project staff, methodologists, and contractors did not vote.

Once evidence statements were final, attention turned to developing recommendations. Recommendations were developed using a process similar to that used for evidence statements. For approval of a recommendation rated E (expert opinion) at least 75 percent of the expert panel members had to vote "yes." For both evidence statements and recommendations, voting could be open so that differing viewpoints could be identified easily and further discussion and revisions facilitated to address areas of disagreement (e.g., by crafting language or dividing an evidence statement into more than one statement). Voting also could be by confidential ballot if the group so chose.

For both evidence statements and recommendations, a record of the vote count (for, against, recusal) was made without attribution. The ideal was 100 percent consensus, but a 2/3 majority was considered acceptable. In cases where a 2/3 majority was not reached in the initial vote, further discussion and clarification was used to create a consensus majority.

Description of Methods for Grading the Body of Evidence

The NHBLI Adult Cardiovascular Disease Guidelines Project applied related but distinct processes for grading the bodies of evidence for CQs, for bodies of evidence for different outcomes included within CQs, and for the subsequent strength of recommendations developed from those bodies of evidence. Each of these processes is described in turn below.

Grading the Body of Evidence

In developing the system for grading the body of evidence, the NHLBI reviewed the following systems: Grading of Recommendations, Assessment, Development, and Evaluation (GRADE), USPSTF, American College of Cardiology/American Heart Association (ACC/AHA), American Academy of Pediatrics, Strength of Recommendation Taxonomy, Canadian Task Force on Preventive Health Care, Scottish Intercollegiate Guidelines Network, and Center for Evidence-Based Medicine in Oxford. In particular, GRADE, USPSTF, and ACC/AHA were considered at length. However, none of those systems fully met the needs of the NHLBI project. The NHLBI, therefore, developed its own hybrid version that incorporated features of those systems. The expert panel and work group members strongly supported the resulting system and, with the methodology team, used it to decide about evidence ratings.

Using a systematic review process, the panel members gathered and summarized the bodies of evidence received (as a result of the screening and quality rating process), then, graded the bodies of evidence.

Once the panel and work group members reached consensus on the wording of the evidence statement, they assigned a grade to the strength of the body of evidence. This grade informs PCPs and other stakeholders about the degree of support the evidence provides for the evidence statement. Three options were identified for grades for the strength of evidence: High, Moderate, or Low.

With assistance from methodologists, the panel and work group members used the types of evidence to grade the strength of evidence as high, moderate, or low. See Table A–1 below.

Table A–1. Quality Rating the Strength of Evidence

Type of Evidence	Strength of Evidence Grade
• Well-designed, well-executed RCTs that adequately represent populations to which the results are applied and directly assess effects on health outcomes; • MAs of such studies. • *There is high confidence that the evidence reflects the true effect. Further research is unlikely to change our confidence in the estimate of effect.*	High
• RCTs with minor limitations affecting confidence in, or applicability of, the results, including minor flaws in design or execution. • Well-designed, well-executed nonrandomized controlled studies and well-designed, well-executed observational studies • MAs of such studies; • *There is moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.*	Moderate
• RCTs with major limitations; • Nonrandomized intervention studies and observational studies with major limitations affecting confidence in, or applicability of, the results; • Uncontrolled clinical observations without an appropriate comparison group (e.g., case series, case reports) • Physiological studies in humans. • MAs of such studies; • *There is low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.*	Low

The strength of the body of evidence represents the degree of certainty, based on the overall body of evidence, that an effect or association is correct. It is important to assess the strength of the evidence as objectively as possible. For rating the overall strength of evidence, the entire body of evidence for a particular summary table and its associated evidence statement was used.

Methodologists provided guidance to the panels and work group for assessing the body of evidence for each outcome or summary table of interest using four domains: 1) risk of bias; 2) consistency; 3) directness; and 4) precision. Each domain was assessed and discussed, and the aggregate assessment was used to increase or decrease the strength of the evidence, as determined

by the NHLBI Evidence Quality Grading System shown above. The four domains are explained in more detail below:

Risk of bias. Risk of bias refers to the likelihood that the body of included studies for a given question or outcome is biased due to flaws in the design or conduct of the studies. Risk of bias and internal validity are similar concepts that are inversely correlated. A study with a low risk of bias has high internal validity and is more likely to provide correct results than one with high risk of bias and low internal validity. At the individual study level, risk of bias is determined by rating the quality of each individual study using standard rating instruments, such as the NHLBI study quality rating tools presented and discussed in the previous section of this report. Overall, risk of bias for the body of evidence regarding a particular question, summary table, or outcome is then assessed by the aggregate quality of studies available for that particular question or outcome. Panel and work group members reviewed the individual study quality ratings with methodologists to determine the aggregate quality of the studies available for a particular question, summary table, or outcome. If the risk of bias is low, it increases the strength of evidence rating for the strength of the overall body of evidence; if the risk of bias is high, it decreases the strength of evidence rating.

Consistency. Consistency is the degree to which reported effect sizes are similar across the included studies for a particular question or outcome. Consistency enhances the overall strength of evidence and is assessed through effect sizes being in the same direction (i.e., multiple studies demonstrate an improvement in a particular outcome), and the range of effect sizes across studies being narrow. Inconsistent evidence is reflected in effect sizes that are in different directions, a broad range of effect sizes, non-overlapping CIs, or unexplained clinical or statistical heterogeneity. Studies included for a particular question or outcome can have effect sizes that are

consistent, inconsistent, or unknown (or not applicable). The latter occurs in situations when there is only a single study. For the NHLBI project, consistent with the Evidence-based Practice Center (EPC) approach, evidence from a single study generally should be considered insufficient for a high strength of evidence rating because a single trial, no matter how large or well designed, may not provide definitive evidence of a particular effect until confirmed by another trial. However, a very large, multi-centered, well-designed, well-executed RCT that performs well in the other domains could in some circumstances be considered high quality evidence after thoughtful consideration.

Directness. Directness has two aspects: the direct line of causality and the degree to which findings can be extended from a specific population to a more general population. The first defines directness as whether the evidence being assessed reflects a single direct link between the intervention (or service, approach, exposure, etc.) of interest and the ultimate health outcome under consideration. Indirect evidence relies on intermediate or surrogate outcomes that serve as links along a causal pathway. Evidence that an intervention results in changes in important health outcomes (e.g., mortality, morbidity) increases the strength of the evidence. Evidence that an intervention results in changes limited to intermediate or surrogate outcomes (e.g., a blood measurement) decreases the strength of the evidence. However, the importance of each link in the chain should be considered, including existing evidence that a change in an intermediate outcome affects important health outcomes.

Another example of directness involves whether the bodies of evidence used to compare interventions are the same. For example, if Drug A is compared to placebo in one study and Drug B is compared to placebo in another study, using those two studies to compare Drug A versus

Drug B yields indirect evidence and provides a lower strength of the evidence than direct head-to-head studies of Drug A versus Drug B.

The second aspect of directness refers to the degree to which participants or interventions in the study are different from those to whom the study results are being applied. This concept is referred to as applicability. If the population or interventions are similar, the evidence is direct and strengthened. If they are different, the evidence is indirect and weakened.

Precision. Precision is the degree of certainty about an estimate of effect for a specific outcome of interest. Indicators of precision are statistical significance and CIs. Precise estimates enabled firm conclusions to be drawn about an intervention's effect relative to another intervention or control. An imprecise estimate is where the CI is so wide that the superiority or inferiority of an intervention cannot be determined. Precision is related to the statistical power of the study. An outcome that was not the primary outcome or not prespecified will generally be less precise than the primary outcome of a study. In MA, precision is reflected by the CI around the summary effect size. For SRs, which include multiple studies but no quantitative summary estimate, the quantitative information from each study should be considered in determining the overall precision of the body of included studies, since some studies may be more precise than others. Determining precision across many studies without conducting a formal meta-analysis is challenging and requires judgment. A more precise body of evidence increases the strength of evidence and less precision reduces the strength of a body of evidence.

Following discussion of the four criteria for the strength of evidence grading options, in some cases, the expert panels and work groups also considered other factors. For example, the objectivity of an outcome measure needs to be assessed. Total mortality (usually recorded

accurately) is a more objective measure than angina. Similarly, urinary sodium excretion is a more objective measure than dietary sodium intake reported by study subjects through recall. And measured height and weight, used to calculate a study subject's BMI, is a more objective measure than self-reported weight and height.

After the panel and work group members reviewed and discussed this range of factors, they voted on the final grade for the strength of evidence for each evidence statement. Methodologists provided analysis and recommendations regarding strength of evidence grading but did not participate in the voting process. A simple majority vote was sufficient to identify the strength of evidence grade. However, in most cases, the panels and work groups discussed the results if there were dissenting opinions, until they achieved consensus or large majorities for the votes on the strength of evidence.

Policy and Procedures for the Use of Existing Systematic Reviews and Meta-Analyses

SRs and MAs are routinely used in evidence reviews, and well-conducted SRs or MAs of RCTs are generally considered to be among the highest forms of evidence. As a result, SRs or MAs could be used to inform guideline development in the NHLBI CVD adult guidelines project if certain criteria were met. AHRQ has published guidance on using existing SRs, which has inform the development of the NHLBI criteria (431).

To use existing SRs or MAs to inform the guideline recommendations, the project needed to identify: (1) those studies relevant to the topic of interest, (2) those where the risk of bias was low, and (3) those that were recent. The first item was addressed by examining the research

question and component studies in the SRs or MA as they related to the NHLBI CQs. The second item was addressed using a quality assessment tool and the third by examining publication dates.

In general, the project used the following process in using SRs and MA:

- Eligibility of SRs and MA was determined by the methodologists and consulting with panels/workgroups as needed.

- Data were not formally abstracted from SRs or MA using the database system to create individual evidence tables. Data from the SRs or MA used for CQ1 and CQ2 were pulled from the studies and included in summary tables, but not in individual evidence tables. The citations were included in the reference list.

- SRs or MA were rated using the quality assessment tool for this project. SRs or MA were used to develop recommendations if they were rated "good" or "fair " or were comprehensive reviews commissioned by the Federal government. SRs or MA rated as "poor" were only used when there were no eligible good or fair publications; this occurred for Obesity Question 2.

- If an existing SR or MA was used to develop recommendations:

  - Multiple eligible SRs and MA addressing the same topic were identified through a systematic search to minimize bias. The SRs or MA used were summarized in text, table, or appendix.

  - Rating the body of evidence followed the same system used for the de novo SRs conducted for this project and resulted in a High [SRs/MA rated "good" only], Moderate, or Low

rating based on number, type, and quality of the studies in the MA or SR. In most cases, the number of SRs/MA was also considered when rating the body of evidence.

- Recommendation strength took into account whatever evidence was available in the SRs or MA used to make the recommendation, including issues like strength of the evidence, applicability of the evidence, consistency of the evidence, and others. Any level of recommendation could be made, as long as it was supported by the evidence being used to make the recommendation: Grade A (Strong) [a strong recommendation only can be given if the SRs/MA used to make the recommendation are rated as Good], B (Moderate), C (Weak), (D) Against, (E) Expert Opinion, (N) No recommendation.

Three criteria were used in to determine when SRs or MA could be used.

Situation #1—When a SR or MA addresses a topic relevant to the NHLBI CVD guidelines that was not covered by an existing CQ (e.g., effects of physical activity on CVD risk):

A. For an SR or MA to be examined for relevance to the topic of interest, the topic needed to be prespecified in the form of a CQ using the PICO structure (population, intervention/exposure, comparator, and outcome). If only portion(s) of an SR were relevant, those relevant portions that were reported separately could be used. For example, in the Department of Health and Human Services' (DHHS) 2008 systematic review on physical activity, the effects of physical activity on CVD was relevant and was used to make recommendations because they were reported in a separate chapter. However, the effects of physical activity on mental health would not be relevant and, therefore, were not used in crafting the recommendations.

B. SRs or MA could be used if they were recent, i.e., published within 3 years of the end date of the NHLBI systematic review publication window (December 31, 2009), or identified by the panel or workgroup if published after the end date of the project literature search and before the panel began to deliberate recommendations. If the end date of the SR or MA literature search was before December 31, 2009, panel or work group members could conduct a bridging literature search through December 31, 2009 in the following situations: 1) if they believed it was necessary to review relevant studies, published after the end date, and 2) if the bridging literature search covered the period up to one year before the literature search cut-off date of the SR or MA and extended no later than December 31, 2009.

Situation #2—If the NHLBI literature review identified an existing SR or MA that could possibly replace the NHLBI's review of a CQ or subquestion:

A. The SR or MA was examined for consistency between the studies in the SR or MA and the CQ I/E criteria. Component studies had to meet the I/E criteria; however, smaller sample sizes were allowed, as were studies published before the beginning of the NHLBI project's search date window, as long as a truly systematic approach was used. If the end date of the SR or MA literature search was before December 31, 2009, panel or work group members could conduct a bridging literature search through December 31, 2009 in these situations: 1) if they believed it was necessary to review relevant studies, published after the end date, and 2) if the bridging literature search covered the period up to one year before the literature search cut-off date of the SR or MA and extended no later than December 31, 2009.

Situation #3—If the NHLBI literature review identified an existing SR or MA that addressed the same or a similar CQ or subquestion as one undergoing NHLBI review:

A. SR or MA component articles that met all the I/E criteria for the CQ, but were not identified in the NHLBI literature search, could be added to the included studies in the NHLBI review and treated the same way (i.e., abstracted, quality rated, and added to evidence and summary tables).

APPENDIX 3: QUESTION SPECIFIC METHODS

Search Strategy Overview and Syntax of Queries

This section describes how search strategies for the NHLBI guidelines initiative were constructed and explains how to interpret search strategies that are documented in the following section.

A search strategy is an expression of conditions connected by the logical operators AND, OR, and NOT. Parentheses are used to group conditions. Each condition is described by attributes, operators, and values. Table A–2 shows examples of queries and descriptions of results. A complete list of attributes used in search strategies with their explanations is listed in Table A–3. Commonly used macro queries are defined in Table A–4.

Table A–2. Examples of Simple Queries

Query	Results
title=weight loss	Articles with phrase “weight loss” in article title
title, abstract=weight loss	Articles with phrase “weight loss” in article title or its abstract
weight loss	When attribute name is skipped, “title, abstract” is assumed; therefore, the results are equivalent to query: title, abstract=weight loss
Y title=(weight loss or obesity)	Articles with phrases “weight loss” or “obesity” in article title
title=obesity and abstract=(mortality or morbidity)	Articles with “obesity” in the title and “mortality” or “morbidity” in the abstract.
((subject=Cardiovascular Diseases) with (qualifier=(prevention or epidemiology)))	Articles with MeSH heading “Cardiovascular Diseases” and subheadings ‘prevention’ or ‘epidemiology’
qualifier=mortality	Articles with MeSH subheading ‘mortality’
title, abstract, genre, subject=random?	Articles that include any word starting with ‘random,’ e.g., ‘randomized,’ ‘randomised,’ etc.
abstract=?cholesterol?	Articles with abstracts including any word that includes subword ‘cholesterol,’ e.g., hypocholesterolemia
not journal Title=“ACP journal club”	Exclude articles from “ACP journal club”
publication Year >1997 and publication Year <2010	Articles from 1998 to 2009
(CVD %2 event?)	Articles with ‘CVD’ word in proximity of two words from word stem ‘event’

Table A–3. Attributes, Their Values, and Explanation

Attribute	Values
abstract	Text of abstract
title	Text of title
<no attribute specified>	Combined text of title and abstract
Journal Title	Journal name (as in PubMed)
PublicationYear	Year of the publication, e.g., 2000
genre	Publication type (as in Pubmed)
language	eng for English
subject	MeSH subject headings
Major Subject	MeSH major subject headings
qualifier	MeSH subheadings
substance	MeSH substances
Record Content Source	e.g., 'Pubmed,' 'embase, 'cinahl'
Record Status	e.g., 'delete'
Pubmed id	Pubmed identifier
Uu id	Internal unique identifier

Table A–4. Common Macro Queries Used in Search Strategies

Macro Name	Query
{Randomized Controlled Trials}	(((RecordContentSource=pubmed AND (genre=randomized controlled trial OR subject=random allocation OR subject=double-blind method OR subject=single-blind method OR (subject="Randomized Controlled Trials as Topic" and abstract=? and (title=trial or ((title=study or subject,genre=stud?) and subject=outcome?))))) OR ((? NOT RecordContentSource=pubmed) AND (genre=randomized OR (title,abstract=randomized AND title,abstract=controlled AND title,abstract=trial) OR title,abstract=random? OR subject=random allocation OR title,abstract=placebo OR subject=double-blind method OR subject=single-blind method))) AND language=eng?) NOT (title=(case report or commentary) OR genre=(letter or abstract or newspaper article or comment?))
{Systematic Review}	(((title=systematic review OR genre=meta-analysis OR title=meta-analysis OR title=systematic literature review OR (title,abstract=systematic review AND genre=review) OR genre=consensus development conference OR genre=practice guideline OR journalTitle=("Cochrane Database of Systematic Reviews" OR "Health technology assessment" OR "Evidence report/technology assessment (Summary)")) OR ((title=evidence based OR subject=evidence-based medicine OR title=best practice? OR title,abstract=evidence synthesis) AND (genre=review OR subject=diseases category OR subject=behavior and behavior mechanisms OR subject=therapeutics OR genre=evaluation studies OR genre=validation studies OR genre=guideline)) OR ((systematic OR systematically OR title,abstract=critical OR (study selection) OR (predetermined OR inclusion AND criteri?) OR exclusion criteri? OR "main outcome measures" OR "standard of care" OR "standards of care") AND (title,abstract=survey OR title,abstract=surveys OR overview? OR title,abstract=review OR title,abstract=reviews OR search? OR handsearch OR title,abstract=analysis OR title,abstract=critique OR appraisal OR

Macro Name	Query
	(reduction AND risk AND (death OR recurrence))) AND (title,abstract=literature OR title,abstract=articles OR title,abstract=publications OR title,abstract=publication OR title,abstract=bibliography OR title,abstract=bibliographies OR title,abstract=published OR unpublished OR citation OR citations OR title,abstract=database OR title,abstract=internet OR title,abstract=textbooks OR references OR scales OR papers OR datasets OR title,abstract=trials OR meta-analy? OR (title,abstract=clinical AND title,abstract=studies) OR subject,title,abstract=treatment outcome))) AND language=eng?) NOT (title=(case report or commentary) OR genre=(letter or abstract or newspaper article or comment?))
{Cardiovascular Diseases}	Term in parentheses is MeSH-exploded and matched against subject headings, titles, and abstracts
{Non-Westernized Countries}	subject=("Africa" OR "Africa Northern" OR "Algeria" OR "Egypt" OR "Libya" OR "Morocco" OR "Tunisia" OR "Africa South of the Sahara" OR "Africa Central" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Congo" OR "Gabon" OR "Democratic Republic of the Congo" OR "Equatorial Guinea" OR "Africa Eastern" OR "Burundi" OR "Ethiopia" OR "Kenya" OR "Rwanda" OR "Somalia" OR "Sudan" OR "Tanzania" OR "Uganda" OR "Djibouti" OR "Eritrea" OR "Africa Southern" OR "Angola" OR "Botswana" OR "Lesotho" OR "Malawi" OR "Mozambique" OR "Namibia" OR "South Africa" OR "Swaziland" OR "Zambia" OR "Zimbabwe" OR "Africa Western" OR "Benin" OR "Burkina Faso" OR "Gambia" OR "Ghana" OR "Guinea Bissau" OR "Cote d Ivoire" OR "Liberia" OR "Mali" OR "Mauritania" OR "Niger" OR "Nigeria" OR "Senegal" OR "Sierra Leone" OR "Togo" OR "Guinea" OR "Cape Verde" OR "Americas" OR "Central America" OR "Belize" OR "Costa Rica" OR "El Salvador" OR "Guatemala" OR "Honduras" OR "Nicaragua" OR "Panama" OR "Panama Canal Zone" OR "Latin America" OR "South America" OR "Argentina" OR "Bolivia" OR "Brazil" OR "Chile" OR "Colombia" OR "Ecuador" OR "French Guiana" OR "Guyana" OR "Paraguay" OR "Peru" OR "Suriname" OR "Uruguay" OR "Venezuela" OR "Caribbean Region" OR "West Indies" OR "Barbuda and Antigua" OR "Bahamas" OR "Barbados" OR "Cuba" OR "Dominican Republic" OR "Haiti" OR "Jamaica" OR "Martinique" OR "Netherlands Antilles" OR "Puerto Rico" OR "Trinidad and Tobago" OR "Virgin Islands of the United States" OR "Dominica" OR "Grenada" OR "Guadeloupe" OR "Saint Lucia" OR "Saint Vincent and the Grenadines" OR "Saint Kitts and Nevis" OR "Antarctic Regions" OR "Arctic Regions" OR "Asia" OR "Asia Central" OR "Kazakhstan" OR "Kyrgyzstan" OR "Tajikistan" OR "Turkmenistan" OR "Uzbekistan" OR "Asia Southeastern" OR "Borneo" OR "Brunei" OR "Myanmar" OR "Cambodia" OR "Indonesia" OR "Laos" OR "Malaysia" OR "Mekong Valley" OR "Philippines" OR "Singapore" OR "Thailand" OR "Vietnam" OR "East Timor" OR "Asia Western" OR "Bangladesh" OR "Bhutan" OR "India" OR "Sikkim" OR "Middle East" OR "Afghanistan" OR "Bahrain" OR "Iran" OR "Iraq" OR "Jordan" OR "Kuwait" OR "Lebanon" OR "Oman" OR "Qatar" OR "Saudi Arabia" OR "Syria" OR "Turkey" OR "United Arab Emirates" OR "Yemen" OR "Nepal" OR "Pakistan" OR "Sri Lanka" OR "Far East" OR "China" OR "Hong Kong" OR "Tibet" OR "Japan" OR "Tokyo" OR "Korea" OR "Macau" OR "Mongolia" OR "Taiwan" OR "Atlantic Islands" OR "Azores" OR "Bermuda" OR "Falkland Islands")

To increase the readability of search strategies, conditions are grouped in meaningful components.

There are three major types of components: study type query, Boolean search, and Boolean filter.

These three components are connected with the AND operator; thus, a citation must satisfy all three component queries to be retrieved. The I/E criteria for each question, which was defined using the PICOTS structure, are implemented in search strategies using the study type query, Boolean search, and Boolean filter.

- Study type query: consists of expressions that retrieve the study designs that are eligible for inclusion in the body of evidence as defined in the criteria (i.e., RCTs, SRs, prospective cohort studies, etc.)
- Boolean search: implements expressions for (PICOTS)
- Boolean filter: implements an extension of search or comparator criterion

Each of the components may use NOT queries to implement exceptions.

In addition to the strict Boolean strategy, results are ranked using keywords specified for integrated ranking of the TeraText Rank Engine and Content Analyst Conceptual Engine. Ranking helps to identify the most relevant citations first, as the titles and abstracts are analyzed for the presence and frequency of the keywords.

Critical Question 1: Search Strategy

Among overweight and obese adults, does achievement of reduction in body weight with lifestyle and pharmacological interventions affect CVD risk factors, CVD events, morbidity, and mortality?

a. Does this effect vary across population subgroups defined by the following demographic and clinical characteristics:

- Age
- Sex
- Race/ethnicity
- BMI

- Baseline waist circumference (WC)
- Presence or absence of comorbid conditions
- Presence or absence of CVD risk factors

b. What amount (shown as percent lost, pounds lost, etc.) of weight loss is necessary to achieve benefit with respect to CVD risk factors, morbidity, and mortality?

- Are there benefits on CVD risk factors, CVD events morbidity, and mortality from weight loss?
- What are the benefits of more significant weight loss?

c. What is the effect of sustained weight loss for 2 or more years in individuals who are overweight or obese on CVD risk factors, CVD events, and health and psychological outcomes?

- What percent of weight loss needs to be maintained at 2 or more years to be associated with health benefits?

Study Type Query

Study types eligible for CQ1: SRs or MA).

- {Systematic Review}

Boolean Search

(

- (publicationYear >1997)
- AND (subject,title,abstract=("Overweight" or "Obesity" or "Obesity Morbid" or "Body Mass" or "Waist Circumference") or obese or majorSubject=("Weight Loss" or "Diet, Reducing"))
- AND (subject,title,abstract=("Weight Loss" or "Diet, Reducing") or (weight %5 reduc?))
- AND ((subject,qualifier,abstract,title=(mortality or morbidity or prevalence or incidence or physiopathology or epidemiology or "Treatment outcome" or therapy or "therapeutic use" or Risk factor? or "Fatal Outcome" or "Survival Rate" or Myocardial Infarction? or "Myocardial Stunning" or "No-Reflow Phenomenon" or "Shock, Cardiogenic" or Heart Failure? or "Dyspnea, Paroxysmal" or "Edema, Cardiac" or Stroke? or "Kidney Failure, Chronic") or death? or died or fatal or ((CVD or CV or cardiovascular or CHF or heart failure) %2 (event?

or hospitalization)) or Chronic Kidney Failure or CKD or Chronic Kidney Disease or End Stage Renal or ESRD)

  - or (((subject=("Fatty Liver")) with (qualifier=(blood or diagnosis))) not subject=Alcohol?) or nonalcoholic steatohepatitis or NASH
  - or ((subject=(Depression)) with (qualifier=(blood or diagnosis)))
  - or ((subject=(Hypertension or Cholesterol or Diabetes or Metabolic Syndrome X)) with (qualifier=(blood or diagnosis)))
  - or subject,title,abstract=("Blood pressure" and (systol? or diastol?)) or BP or SBP or DPB or hypertensive or non-hypertensive or blood pressure goal?
  - or ((subject=(Triglycerides or "Cholesterol" or "Apolipoproteins B" or Apolipoprotein B? or "Apolipoprotein A-I" or "Apolipoproteins A" or Apolipoproteins or "Lipoprotein(a)" or "Apoprotein(a)")) with (qualifier=(blood or metabolism))) or Triglyceride? or HDL Cholesterol or HDL-C or Apolipoprotein B? or apoB or Apolipoprotein A? or apoA-1 or Lp(a) or "Lipoprotein (a)" or "Apoprotein(a)" or total cholesterol or TC or LDL particle number or LDL-P or (LDL and subject,abstract,title="Particle Size") or lipid goal?
  - or subject="Glucose Tolerance Test" or ((subject=(Blood Glucose or Insulin or "Hemoglobin A, Glycosylated")) with (qualifier=(blood or diagnostic))) or (fasting %2 glucose) or (fasting %2 insulin) or A1c or HOMA or IVGTT or OGTT or glycemic control goal?
  - or ((subject="C-Reactive Protein") with (qualifier=(metabolism or analysis))) or hs-CRP or CRP or hsCRP or "C-reactive protein"
  -)

- AND ((((Subject=(Obesity or Overweight)) with (qualifier=("drug therapy" or epidemiology)))) or placebo
  - or subject,title,abstract=("Anti-Obesity Agent?" or "Appetite Depressant?")
  - or subject,title,abstract=(Diethylpropion or Phenmetrazine or Phentermine or Phenylpropanolamine)
  - or substance,abstract,title=(amylin or benfluorex or butenolide or "FG 7142" or lipid mobilizing substance or norpseudoephedrine or oleoyl-estrone or orlistat or perflubron or pyroglutamyl-histidyl-glycine or satietin or sibutramine or topiramate)
  - or qualifier=("therapeutic use" or "drug effects")
  - or qualifier="diet therapy"
  - or subject=("Life style" or "Life Change Events" or Lifestyle or "Risk Reduction Behavior" or "Behavior Therapy" or Exercise or "Physical Fitness") or "lifestyle intervention" or "energy intake" or cardiorespiratory fitness
  - or majorSubject=("Weight Loss" or Obesity or Overweight or "Body Mass Index" or Diet or "Psychotherapy, Group")
  - or subject,title,abstract="Combined Modality Therapy"

  - or ((((Subject=(Obesity or Overweight)) with (qualifier="diet therapy"))) or (Subject=(Obesity or Overweight) and Subject=Diet))
  - or (diet %2 exercise)
  - or ((pharmacological or non-pharmacological) %2 intervention?)
  -)

- AND (subject,title,abstract="Body Weight" or subject="Body Weight Changes"
  - or subject,title,abstract="Body Mass Index" or BMI
  - or subject,title,abstract=("Weight Loss" or weight)
  - or subject,title,abstract=("Waist-Hip Ratio" or "Waist Circumference")
  - or subject,title,abstract=("Body Fat Distribution" or Adiposity))
  - **)**
- NOT {Non-Westernized Countries}
- NOT majorSubject=("Dietary Supplements")
- NOT majorSubject=(Accreditation)
- NOT majorSubject=("Digestive System Surgical Procedures" or "Bariatric Surgery" or "Gastric Bypass" or "Gastric Balloon" or Laparoscopy or Gastroplasty or Coronary Artery Bypass or Gastrectomy or "Biliopancreatic Diversion")
- NOT (((subject=("Digestive System Surgical Procedures" or "Bariatric Surgery" or "Gastric Bypass" or "Gastric Balloon" or Laparoscopy or Gastroplasty or Coronary Artery Bypass or Gastrectomy or Biliopancreatic Diversion)) with (qualifier=(instrumentation or methods or adverse effects or economics or standards or statistics))))
- NOT subject=("Postoperative Complications" or Reoperation or "Postoperative Period" or "Length of Stay" or "Reconstructive Surgical Procedures" or "Equipment and Supplies" or "Preoperative Care" or "Postoperative Care" or "Prenatal Care" or "Weight Gain and Pregnancy" or "Pregnancy Complications")
- NOT subject=("Equipment Design" or "Advertising as Topic")
- NOT (subject=("Pilot Projects") or pilot study)
- NOT subject=((child or adolescent) not (adult or aged))
- NOT subject=("Child Nutrition" or "Child Behavior" or "Child, Preschool" or "Child Development" or "Infant Food")
- NOT subject=(Heel or Foot diseases or Cosmetic techniques or Hair Removal or Hirsutism)

- NOT majorSubject=("Research Design" or Questionnaires)
- NOT (((self-report?) %3 weight) not (qualifier,abstract,title,subject=mortality or subject,title,abstract=(Myocardial Infarction or Heart Failure or Stroke or CVD event? or CHD event?)))
- NOT ((week or days) not (week? or month? or year?))
- NOT (subject=(Animals or Venoms))
- NOT (title=(binge eating or schizophrenia))
- NOT (genre=randomized)
- NOT (recordStatus=delete)

Critical Question 1: Search Strategy Results and PRISMA Diagram

CQ1 was initially intended to be a de novo SR of original studies plus SRs/MAs). In 2011, the question was de-scoped and restricted to SRs/MAs only. The initial and subsequent exclusive supplemental SRs/MAs search included the bibliographic databases listed below. The search strategy presented above is the final strategy, which queries for SRs/MAs.

- PubMed from January 2000 to October 2011
- CINAHL from January 2000 to July 2008
- EMBASE from January 2000 to July 2008
- PsycInfo from January 2000 to July 2008
- Evidence-based Medicine Cochrane Libraries from January 2000 to July 2008
- Biological Abstracts from January 2004 to July 2008
- Wilson Social Sciences Abstracts from January 2000 to July 2008

The literature search for CQ1 included an electronic search of the Central Repository for SRs/MAs published in the literature from January 2000 to October 2011. The Central Repository contains citations pulled from seven literature databases: PubMed, CINAHL, EMBASE, PsychInfo,

EBM, Biological Abstracts, and Wilson Social Sciences Abstracts. The search produced 1,630 citations, with 3 additional citations identified from non-search sources (i.e., by the panel members) (19-21).

Figure 1 below of the PRISMA diagram outlines the flow of information from the literature search through the various steps used in the systematic review process.

Two reviewers independently screened the titles and abstracts of 1,633 publications against the I/E criteria, resulting in 936 publications being excluded and 697 publications being retrieved for full-text review to further assess eligibility. Then, two reviewers independently screened and assessed the 697 full-text publications for eligibility by applying the I/E criteria; 669 of these publications were excluded based on one or more of the I/E criteria (see specified rationale as noted in the PRISMA).

Forty-two of the 697 full-text publications met the criteria and were included. The quality (internal validity) of these 42 publications was assessed using the quality assessment tool developed to assess SRs/MAs or RCTs (see Appendix 2). Of these, 14 publications were rated poor quality; rationales for the poor quality studies are included in Appendix 3. The remaining 28 publications were rated good or fair quality and included in the evidence base that was used to formulate the evidence statements and recommendations.

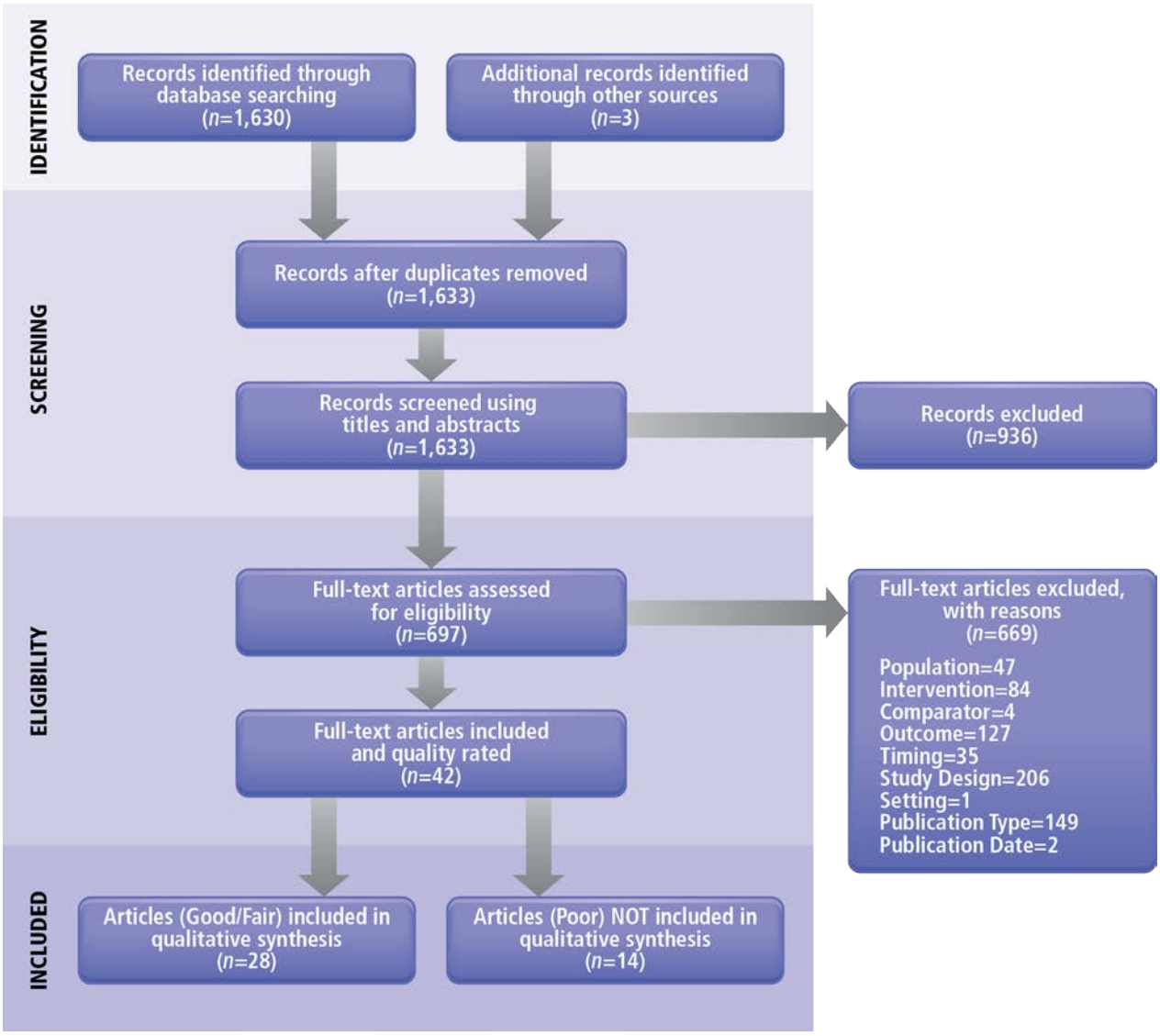
The NHLBI approved using relevant data from an RCT study (i.e., Look AHEAD). The following is the rationale. Look AHEAD is a prospective, multicenter, randomized clinical trial that examined the effects of ILI vs. usual diabetes care, referred to as diabetes support and education,on CV morbidity and mortality in 5,145 overweight or obese participants with type 2 diabetes. This single trial provides data on more patients than the two MAs by Norris (50) and

Norris (47) (*N*=4,659), almost as many as the Norris (49) (*N*=5,956) and Orozco (62) (*N*=5,956). They have provided 4-year comparison outcome data (20) and, more importantly, 1-year dose-response data that relates the amount of weight loss to predefined CVD risk factors (19).

Subsequent to receiving approval to include relevant data from Look AHEAD, an additional search was made (of the de novo citations included during the early screening stages) for RCTs of similar size to the Look AHEAD (≥5,000); through this process; no additional relevant studies were found.

A total of 42 publications were included in the CQ1 evidence base; 39 were SRs/MA and 3 were RCTs. The panel members reviewed the final articles on the include list along with their quality ratings and had the opportunity to raise questions. For CQ1, panel members created spreadsheets (containing key information from the SRs/MAs and the Look AHEAD studies); these spreadsheets (cross-checked by the methodology and SR teams) formed the basis for panel deliberations.

Figure A–1. PRISMA Diagram Showing Selection of Articles for CQ1.



Key:
Details for each exclusion rationale are determined by the I/E criteria for the question, reproduced below. The I/E criteria are also available in Section 5a.

Table A–5. Criteria for Selection of Publications for CQ1

	Inclusions	Exclusions
Population	Adults	• Children • Animals studies
Intervention	Single or multi-lifestyle or pharmacologic interventions	• Any pharmacological agents that are not the FDA-approved for long-term treatment of obesity • Bariatric surgical interventions (LAGB; laparascopic RYGB; open RYGB;

	Inclusions	Exclusions
		biliopancreatic bypass/duodenal switch; GS)
Comparator	• No intervention (except for in pharmacological interventions where the comparator can be lifestyle) • Usual care, control, or minimal treatment	
Outcome	Reduction in body weight as measured by: • Weight (kg, lbs, %) • Body fat measures: (BMI and BMI change) • WC • Waist-hip ratio • Percent body fat (includes body composition changes) • Weight loss maintenance • Percent reduction of excess weight Must have one a body weight measure plus one or more of the following outcomes <u>CVD Events (allows for self-reported weight)</u> • Myocardial infarction • Heart Failure • Hospitalization for HF or stroke <u>CVD Risk Factors</u> • SBP or DBP • Total cholesterol, HDL-C), LDL-C, Non-HDL-C, triglycerides • Fasting insulin, fasting glucose, HbA1c, diagnosis of diabetes • Smoking status • CRP	Self-reported weight (only allowed in studies reporting CVD events; for risk factors, the studies have to report measured weight) Studies that combine weight loss and weight maintenance after successful weight loss results in a manner that does not allow the two study designs to be independently assessed.
	<u>Morbidity</u> • CHD/CVD • Chronic renal failure • Nonalcoholic steatohepatitis • Depression <u>Mortality</u> • CVD-related • All-cause <u>Body composition changes</u> <u>Quality of Life</u> • Function • Disability	
Timing	• Intervention period: no limits	Follow-up of less than 6 mos

	Inclusions	Exclusions
	• Follow-up period is 6 mos or more, with breakdowns where possible by: ≥6 months to 12 mos; greater than one yr.	
Setting	Westernized countries: • United States • European Union • Australia • New Zealand • Israel Any clinical or research setting	Countries not applicable to western weight goals and diets
Study Design	• SRs of RCTs or controlled clinical trials	All other studies
Publication Type	Published SRs/MAs studies	• Unpublished literature – Unpublished industry-sponsored trials – Other unpublished data • FDA Medical and Statistical reviews • Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Publication Time Frame	• Search for SRs/MAs between 2000 and October 2011	• Studies published before 2000

Critical Question 2: Search Strategy

a. Are the current cut-point values for overweight (BMI 25.0 to 29.9 kg/m^2) and obesity (BMI ≥30 kg/m^2) compared with BMI 18.5 to 24.9 kg/m^2 associated with elevated CVD-related risk (defined below)? Are the WC cutpoints of >102 cm (M) and >88 cm (F) associated with elevated CVD-related risk (defined below)? How do these cut-points compare with other cutpoints in terms of elevated CVD risk?

- Fatal and non-fatal CHD, stroke, and CVD
- Overall mortality
- Incident type 2 diabetes mellitus
- Incident dyslipidemia

- Incident hypertension

b. Are differences across population subgroups in the relationships of BMI and WC cut-points with CVD sufficiently large to warrant different cutpoints? If so, what should they be?

- Fatal and non-fatal CHD, stroke, and CVD
- Overall mortality
- Incident type 2 diabetes mellitus
- Incident dyslipidemia
- Incident hypertension
- Groups being considered include:
- Age
- Sex (both M and F)
- Race/ethnicity (African American, Hispanic, Native American, Asian, Caucasian)

c. What are the associations between maintaining weight and weight gain with elevated CVD-related risk in normal weight, overweight, and obese adults?

Study Type Query

Study types eligible for CQ2: SRs, MAs, or pooled analyses focusing only on CHD, CVD, and mortality as outcomes.

- ({Systematic Review} or
  - ((subject=(Longitudinal Studies) or pooling or pooled or collaborative anal? or genre,title,abstract=Multicenter or (stratif? %5 study center) or Mantel? or Peto or DerSimonian or Laird or Woolf or subject,title,abstract=(Bayesian or (Sensitivity and Specificity)) or random effects or Meta-regression or (integrat? anal?) or between-study variance or ((variance or heterogeneity) %2 stud?)) **and**
  - majorSubject,title=("Body Mass" or "Waist Circumference" or BMI or Anthropometry or "Body Weights and Measures")))
- AND
- ({Cardiovascular Diseases} or

- subject,qualifier,title,abstract=mortality or death? or died or subject=("Cause of Death" or "Fatal Outcome" or "Survival Rate") or subject,title,abstract=(Diabetes or "Glucose Metabolism Disorders" or "Metabolic Syndrome X" or Dyslipid? or Hyperlipid? or Hypercholesterol? or Hyperlipoprotein? or Hypertriglycerid? or "Tangier Disease" or "Smith Lemli Opitz Syndrome" or "Hyperglycemia" or "Glucose Intolerance" or "Prediabetic State" or "Insulin Resistance")

Boolean Search

- (subject,title,abstract=("Body Mass" or "Waist Circumference" or BMI or Anthropometry or "Body Weights and Measures")
  AND ((publicationYear>1999 and publicationYear<2012)))
- NOT {Non-Westernized Countries}NOT (majorSubject=(Angioplasty or Laparoscopy))
- NOT (subject=”Postoperative Complications”)
- NOT (subject,title,abstract=malnutrition)
- NOT (subject=(Vaccines))
- NOT ((subject=("Bariatric Surgery" or Gastroplasty or Gastric Bypass)) with (qualifier="adverse effects"))
- NOT ((subject=(Obesity)) with (qualifier=surgery))
- NOT (title=chemotherapy)
- NOT (subject=("Single-blind method" or "Double-blind method") or genre=Randomized)
- NOT subject=("Postoperative Complications" or Reoperation or "Postoperative Period" or "Length of Stay" or "Reconstructive Surgical Procedures" or "Equipment and Supplies" or "Preoperative Care" or "Postoperative Care" or "Prenatal Care" or "Weight Gain and Pregnancy" or "Pregnancy Complications")
- NOT subject=("Equipment Design" or "Advertising as Topic")
- NOT (subject=("Pilot Projects") or pilot study)
- NOT subject=((child or adolescent) not (adult or aged))
- NOT subject=("Child Nutrition" or "Child Behavior" or "Child Development" or "Infant Food")
- NOT subject=(Heel or Foot diseases or Cosmetic techniques or Hair Removal or Hirsutism)

Critical Question 2: Search Strategy Results and PRISMA Diagram

CQ 2 was initially intended to be a de novo SR of original studies plus SRs and MAs. In 2011, CQ2 was de-scoped and restricted to SRs/MAs only. The initial and subsequent exclusive supplemental SRs/MAs search included the bibliographic databases listed below. The search strategy presented above is the final strategy, which queries for SRs/MAs.

- PubMed from January 2000 to October 2011
- CINAHL from January 2000 to July 2008
- EMBASE from January 2000 to July 2008
- PsycInfo from January 2000 to July 2008
- Evidence-Based Medicine Cochrane Libraries from January 2000 to July 2008
- Biological Abstracts from January 2004 to July 2008
- Wilson Social Sciences Abstracts from January 2000 to July 2008

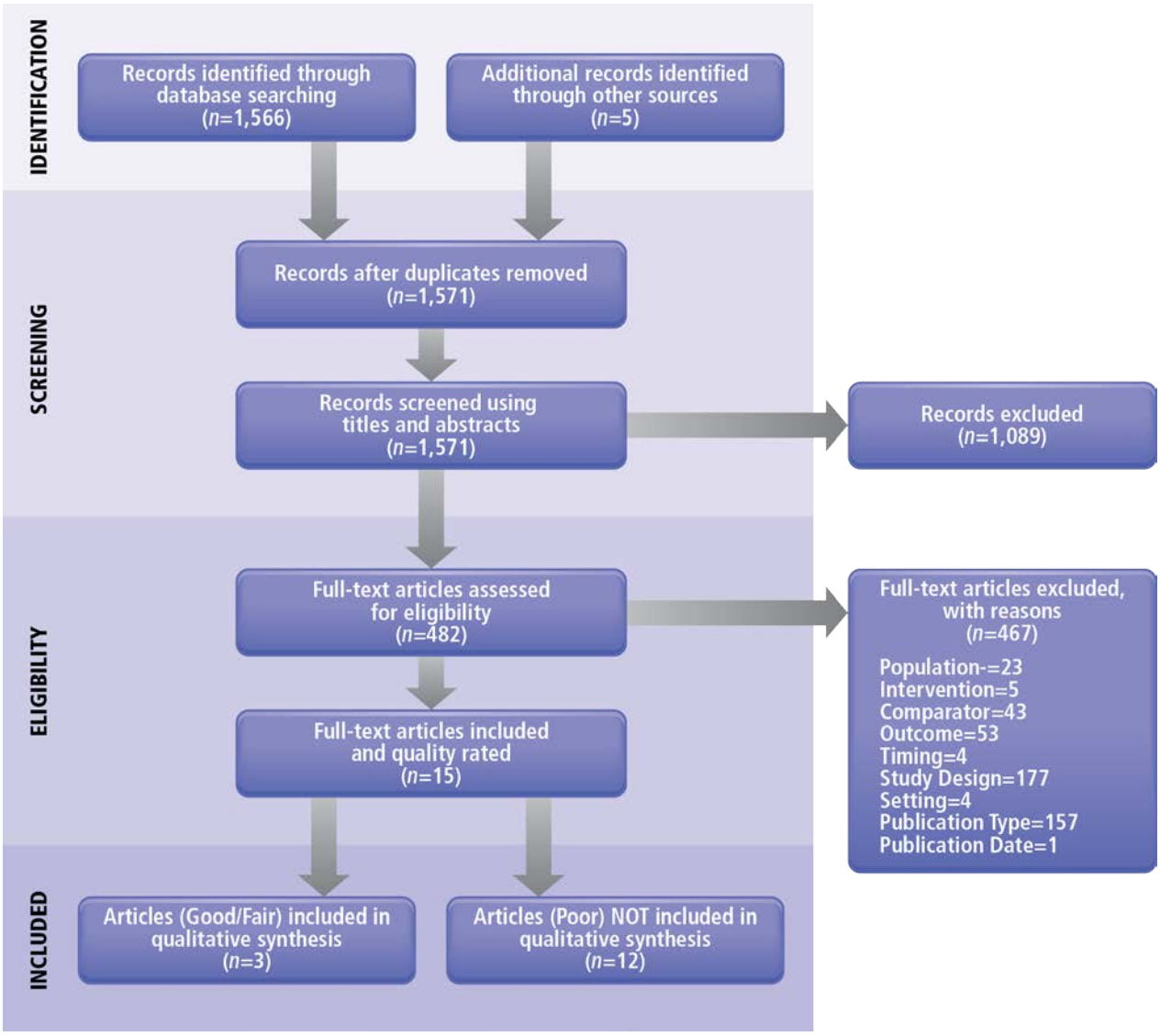
The literature search for CQ2 included an electronic search of the Central Repository for SRs/MAs published in the literature from January 2000 to October 2011. The Central Repository contains citations pulled from seven literature databases: PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts. The search produced 1,566 citations, with 5 additional citations identified from non-search sources (i.e., by the panel members). Three of the five citations met the criteria and were eligible for inclusion in the CQ2 evidence base (64-66). In contrast, the other two citations did not meet the criteria and were excluded from the CQ2 evidence base (67,68).

Figure A–2, the PRISMA diagram, outlines the flow of information from the literature search through the various steps used in the SR process.

Two reviewers independently screened the titles and abstracts of 1,571 publications against the I/E criteria, resulting in 1,089 publications being excluded and 482 publications being retrieved for full-text review to further assess eligibility. Next, two reviewers independently screened and assessed 482 full-text publications for eligibility by applying the I/E criteria; 467 of these publications were excluded based on one or more of the I/E criteria (see specified rationale as noted in the PRISMA).

Fifteen of the 482 full-text publications met the criteria and were included. The quality (internal validity) of these 15 publications was assessed using the quality assessment tool developed to assess SRs/MAs (see Appendix 2). Of these, 12 publications were rated as poor quality; however, they were used as part of the evidence base since NHLBI policy indicated that poor studies could be used as part of the evidence base if the majority of included studies were not rated good or fair. Rationales for the poor quality studies are included in Appendix 3. The remaining three SRs/MAs were rated good or fair quality and included in the evidence base that was used to formulate the evidence statements and recommendations. Panel members reviewed the final articles on the include list, along with their quality ratings, and had the opportunity to raise questions. Some SRs/MAs previously deemed to be of poor quality were upgraded to fair quality upon closer review by the methodology team, who made the final decision (78,79). For this question, panel members created spreadsheets containing key information from the SRs/MAs; these spreadsheets, cross-checked by the methodology and SR teams), formed the basis for panel deliberations.

Figure A–2. PRISMA Diagram Showing Selection of Articles for CQ2



Key:
Details for each exclusion rationale are determined by the I/E criteria for the question, reproduced below. The I/E criteria are also available in Section 6a.

Table A–6. Criteria for Selection of Publications for CQ2

	Inclusions	Exclusions
Population	• Adults • Normal weight (BMI 18.5 to 24.9) or • Overweight (BMI 25.0 to 29.9) or • Obese (BMI ≥30.0)	• Children • Animals studies • Studies on specific populations (e.g., sample with coronary artery disease, cancer)
Intervention	No interventions	Studies not reporting BMI or WC cutpoints

	Inclusions	Exclusions
Comparator	• BMI: must compare 2 or more BMI categories or include BMI as a continuous variable • WC : must compare 2 or more WC categories or include WC as a continuous analysis	Studies not reporting BMI or WC cutpoints
Outcome	*Study must report BMI or WC as an independent variable* Must have one or more of the following outcomes: <u>CVD Events</u> • Myocardial infarction • Heart failure • Hospitalization for heart failure • Stroke <u>CVD Risk</u> • Elevated SBP or DBP • Dyslipidemia as measured by total cholesterol, HDL-C, LDL-C, Non-HDL-C, triglycerides • Dysglycemia as measured by fasting insulin, fasting glucose, HbA1c (includes prediabetes), incident cases of type 2 diabetes <u>Morbidity</u> • CHD/CVD • Diabetes <u>Mortality</u> • CVD-related • Overall	**Studies focused on predicting risk** ***Note: No longer excluding self-reported weight data***
Timing	• Intervention or exposure period: no limits • Follow-up period is 6 mos or more	• Follow-up of less than 6 mos
Study Design	• SRs (qualitative summary or narrative review article), or MAs (quantitative summary of published data) or pooled analyses (an analysis of independent primary studies that do not have identical protocols for all measures and are collected in more than one distinct examination center) focusing only on CHD, CVD, and mortality as outcomes) • Sample size:	• Case series, case reports • Cross-sectional studies

	Inclusions	Exclusions
	– For fatal and non-fatal CHD, stroke, and CVD, overall mortality, type 2 diabetes mellitus, dysglycemia (impaired glucose tolerance, impaired fasting glucose, prediabetes): sample size ≥1,000 incident outcomes or ≥500 for minority groups – For abnormal lipids (LDL, HDL, triglycerides), hypertension or increased blood pressure, and elevated CRP: sample size ≥500	
Setting	The majority (>50%) of studies in MAs, SRs, or pooled analyses from Westernized countries: • United States • Canada • Europe • Australia • New Zealand • Israel Any clinical or research setting	
Publication Type	Published SRs/MAs and pooled studies	• Studies examining a single cohort • Other unpublished literature – Unpublished data – Unpublished industry-sponsored trials • FDA Medical and Statistical reviews • Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Publication Time Frame	• Searches for SRs/MA and pooled studies were conducted between 2000 and October 2011	• Studies published before 2000

Critical Question 3: Search Strategy

CQ3 has two parts:

a. In overweight or obese adults, what is the comparative efficacy/effectiveness of diets of differing forms and structures (macronutrient content, carbohydrate and fat quality, nutrient

density, amount of energy deficit, dietary pattern) or other dietary weight loss strategies (e.g., meal timing, portion controlled meal replacements) in achieving or maintaining weight loss?

b. During weight loss or weight maintenance after weight loss, what are the comparative health benefits or harms of the above diets and other dietary weight loss strategies?

Study Type Query

Study types eligible for CQ3: RCTs, SRs of RCTs, or controlled clinical trials. No restrictions on sample size.

Exclusions: Case series, case reports, before-after studies, unpublished literature, unpublished industry-sponsored trials, other unpublished data, FDA Medical and Statistical reviews, theses, studies published only as abstracts, letters, commentaries and opinion pieces, and non-SRs. Results are not compared according to randomized treatment assignments. Dropout rate ≥40 percent after 6 months.

- {RCT} OR {Systematic Review} OR
- NOT genre,title,subject=(case reports or case study or case series or before after)
- NOT (title=(case report or commentary) OR genre=(letter or abstract or newspaper article or comment?))

Boolean Search

(

(publicationYear>1997 and publicationYear<2010 and language=eng?)

- AND (overweight? or obesity or obese or subject=(obesity or overweight) or (("body mass index" or BMI) %3 (2? or 3? or 4?)) or majorSubject=("Weight Loss" or "Diet, Reducing"))
- AND (diet? or meal? or low-glycemic index or glycemic load or therapeutic lifestyle change? or TLC or energy density or portion control or volumetrics or subject=(diet or dietary or Energy Intake or Caloric Restriction))

- AND (weight %3 los? or weight reduc? or weight maintenance or subject="weight loss" or subject="body weight" or subject="weight reduction" or majorSubject="Diet, Reducing")

)

- NOT majorSubject=(Accreditation)
- NOT (((subject=("Digestive System Surgical Procedures" or "Bariatric Surgery" or "Gastric Bypass" or "Gastric Balloon" or Laparoscopy or Gastroplasty or Coronary Artery Bypass or Gastrectomy or Biliopancreatic Diversion)) with (qualifier=(instrumentation or methods or adverse effects or economics or standards or statistics))))
- NOT subject=("Postoperative Complications" or Reoperation or "Postoperative Period" or "Length of Stay" or "Reconstructive Surgical Procedures" or "Equipment and Supplies" or "Preoperative Care" or "Postoperative Care" or "Prenatal Care" or "Weight Gain and Pregnancy" or "Pregnancy Complications")
- NOT subject=("Equipment Design" or "Advertising as Topic")
- NOT (subject=("Pilot Projects") or pilot study)
- NOT subject=((child or adolescent) not (adult or aged))
- NOT subject=("Child Nutrition" or "Child Behavior" or "Child, Preschool" or "Child Development" or "Infant Food")
- NOT subject=(Heel or Foot diseases or Cosmetic techniques or Hair Removal or Hirsutism)
- NOT subject=("Africa" OR "Africa Northern" OR "Algeria" OR "Egypt" OR "Libya" OR "Morocco" OR "Tunisia" OR "Africa South of the Sahara" OR "Africa Central" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Congo" OR "Gabon" OR "Democratic Republic of the Congo" OR "Equatorial Guinea" OR "Africa Eastern" OR "Burundi" OR "Ethiopia" OR "Kenya" OR "Rwanda" OR "Somalia" OR "Sudan" OR "Tanzania" OR "Uganda" OR "Djibouti" OR "Eritrea" OR "Africa Southern" OR "Angola" OR "Botswana" OR "Lesotho" OR "Malawi" OR "Mozambique" OR "Namibia" OR "South Africa" OR "Swaziland" OR "Zambia" OR "Zimbabwe" OR "Africa Western" OR "Benin" OR "Burkina Faso" OR "Gambia" OR "Ghana" OR "Guinea Bissau" OR "Cote d Ivoire" OR "Liberia" OR "Mali" OR "Mauritania" OR "Niger" OR "Nigeria" OR "Senegal" OR "Sierra Leone" OR "Togo" OR "Guinea" OR "Cape Verde" OR "Americas" OR "Central America" OR "Belize" OR "Costa Rica" OR "El Salvador" OR "Guatemala" OR "Honduras" OR "Nicaragua" OR "Panama" OR "Panama Canal Zone" OR "Latin America" OR "South America" OR "Argentina" OR "Bolivia" OR "Brazil" OR "Chile" OR "Colombia" OR "Ecuador" OR "French Guiana" OR "Guyana" OR "Paraguay" OR "Peru" OR "Suriname" OR "Uruguay" OR "Venezuela" OR "Caribbean Region" OR "West Indies" OR "Barbuda and Antigua" OR "Bahamas" OR "Barbados" OR "Cuba" OR "Dominican Republic" OR "Haiti" OR "Jamaica" OR "Martinique" OR "Netherlands Antilles" OR "Puerto Rico" OR "Trinidad

and Tobago" OR "Virgin Islands of the United States" OR "Dominica" OR "Grenada" OR "Guadeloupe" OR "Saint Lucia" OR "Saint Vincent and the Grenadines" OR "Saint Kitts and Nevis" OR "Antarctic Regions" OR "Arctic Regions" OR "Asia" OR "Asia Central" OR "Kazakhstan" OR "Kyrgyzstan" OR "Tajikistan" OR "Turkmenistan" OR "Uzbekistan" OR "Asia Southeastern" OR "Borneo" OR "Brunei" OR "Myanmar" OR "Cambodia" OR "Indonesia" OR "Laos" OR "Malaysia" OR "Mekong Valley" OR "Philippines" OR "Singapore" OR "Thailand" OR "Vietnam" OR "East Timor" OR "Asia Western" OR "Bangladesh" OR "Bhutan" OR "India" OR "Sikkim" OR "Middle East" OR "Afghanistan" OR "Bahrain" OR "Iran" OR "Iraq" OR "Jordan" OR "Kuwait" OR "Lebanon" OR "Oman" OR "Qatar" OR "Saudi Arabia" OR "Syria" OR "Turkey" OR "United Arab Emirates" OR "Yemen" OR "Nepal" OR "Pakistan" OR "Sri Lanka" OR "Far East" OR "China" OR "Hong Kong" OR "Tibet" OR "Japan" OR "Tokyo" OR "Korea" OR "Macau" OR "Mongolia" OR "Taiwan" OR "Atlantic Islands" OR "Azores" OR "Bermuda" OR "Falkland Islands")

- NOT majorSubject=("Research Design" or Questionnaires)
- NOT (subject=(Animals or Venoms))
- NOT (recordStatus=delete)

Boolean Filter

The Boolean filter in the CQ3 search strategy implements the intervention criterion to reflect dietary weight loss intervention.

(abstract,title,qualifier="diet therapy" and abstract,title,subject="weight loss")

- OR ((qualifier="diet therapy" or (diet? %3 therap?) or majorSubject=(Diet or "caloric restriction" or "glycemic index")) and (weight %3 los? or weight reduc? or weight maintenance or subject="weight loss"))
- OR (title,abstract,subject=diet? and majorSubject="weight loss")
- OR ((subject="weight loss") with (qualifier=physiology))
- OR ((overweight? or obes?) and diet? and (weight loss or weight %2 reduc?))
- OR (majorSubject="Diet, Reducing")
- OR genre=(Comparative Study or Meta-Analysis)

Critical Question 3: Search Strategy Results and PRISMA Diagram

The following databases were searched for RCTs and SRs and MAs of RCTs or controlled clinical trials to answer CQ3:

- PubMed from January 1998 to December 2009
- CINAHL from January 1998 to July 2008
- EMBASE from January 1998 to July 2008
- PsycInfo from January 1998 to July 2008
- Evidence-based Medicine Cochrane Libraries from January 1998 to July 2008
- Biological Abstracts from January 2004 to July 2008
- Wilson Social Sciences Abstracts from January 1998 to July 2008

The literature search for CQ3 included an electronic search of the Central Repository for randomized clinical trials or controlled clinical trials published in the literature from January 1998 to December 2009. The Central Repository contains citations pulled from seven literature databases (PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts). The search produced 1,416 citations, with 6 additional citations identified from non-search sources, i.e., by panel members or hand search of SRs/MAs (obtained through the electronic search). Two of the six citations were published after December 31, 2009. Per NHLBI policy, certain lifestyle and obesity intervention studies published after the closing date could be allowed as exceptions. These studies must be RCTs in which each study arm contained at least 100 participants and was identified by experts' knowledgeable of the literature. One of the two citations published after December 2009 met the criteria and was eligible for inclusion in the CQ3 evidence base [Foster, 2010]. In contrast, the other citation did not meet the criteria and was excluded from the CQ3 evidence base [Larsen, 2010]. The remaining 4 citations were identified through non-search sources (i.e., hand search) by cross-checking the references

listed in 28 SRs/MAs. The SRs/MAs were only used for manual searches and were not part of the final evidence base. This manual cross-check was done to ensure that major studies were not missing from the evidence base. As a result of this cross-check, two of six studies were screened and found eligible for inclusion (94,95). Subsequently, the quality of these studies was rated as poor.

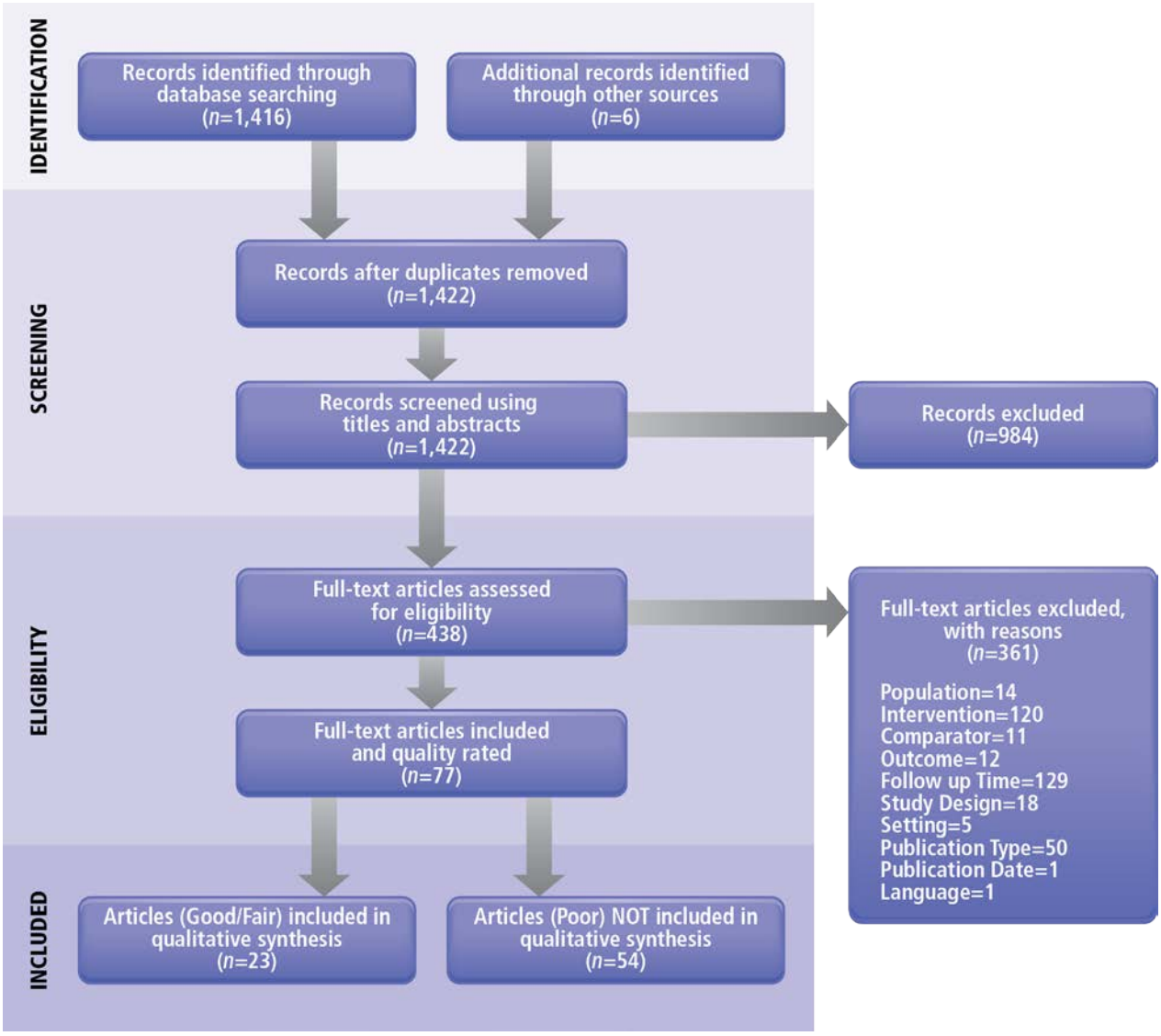
Figure 3, the PRISMA diagram for CQ3, outlines the flow of information from the literature search through the various steps used in the SR process.

Two reviewers independently screened the titles and abstracts of 1,422 publications against the I/E criteria, resulting in 984 publications being excluded and 438 publications being retrieved for full-text review to further assess eligibility. Next, two reviewers independently screened 438 full-text publications and assessed eligibility by applying the I/E criteria; 361 of these publications were excluded based on one or more of the I/E criteria (see specified rationale as noted in the PRISMA). Furthermore, the CQ3 work group noted that since the focus of the CQ is solely on the effect of different dietary approaches to weight loss, other possible interventions could not differ. So, studies were excluded if treatment arms differed in their behavioral approach, i.e., the amount of participant contact and amount or method of prescribed physical activity.

Seventy-seven of the 438 full-text publications met the criteria and were included. The quality (internal validity) of these 77 publications was assessed using the quality assessment tool developed to assess RCTs (see Appendix 2). Of these, 54 publications were excluded because they were rated as poor quality; 52 of these studies were rated poor due to the ITT and attrition rates. Rationales for all poor quality studies are included in Appendix 3. The remaining 17 RCTs (23 articles) were rated good or fair quality and included in the evidence base that was used

to formulate the evidence statements and recommendations. Panel members reviewed the final studies on the include list along with their quality ratings and had the opportunity to raise questions. Some trials previously deemed to be of fair or good quality were downgraded to poor quality upon closer review of evidence tables. These trials used completers analyses rather than ITT analysis and had overall attrition rates exceeding 10 percent. If the study reported only an analysis of completers and had attrition at <10 percent, it was allowed in the evidence base. Methodologists worked with the SR team to reevaluate these trials and make a final decision. Evidence tables and summary tables consisted only of data from the original publications of eligible RCTs; these tables formed the basis for panel deliberations.

Figure A–3. PRISMA Diagram Showing Selection of Articles for CQ3



Key:
Details for each exclusion rationale are determined by the inclusion and exclusion criteria for the question, reproduced below. The inclusion and exclusion criteria are also available in Section 7.2

Table A–7. Criteria for Selection of Publications for CQ3

	Inclusions	Exclusions
Population	Overweight (BMI 25.0 to 29.9) or obese (BMI ≥30.0) adults	• Children • Animals studies • Population not overweight (BMI 25.0 to 29.9) or obese (BMI ≥30.0) at baseline
Intervention	Diet defined as: • Low-calorie	• All other non-diet weight loss interventions

	Inclusions	Exclusions
	• VLCD • Low-fat • High-fiber • High-protein • High-carbohydrate • Low-carbohydrate • Scheduling (meals and meal pattern) • CHO counting • Meal replacement • Low-glycemic index • Glycemic load • DASH • Omni • Atkins • Vegetarian • Therapeutic Lifestyle Changes • Portfolio • Ketogenic • Mediterranean • South Beach • Zone • Ornish • Pritikin • Energy density • Portion control • Volumetrics	
Comparator	• No dietary intervention • Other dietary interventions • Multi-component intervention–if physical activity and behavior components standardized across treatment groups	• Bariatric surgical interventions (LAGB; laparascopic RYGB; open RYGB; biliopancreatic bypass/duodenal switch; GS) • Physical activity • Pharmacotherapy • Multi-component interventions
Outcome	Reduction in body weight as measured by: • Weight (kg, lbs, %) • BMI and BMI change, • WC • Waist-hip ratio, • % body fat • % reduction of excess weight • Weight loss maintenance **Must have one or more of the following outcomes:**	Outcomes by measure of self-report

	Inclusions	Exclusions
	Body weight measures **CVD Events** • Myocardial infarction • Heart failure • Hospitalization for heart failure or stroke **CVD Risk Factors** • SBP or DBP • Total cholesterol, HDL-C, LDL-C, Non-HDL-C, triglycerides • Fasting insulin, fasting glucose, HbA1c • CRP **Morbidity** • CHD/CVD • Chronic renal failure **Mortality** • CVD-related • All-cause	
Timing	• Intervention period: ≥3 mos • Follow-up period: ≥6 mos as measured from randomization.	• Intervention less than 3 mos • Follow-up of less than 6 mos
Setting	Westernized countries: • United States • European Union • Australia • New Zealand • Israel Any clinical or research setting	Countries not applicable to western weight goals and diets
Study Design	• RCTs • Sample size at least 15 subjects per treatment arm	• SRs of RCTs or controlled clinical trials • Case series, case reports, before-after studies • Results are not compared according to randomized treatment assignments • Dropout rate ≥40 percent after 6 mos
Language	• Abstract must be available in English	• Studies where the abstract only, and not the full text, is available in English • Full text translation into English must be feasible
Publication Type	• Published studies	• SRs/MAs • Unpublished literature – Unpublished industry-sponsored trials – Other unpublished data • FDA Medical and Statistical reviews

	Inclusions	Exclusions
		• Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Publication Time Frame	• Studies published in years 1998–2009 • Sentinel articles published after 2009 were also screened, provided they were RCTs and had ≥100 participants per treatment arm.	• Studies published before 1998

Critical Question 4: Search Strategy

CQ4 has two parts:

a. Among overweight and obese adults, what is the efficacy/effectiveness of a comprehensive lifestyle intervention program (i.e., comprised of diet, physical activity, and behavior therapy) in facilitating weight loss or maintenance of lost weight?

b. What characteristics of delivering comprehensive lifestyle interventions (e.g., frequency and duration of treatment, individual vs. group sessions, onsite vs. phone/e-mail contact) are associated with greater weight loss and weight loss maintenance?

Study Type Query

Study types eligible for CQ4:

1. For efficacy/effectiveness: RCTs, SRs. Sufficient information must have been presented about the intervention to replicate the study.
2. For adverse effects: RCTs, controlled clinical trials, SRs, cohort studies with a contemporaneous comparison group, case-control studies, large observational studies.
3. Post hoc analyses of large RCTs if analyses of randomized comparisons are included.

4. Exclusions: Case series, case reports, before-after studies, unpublished literature, unpublished industry-sponsored trials, other unpublished data, FDA Medical and Statistical reviews, theses, studies published only as abstracts, letters, commentaries and opinion pieces, non-SRs.

- {RCT} OR {Systematic Review} OR
- (subject=("Epidemiologic Studies" or "Cross Sectional Studies" or "Cohort Studies" or "Longitudinal Studies" or "Follow Up Studies" or "Prospective Studies" or "Case Control Studies" or "Cross-Over Studies" or "Retrospective Studies" or "Seroepidemiologic Studies" or "HIV Seroprevalence") OR
- (subject=("Controlled Clinical Trials as Topic" or "Randomized Controlled Trials as Topic") and abstract=?) OR
- genre=("Controlled Clinical Trial" OR "Validation Studies" OR "Multicenter Study" OR "Evaluation Studies") OR
- observational stud? or epidemiologic stud? or cross sectional stud? or cohort stud? or longitudinal stud? or follow up stud? or prospective stud? or case control stud? or cross-over stud? or retrospective stud? or title,subject=random? OR
- (((subject=(Obesity or Overweight)) with (qualifier=(epidemiology or etiology or mortality or ethnology))) not genre=review)) AND language=eng?)
- NOT genre,title,subject=(case reports or case study or case series or before-after)
- NOT (title=(case report or commentary) OR genre=(letter or abstract or newspaper article or comment?))

Boolean Search

(

- (publicationYear>1997 AND publicationYear<2010 AND language=eng? and abstract=?)
- AND (subject,title,abstract=("weight loss" or "weight reduction" or "weight maintenance") or (weight %5 reduc?))
- AND (subject,title,abstract=(Overweight or Obesity or Obesity Morbid or Prader Willi Syndrome) or ("weight loss" %2 maintenance) or obese or (("body mass index" or BMI or BMIs) !13 (2? or 3? or 4?)))
- AND (subject,title,abstract=("Body Weight Changes" or "Weight Gain" or "Weight Loss" or "Emaciation" or "Cachexia") or (weight %2 change?) or "baseline weight" or subject,title,abstract=("Body Mass Index" or "Waist Circumference" or "Waist-Hip Ratio" or

"Body Fat Distribution" or "Adiposity") or "percent body fat" or "Percent reduction of excess weight" or BMI or BMIs or WC or WCs or kg)

- AND (subject,title,abstract=("Life Style" OR "Self care" or "Life Change Events" OR "Risk Reduction Behavior" OR "Behavior Therapy" OR "Aversive Therapy" OR "Biofeedback Psychology" OR "Desensitization Psychologic" OR "Implosive Therapy" OR "Relaxation Therapy" OR "Meditation" OR "Cognitive Therapy" OR "Sleep Phase Chronotherapy" OR "Diet" OR "Fasting" OR "Energy Intake" OR "Caloric Restriction" OR meal replacement? or "Diet Therapy" or "Exercise" OR "Motor Activity" or "physical activity" OR "Freezing Reaction Cataleptic" OR "Immobility Response Tonic" OR "Running" OR "Jogging" OR "Swimming" OR "Walking" OR Resistance Training OR "self-monitoring" OR "self-regulation" OR "Diet Records" OR "activity records" OR lifestyle) or ((subject=(Obesity or Overweight)) with (qualifier=therapy)))
)

- NOT (Subject,title=("Complementary Therapies" or Acupressure or Electroacupuncture or Meridians or Moxibustion or Anthroposophy or Auriculotherapy or Holistic Health or Homeopathy or "Medicine, Traditional" or "Mind-Body Therapies" or Aromatherapy or Biofeedback or "Breathing Exercises" or Hypnosis or "Imagery (Psychotherapy)" or "Laughter Therapy" or Meditation or "Mental Healing" or "Mind-Body Relations (Metaphysics)" or Psychophysiology or "Relaxation Therapy" or "Tai Ji" or "Therapeutic Touch" or Yoga or "Musculoskeletal Manipulations" or Massage or "Myofunctional Therapy" or Naturopathy or Organotherapy or "Tissue Therapy" or Phytotherapy or Aromatherapy or "Eclecticism, Historical" or Reflexotherapy or Rejuvenation or "Sensory Art Therapies" or "Acoustic Stimulation" or "Art Therapy" or "Color Therapy" or "Dance Therapy" or "Music Therapy" or "Play Therapy" or Psychodrama or Speleotherapy or "Spiritual Therapies" or "Faith Healing" or Magic or "Medicine, African Traditional" or Meditation or "Mental Healing" or Occultism or Radiesthesia or Shamanism or Witchcraft or Yoga))

- NOT ((subject=Obesity) with (qualifier=Surgery))

- NOT (subject=Drug Therapy or ((subject="Weight Loss") with (qualifier="drug therapy")))

- NOT (majorSubject=Agents)

- NOT ((subject=(Agents) or qualifier=(surgery or drug therapy or therapeutic use or administration or pharmaco?)) not (subject=(Diet or Behavior or Exercise or Physical or Life Style or Counseling or Cognitive or Combined Modality Therapy) or qualifier="diet therapy"))

- NOT (majorSubject=(Alcohol Drinking or Practice Guidelines or Bone))

- NOT majorSubject=("Dietary Supplements")

- NOT majorSubject=("Digestive System Surgical Procedures" or "Bariatric Surgery" or "Gastric Bypass" or "Gastric Balloon" or Laparoscopy or Gastroplasty or Coronary Artery Bypass or Gastrectomy or "Biliopancreatic Diversion")

- NOT (((subject=("Digestive System Surgical Procedures" or "Bariatric Surgery" or "Gastric Bypass" or "Gastric Balloon" or Laparoscopy or Gastroplasty or Coronary Artery Bypass or Gastrectomy or Biliopancreatic Diversion)) with (qualifier=(instrumentation or methods or adverse effects or economics or standards or statistics))))

- NOT subject=("Postoperative Complications" or Reoperation or "Postoperative Period" or "Length of Stay" or "Reconstructive Surgical Procedures" or "Equipment and Supplies" or "Preoperative Care" or "Postoperative Care" or "Prenatal Care" or "Weight Gain and Pregnancy" or "Pregnancy Complications")

- NOT subject=("Equipment Design" or "Advertising as Topic")

- NOT subject=(Heel or Foot diseases or Cosmetic techniques or Hair Removal or Hirsutism)

- NOT subject=("Africa" OR "Africa Northern" OR "Algeria" OR "Egypt" OR "Libya" OR "Morocco" OR "Tunisia" OR "Africa South of the Sahara" OR "Africa Central" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "Congo" OR "Gabon" OR "Democratic Republic of the Congo" OR "Equatorial Guinea" OR "Africa Eastern" OR "Burundi" OR "Ethiopia" OR "Kenya" OR "Rwanda" OR "Somalia" OR "Sudan" OR "Tanzania" OR "Uganda" OR "Djibouti" OR "Eritrea" OR "Africa Southern" OR "Angola" OR "Botswana" OR "Lesotho" OR "Malawi" OR "Mozambique" OR "Namibia" OR "South Africa" OR "Swaziland" OR "Zambia" OR "Zimbabwe" OR "Africa Western" OR "Benin" OR "Burkina Faso" OR "Gambia" OR "Ghana" OR "Guinea Bissau" OR "Cote d Ivoire" OR "Liberia" OR "Mali" OR "Mauritania" OR "Niger" OR "Nigeria" OR "Senegal" OR "Sierra Leone" OR "Togo" OR "Guinea" OR "Cape Verde" OR "Americas" OR "Central America" OR "Belize" OR "Costa Rica" OR "El Salvador" OR "Guatemala" OR "Honduras" OR "Nicaragua" OR "Panama" OR "Panama Canal Zone" OR "Latin America" OR "South America" OR "Argentina" OR "Bolivia" OR "Brazil" OR "Chile" OR "Colombia" OR "Ecuador" OR "French Guiana" OR "Guyana" OR "Paraguay" OR "Peru" OR "Suriname" OR "Uruguay" OR "Venezuela" OR "Caribbean Region" OR "West Indies" OR "Barbuda and Antigua" OR "Bahamas" OR "Barbados" OR "Cuba" OR "Dominican Republic" OR "Haiti" OR "Jamaica" OR "Martinique" OR "Netherlands Antilles" OR "Puerto Rico" OR "Trinidad and Tobago" OR "Virgin Islands of the United States" OR "Dominica" OR "Grenada" OR "Guadeloupe" OR "Saint Lucia" OR "Saint Vincent and the Grenadines" OR "Saint Kitts and Nevis" OR "Antarctic Regions" OR "Arctic Regions" OR "Asia" OR "Asia Central" OR "Kazakhstan" OR "Kyrgyzstan" OR "Tajikistan" OR "Turkmenistan" OR "Uzbekistan" OR "Asia Southeastern" OR "Borneo" OR "Brunei" OR "Myanmar" OR "Cambodia" OR "Indonesia" OR "Laos" OR "Malaysia" OR "Mekong Valley" OR "Philippines" OR "Singapore" OR "Thailand" OR "Vietnam" OR "East Timor" OR "Asia Western" OR "Bangladesh" OR "Bhutan" OR "India" OR "Sikkim" OR "Middle East" OR "Afghanistan" OR "Bahrain" OR "Iran" OR "Iraq" OR "Jordan" OR "Kuwait" OR "Lebanon" OR "Oman" OR "Qatar" OR "Saudi Arabia" OR "Syria" OR "Turkey" OR "United Arab Emirates" OR "Yemen" OR "Nepal" OR "Pakistan" OR "Sri Lanka" OR "Far East" OR "China" OR "Hong Kong" OR "Tibet" OR "Japan" OR "Tokyo" OR "Korea" OR "Macau" OR "Mongolia" OR "Taiwan" OR "Atlantic Islands" OR "Azores" OR "Bermuda" OR "Falkland Islands")

- NOT (subject=(Animals or Venoms))

- NOT subject,title=(Anorexia Nervosa or Bulimia or Binge-Eating Disorder or Coprophagia or Female Athlete Triad Syndrome or Pica or Somatoform Disorders or Body Dysmorphic Disorders or Conversion Disorder or Hypochondriasis or Neurasthenia or Antipsychotic Agents or Genetic Predisposition to Disease or Epilepsy or HIV or Child or pediatric or Thinness or Acupuncture or Enteral Nutrition or Enteral tube feeding)

- NOT subject,title=(Weight Lifting or Accidental Falls or Weight-Bearing or Femur Neck or Lumbar Vertebrae or Pelvic Bones)

- NOT subject,title=("Genetic Predisposition to Disease" or Breast feeding or Electric Impedance or Contraception or Contraceptives or "Transportation of Patients" or Sick Leave or Absenteeism)

Boolean Filter

The Boolean filter in the CQ4 search strategy implements the intervention criterion to reflect comprehensive lifestyle intervention (two or more of the following components: diet, physical activity, or behavior therapy).

- lifestyle intervention? or (long-term %2 (maintenance or weight or effects)) or extended therapy program? or weight reducing program? or weight management or (comprehensive %3 (program? or lifestyle))

- OR subject,title,abstract,qualifier=((diet or Energy Intake or Caloric Restriction or dietary or Fasting)
  - AND (behavio? or cognitive or psychotherapy or problem solving or relapse prevention or psychology or life style or counseling or Aversive Therapy or Biofeedback Psychology or Desensitization Psychologic or Implosive Therapy or Relaxation Therapy or Meditation or Cognitive Therapy or Sleep Phase Chronotherapy))
- OR subject,title,abstract,qualifier=((diet or Energy Intake or Caloric Restriction or dietary or Fasting)
  - AND (physical activity or exercise or fitness or rehabilitation or life style or weight loss education or Motor Activity or Running or Jogging or Swimming or Walking or Resistance Training))
- OR subject,title,abstract,qualifier=((behavio? or cognitive or psychotherapy or problem solving or relapse prevention or psychology or life style or counseling or Aversive Therapy or Biofeedback Psychology or Desensitization Psychologic or Implosive Therapy or Relaxation Therapy or Meditation or Cognitive Therapy or Sleep Phase Chronotherapy)
  - AND (physical activity or exercise or fitness or rehabilitation or life style or weight loss education or Motor Activity or Running or Jogging or Swimming or Walking or Resistance Training))

- OR subject,title,abstract=(Confidence Interval? or Area Under Curve) or AUC
- OR subject=(Combined Modality Therapy)
- OR genre=(Comparative Study or Meta-Analysis)

Critical Question 4: Search Strategy Results and PRISMA Diagram

The following databases were searched for RCTs and SRs and MAs of RCTs or controlled clinical trials to answer CQ4:

- PubMed from January 1998 to December 2009
- CINAHL from January 1998 to July 2008
- EMBASE from January 1998 to July 2008
- PsycInfo from January 1998 to July 2008
- EBM Cochrane Libraries from January 1998 to July 2008
- Biological Abstracts from January 2004 to July 2008
- Wilson Social Sciences Abstracts from January 1998 to July 2008

The literature search for CQ4 included an electronic search of the Central Repository for RCTs or controlled clinical trials published in the literature from January 1998 to December 2009. The Central Repository contains citations pulled from seven literature databases: PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts. The search produced 2,145 citations, with 15 additional citations identified from non-search sources, i.e., by the panel members or hand search of SRs/MAs (obtained through the electronic search). The SRs/MAs were only used for manual searches and were not part of the final evidence base. This manual cross-check was done to ensure that major studies were not missing from the evidence base. Eleven of the 15 citations identified from non-search sources were published after December 31, 2009. Per NHLBI policy, certain lifestyle and obesity intervention studies published after the closing date could be allowed as exceptions. These studies must be RCTs in which each study arm contained at least 100 participants and were identified by experts

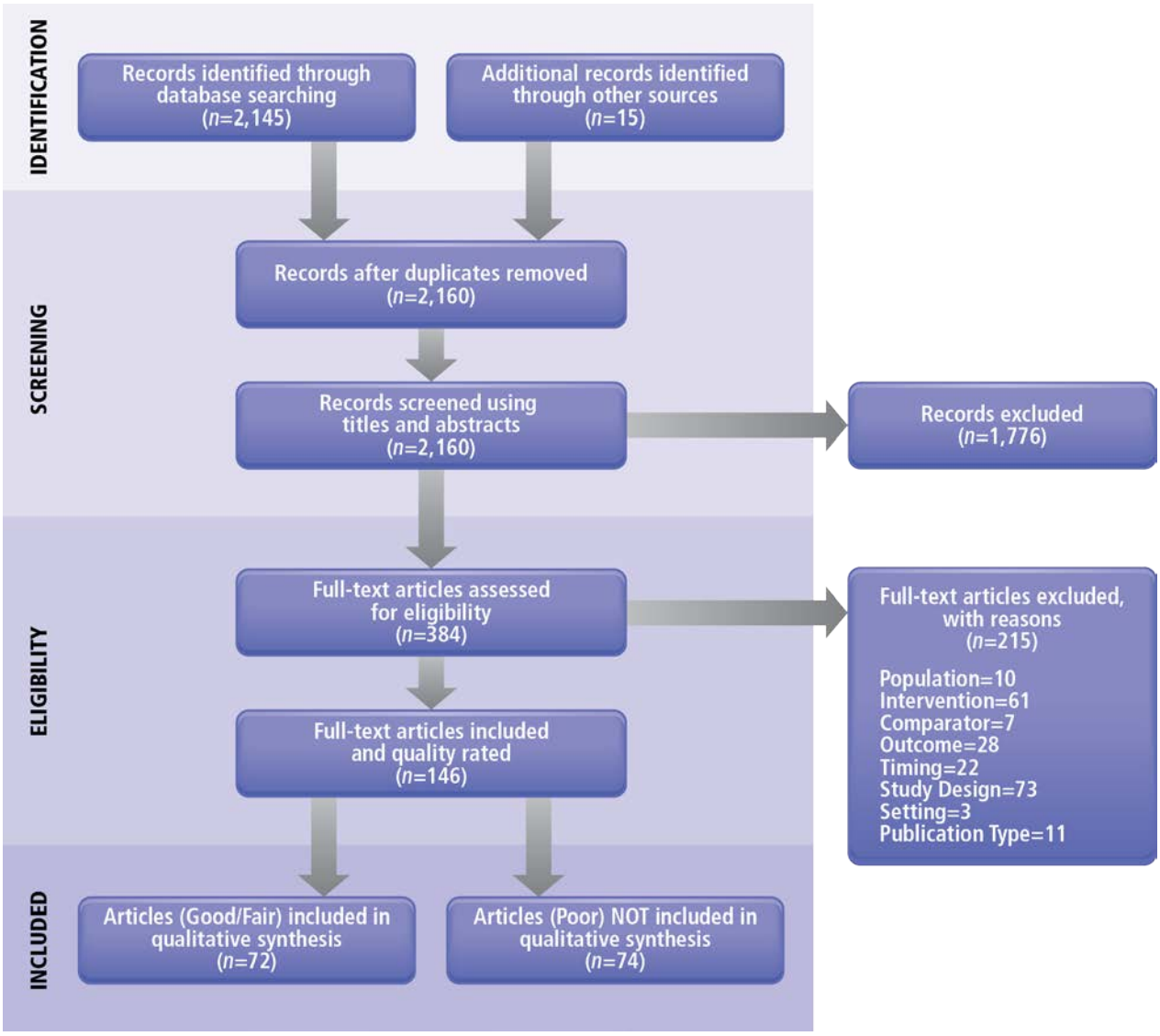
knowledgeable of the literature. Ten of the 11 citations published after December 2009 met the criteria and were eligible for inclusion in the CQ4 evidence base (20,198-206). In contrast, 1 of the 11 citations did not meet the criteria and was excluded from the CQ4 evidence base (207). The remaining four citations, identified through non-search sources, were published before 2009. Of these four, one citation had no abstract, two citations had no indication in the abstract or MeSH terms that they were related to overweight or obese populations, and one citation had no indication in the abstract or MeSH terms that the publication was related to comprehensive lifestyle interventions. Of the 15 citations identified through non-search sources, 14 were screened and found eligible for inclusion; subsequently, two of these studies were rated as poor quality studies.

Two reviewers independently screened the titles and abstracts of 2,160 publications against the I/E criteria, resulting in 1,776 publications being excluded and 384 publications being retrieved for full-text review to further assess eligibility. Next, two independent reviewers independently screened 384 full-text publications, assessing eligibility by applying the I/E criteria; 215 of these publications were excluded based on one or more of the I/E criteria (see specified rationale as noted in the PRISMA).

One hundred and forty-six of the 384 full-text publications met the criteria and were included. The quality (internal validity) of these 146 publications was assessed using the quality assessment tool developed to assess RCTs (see Appendix 2). Of these, 74 publications were excluded because they were rated as poor quality; of them, 43 studies were rated poor due to the ITT and attrition rates. Rationales for the poor quality studies are included in Appendix 3. The remaining 51 trials (72 articles) were rated good or fair quality and included in the evidence base that was used to formulate the evidence statements and recommendations. Panel members reviewed the final studies on the include list, along with their quality ratings, and had the opportunity to raise

questions. Some trials previously deemed to be of fair or good quality were downgraded to poor quality upon closer review of evidence tables. These trials used completers analyses rather than ITT analysis and had overall attrition rates exceeding 10 percent. If the study reported only an analysis of completers and had attrition at <10 percent, it was allowed in the evidence base. Methodologists worked with the SR team to reevaluate these trials and make a final decision. Evidence tables and summary tables consisted only of data from the original publications of eligible RCTs; these tables formed the basis for panel deliberations.

Figure A–4. PRISMA Diagram Showing Selection of Articles for CQ4



Key:
Details for each exclusion rationale are determined by the I/E criteria for the question, reproduced below. The I/E criteria are also available in Section 8a.

Table A–8. Criteria for Selection of Publications for CQ4

	Inclusions	Exclusions
Population	Adults overweight (BMI 25.0 to 29.9) or obese (BMI ≥30.0)	• Children • Animals studies • Population not overweight (BMI 25.0 to 29.9) or obese (BMI ≥30.0) at baseline

	Inclusions	Exclusions
Intervention	Comprehensive lifestyle interventions for weight loss, weight maintenance or weight regain prevention, comprised of all three components: diet, physical activity, behavioral therapy 4a Components • Diet: calorie (energy) restriction/reduction • Physical activity: exercise, increased physical activity • Behavior: behavioral weight control, behavior therapy or treatment, behavior modification 4b • Duration: short term (≤6 mos), intermediate (>6 months and ≤12 mos), long term (>1 yr) • Delivery: – Sessions: group (i.e., meetings, treatment) or individual (i.e., meetings, treatment) – Format: face-to-face (onsite, clinic based); electronic (Internet Web site, e-mail, chat room, individual telephone, group telephone [conference call]); mail; or bibliotherapy • Frequency of contact: daily, weekly, biweekly, monthly, quarterly • Characteristics: self-monitoring, food records, activity records	
Comparator	• Usual care • Minimal or control intervention • No treatment intervention • Comprehensive intervention comprising three components: comparison to a variation of the standard diet, physical activity, and behavior therapy components • Diet comparison trials, which examined the effects of different dietary interventions (in the presence of the same physical activity and behavior therapy components), were evaluated by CQ3.	• Pharmacotherapy • Obesity surgery • Alternative medicine, including hypnosis and others
Outcome	***One or more*** of the following outcomes: • Weight (kg, lbs, %) • Body fat measures (BMI and BMI change, WC, waist-hip ratio, % body fat) • Weight loss maintenance • Percent reduction of excess weight	Outcomes by measure of self-report * Results are not reported according to randomized treatment or treatment groups *Note: Panel determined self-reported weight (only allowed in studies reporting CVD events; for risk factors, the studies have to report measured weight) is not appropriate for this CQ because these would be observational studies

	Inclusions	Exclusions
Timing	• Intervention period: ≥3 mos • Follow-up period: ≥6 mos (defined from the start of randomization)	• Intervention less than 3 mos • Follow-up of less than 6 mos
Setting	Westernized countries: • United States • Canada • European Union • Australia • New Zealand • Israel Any clinical or research setting	
Study Design	• For efficacy/effectiveness: RCTs. (SRs/MAs were used to identify papers potentially missed by the search.) Sufficient information must be presented about the intervention to replicate the study. • For adverse effects: RCTs, controlled clinical trials, cohort studies with a contemporaneous comparison group, case-control studies, large observational studies • Post hoc analyses of large RCTs if analyses of randomized comparisons are included • Sample size: must be ≥15 subjects per treatment arm	• SRs/MAs • Case series, case reports, before-after studies • Results are not compared according to randomized treatment assignments. • Dropout rate ≥40 percent after 6 mos • Studies with <15 subjects per treatment arm
Publication Type	Published studies	• SRs/MAs • Unpublished literature – Unpublished industry-sponsored trials – Other unpublished data • FDA Medical and Statistical reviews • Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Language	• Abstract must be available in English	• Full-text translation into English must be feasible.
Publication Time Frame	• RCTs published in years 1998 to 2009; RCTs published in 2010 and 2011 were included if there were ≥100 participants per treatment arm.	• Studies published before 1998

Critical Question 5: Search Strategy

CQ5 has three parts:

a. Efficacy:

What are the long-term effects of the following surgical procedures on weight loss, weight loss maintenance, CV risk factors, related comorbidities, and mortality?

- LAGB
- Laparascopic RYGB
- Open RYGB
- Biliopancreatic bypass with or without duodenal switch
- SG

What are the long-term effects of the surgical procedures (listed above) in patients with different BMIs and comorbidities?

- BMI <35
- BMI of 35 to 40 with no comorbidities
- BMI ≥35 with comorbidities, and
- BMI ≥40 with no comorbidities

b. Predictors:

What are the predictors associated with long-term effects of the following surgical procedures on weight loss, weight loss maintenance, CV risk factors, related comorbidities, and mortality?

- LAGB
- Laparascopic RYGB
- Open RYGB
- BPD with or without duodenal switch
- SG

What are the predictors associated with long-term effects of the surgical procedures (listed above) in patients with different BMIs and comorbidities?

- BMI <35
- BMI of 35 to 40 with no comorbidities
- BMI ≥35 with comorbidities, and
- BMI ≥40 with no comorbidities.

c. Complications:

What are the short-term (less than 30 days) and long-term (30 days or more) complications of the following bariatric surgical procedures? What are the predictors associated with complications?

- LAGB
- Laparascopic RYGB
- Open RYGB
- BPD with or without duodenal switch
- SG

What are the complications of the surgical procedures (listed above) in patients with different BMIs and comorbidities?

- BMI <35
- BMI of 35 to 40 with no comorbidities
- BMI ≥35 with comorbidities, and
- BMI ≥40 with no comorbidities.

Study Type Query

- {RCT} OR {Systematic Review} OR
- (subject=("Case Control Studies" or "Retrospective Studies" or "Cohort Studies" or "Longitudinal Studies" or "Follow Up Studies" or "Prospective Studies") or (genre,subject="Controlled Clinical Trial?" and qualifier="adverse effects") or case control or longitudinal or prospective? or retrospective? or cohort? or (before %10 after))
- NOT (title=case report OR genre=letter OR genre=newspaper article OR genre=comment OR genre="case reports" OR genre="case study")

Boolean Search

(publicationYear>1997 AND publicationYear<2010 and language=eng? **AND**

(((subject=("Overweight" or "Obesity" or "Obesity Morbid")) with (qualifier=surgery))

- OR ((bariatric %3 (surger? or procedure? or operation?)) or subject=(Gastroplasty or Laparoscopy) or (subject="Anastomosis Roux-en-Y" or subject,abstract,title="Gastric Bypass" or Gastroileal Bypass or Gastrojejunostom? or subject,abstract,title=((Biliopancreatic or Bilio-Pancreatic) %2 (Diversion? or Bypass?)) or "laparoscopic adjustable gastric band?" or "gastric band" or "gastric banding" or ((subject=Duodenum) with (qualifier=surgery)) or "duodenal switch" or "gastric sleeve" or "sleeve gastrectomy" or "Laparascopic Roux-en-Y gastric bypass" or "Open Roux-en-Y gastric bypass" or "Biliopancreatic bypass" or Roux-en-Y)))
- **AND** (subject,title,abstract,qualifier=(mortality or death?) or subject="Hospital Mortality" or subject,title,abstract=("Body Weight" or subject,title,abstract="Body Mass Index" or "Waist Circumference" or "Weight Gain" or "Weight Loss" or "Waist-Hip Ratio" or "Body Fat Distribution" or "Skinfold Thickness" or Adiposity) or BMI or abstract,title,qualifier="adverse effects" or subject=("Postoperative Complications" or "Postgastrectomy Syndromes" or "Dumping Syndrome" or "Postoperative Hemorrhage" or "Postoperative Nausea and Vomiting" or "Surgical Wound")))
- NOT (recordStatus=delete)
- NOT subject=("Africa" OR "Africa Northern" OR "Algeria" ›157 more terms.)
- NOT subject=("Advertising as Topic")
- NOT (subject=(Animals or Venoms))
- NOT subject=((child or adolescent) not (adult or aged))
- NOT subject=("Child Nutrition" or "Child Behavior" or "Child, Preschool" or "Child Development" or "Infant Food")
- NOT subject=(Heel or Foot diseases or Cosmetic techniques or Hair Removal or Hirsutism)

Boolean Filter

The Boolean filter in the CQ5 5 search strategy implements the intervention criterion to reflect exactly the five requested procedures, i.e., LAGB, Laparascopic RYGB, Open RYGB, Biliopancreatic bypass/duodenal switch, and GS.

(

- "Laparoscopic adjustable gastric banding" or "lap-band" or subject,title,abstract=(Laparoscop? and (Gastroplast? or gastric) and band?)
- or "Laparascopic Roux-en-Y gastric bypass" or (subject,title,abstract="Gastric Bypass" and subject,title,abstract=Laparoscop?)
- or "Open Roux-en-Y gastric bypass" or (subject,title,abstract="Gastric Bypass" and subject,title,abstract="Roux-en-Y") or Gastroileal Bypass or Gastrojejunostom?
- or ((Biliopancreatic or Bilio-Pancreatic) %2 (Diversion? or Bypass?)) or "duodenal switch" or subject,title,abstract="Biliopancreatic Diversion" or ((subject=Duodenum) with (qualifier=surgery))
- or "Gastric sleeve" or "sleeve gastrectomy"
- or subject,title,abstract=(("Bariatric Surgery" or "Gastric Bypass" or "gastric banding" or "gastric surgery" or Gastrectomy) and ((Weight or BMI) %3 (loss or gain or reduc?)))
- or genre,title=Meta-analysis)

Critical Question 5: Search Strategy Results and PRISMA Diagram

The following databases were searched for RCTs, observational studies and SRs and MAs of

RCTs or controlled clinical trials, and observational studies to answer CQ5:

- PubMed from January 1998 to December 2009
- CINAHL from January 1998 to July 2008
- EMBASE from January 1998 to July 2008
- PsycInfo from January 1998 to July 2008
- Evidence-based Medicine Cochrane Libraries from January 1998 to July 2008
- Biological Abstracts from January 2004 to July 2008
- Wilson Social Sciences Abstracts from January 1998 to July 2008

The literature search for CQ5 included an electronic search of the Central Repository for RCTs, controlled clinical trials, and observational studies published in the literature from January 1998 to December 2009. The Central Repository contains citations pulled from seven literature databases: PubMed, CINAHL, EMBASE, PsychInfo, EBM, Biological Abstracts, and Wilson Social Sciences Abstracts. The search produced 2,317 citations, with 9 additional citations identified from non-search sources, i.e., by the panel members or hand search of SRs/MA (obtained through the electronic search). The SRs/MAs were only used for manual searches and were not part of the final evidence base. This manual cross-check was done to ensure that major studies were not missing from the evidence base. A similar manual cross-check of citations from the American Society for Metabolic & Bariatric Surgery (ASMBS) position statement on SG was performed in May 2012. Eight of the 9 citations identified from non-search sources were published after December 31, 2009. Per NHLBI policy, certain lifestyle and obesity intervention studies published after the closing date could be allowed as exceptions. These studies must be RCTs in which each study arm contained at least 100 participants and were identified by experts knowledgeable of the literature. Three of the nine citations published after December 2009 met the criteria and were eligible for inclusion in the CQ5 evidence base (340-342). In contrast, five of the nine citations did not meet the criteria and were excluded from the CQ5 evidence base (343-347). The remaining citation, identified through non-search sources, was published before 2009 (348). This citation met the criteria and was eligible for inclusion. Thus, of the nine citations identified through non-search sources, four were screened and found eligible for inclusion; subsequently, all these studies were rated as good quality.

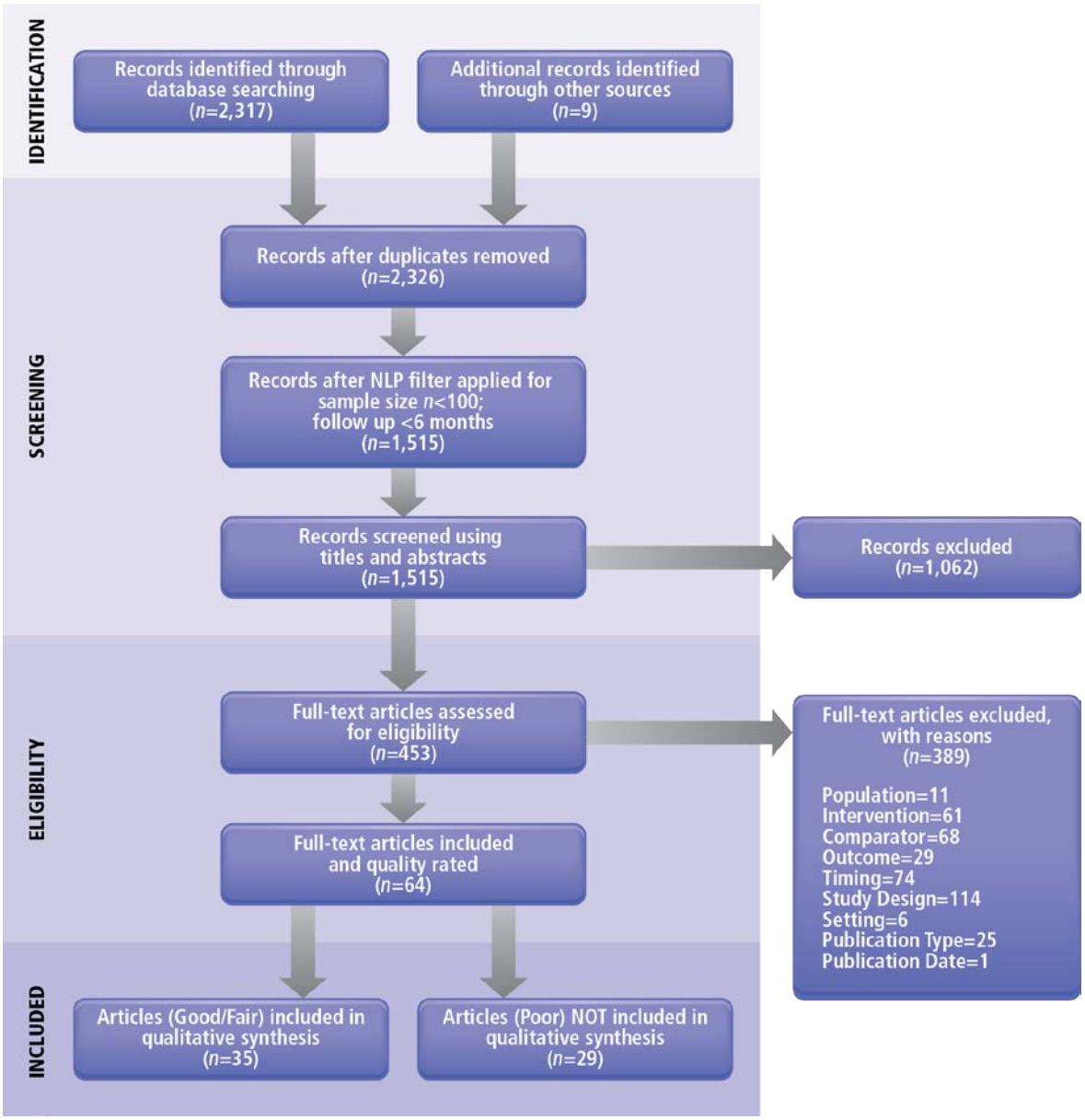
Figure A–5 , the PRISMA diagram for CQ5, outlines the flow of information from the literature search through the various steps used in the SR process.

A natural language processing filter was used to identify studies with sample sizes less than 100, 100 to 299, and/or a follow-up time of less than 6 months. The natural language processing filter was executed against titles and abstracts. Of the 2,317 citations identified through the database search, 811 citations were automatically excluded using the natural language processing filter. Two reviewers independently screened the remaining titles and abstracts of the 1,515 remaining citations against the I/E criteria for each of the three components (Efficacy, Predictors, and Complications). This resulted in 1,062 publications being excluded (on one or more of the I/E criteria for each of the three components of CQ5) and 453 publications being retrieved for full-text review to further assess eligibility.

Sixty-four of the 453 full-text publications met the criteria and were included. The quality (internal validity) of these 64 publications was assessed using the six quality assessment tools that were developed (see Appendix 2). Of these, 29 publications were excluded because they were rated as poor quality; of these, 18 studies were rated poor due to the ITT and/or attrition rates. Rationales for the poor quality studies are included in Appendix 3. The remaining 22 trials (35 articles) that met the criteria for **at least** one of the three components were rated good or fair quality and included in the evidence base. These articles were used to formulate the evidence statements and recommendations. For the Efficacy, Predictors and Complications components, there were 17, 12, and 15 citations rated as good/fair. There were a total of eight citations that were used across more than one component (341,378,379,381,385,394,401,402). Of the 16 citations included for the Efficacy component, 4 were RCTs, and 12 were observational studies. Of the 12 citations included for the Predictors component, 6 were RCTs and 6 were observational studies. And, of the 15 citations included for the Complications component, 4 were RCTs and 11 were observational studies.

Panel members reviewed the final studies on the include list, along with their quality ratings, and had the opportunity to raise questions. Some trials previously deemed to be of fair or good quality were downgraded to poor quality upon closer review of evidence tables. These trials used completers analyses rather than ITT analysis and had overall attrition rates exceeding 10 percent. If the study reported only an analysis of completers and had attrition at <10 percent, it was allowed in the evidence base. Methodologists worked with the SR team to reevaluate these trials and make a final decision. Evidence tables and summary tables consisted only of data from the original publications of eligible RCTs and observational studies; these tables formed the basis for panel deliberations.

Figure A–5. PRISMA Diagram Showing Selection of Articles for CQ5



Key:
Details for each exclusion rationale are determined by the I/E criteria for the question, reproduced below. The I/E criteria are also available in Section 9a.

Table A–9. Criteria for Selection of Publications for CQ5

	Inclusions	Exclusions
Population	Adults	• Children • Animals studies
Intervention	• LAGB • Laparascopic RYGB	• Other bariatric surgical interventions not listed in

	Inclusions	Exclusions
	• Open RYGB • Biliopancreatic bypass with or without duodenal switch • SG Any of the above interventions AND preoperative or postoperative intervention components (can be multi-component): • diet • physical activity • behavioural treatments	inclusions
Comparator	**Efficacy Component:** • Any type of nonsurgical alternate intervention differing from the main study intervention **Predictor and Complication Components:** • Any type of alternate intervention differing from the main study intervention **All Components:** • No care • Usual care • Observational studies may not have prespecified comparison groups (For example, intervention and comparison groups, or exposed and unexposed groups, may emerge over time as patients are being followed for a cohort study.)	
Outcome	**Reduction in body weight as measured by:** • Weight (kg, lbs, %) • Body fat measures: (BMI and BMI change) • WC • Waist-hip ratio • Percent body fat • Weight loss maintenance (weight change from end of treatment to follow-up) • Percent reduction of excess weight Self-reported weight outcomes are permitted *For all but short-term postoperative outcomes, study must report a body weight measure plus one or more of the following outcomes:* **Long- and Short-Term Surgical Complications** • Intraoperative • Short-term postoperative (<30 days) • Long-term postoperative (≥30 days) **Quality of Life** • Function • Disability **CVD Events** • Myocardial infarction • Heart failure • Hospitalization for heart failure or stroke **CVD Risk Factors**	

	Inclusions	Exclusions
	• SBP or DBP • Total cholesterol, HDL-C, LDL-C, Non-HDL-C, triglycerides • Fasting glucose, fasting plasma insulin, HbA1C • Smoking status • CRP **Morbidity** • CHD/CVD • Incidence and remission of diabetes • Incidence and remission of hypertension • Liver disease • Sleep apnea • Depression • Eating disorders • Chronic renal failure **Mortality** • CVD-related • All-cause **Physical activity**	
Timing	**Efficacy and Predictor Components:** • Intervention period: for lifestyle components ≥3 mos • Follow-up periods: – ≥6 mos for lifestyle components – ≥2 yrs for surgery *No follow-up time criteria for complications components	• Intervention periods for lifestyle components of less than 3 mos • Follow-up of less than 6 mos for lifestyle components • Follow-up periods of less than 2 yrs for surgery intervention *No follow-up time criteria for complications components
Setting	**Westernized countries:** • United States • Canada • European Union • Australia • New Zealand • Israel Any clinical or research setting	• Countries not applicable to Western weight goals and diets
Study Design	**Efficacy Component** • RCTs, non-RCTs, prospective cohort studies, retrospective cohort studies, case cohort studies, case control studies, nested case control studies, case-crossover studies, interrupted time series studies **Predictor Component** • RCTs, non-RCTs, prospective cohort studies, retrospective cohort studies, case cohort studies, case control studies, nested case control studies, case-crossover studies, interrupted time series studies, before-after studies	**Efficacy Component** • Before-after studies, time series studies, cross-sectional studies, case series, case reports **Predictor Component** • Time series studies, cross-sectional studies, case series, case reports **Complications Component** • Cross-sectional studies, case reports **All components:** • SRs/MAs

	Inclusions	Exclusions
	Complications Component • RCTs, non-RCTs, prospective cohort studies, retrospective cohort studies, case cohort studies, case control studies, nested case control studies, case-crossover studies, interrupted time series studies, before-after studies, time series studies, case series **Sample Size Criteria for Predictor and Complications Components Only:** • Sample size requirements only for observational studies: ≥100 for studies with 10 or more years of follow-up or studies on duodenal switch procedures or sleeve procedures; ≥500 for all other observational studies	• Dropout rate ≥35% overall at 1 yr
Language	• Abstract must be available in English	• Full-text translation into English must be feasible
Publication Type	Published studies	• SRs/MAs • Unpublished literature – Unpublished industry-sponsored trials – Other unpublished data • FDA Medical and Statistical reviews • Theses • Studies published only as abstracts • Letters • Commentaries and opinion pieces • Non-SRs
Publication Time Frame	• Studies published in years 1998–2009	• Studies published before 1998

Critical Questions and Quality Ratings of Studies

For each CQ, this section includes a table that lists studies rated as fair or good and a table listing studies rated as poor.

Critical Question 1

Among overweight and obese adults, does achievement of reduction in body weight with lifestyle and pharmacological interventions affect CVD risk factors, CVD events, morbidity, and mortality?

a. Does this effect vary across population subgroups defined by the following demographic and clinical characteristics:

- Age
- Sex
- Race/ethnicity
- Baseline BMI
- Baseline WC
- Presence or absence of comorbid conditions
- Presence or absence of CVD risk factors

b. What amount (shown as percent lost, pounds lost, etc.) of weight loss is necessary to achieve benefit with respect to CVD risk factors, morbidity, and mortality?

- Are there benefits on CVD risk factors, CVD events morbidity, and mortality from weight loss?
- What are the benefits of more significant weight loss?

c. What is the effect of sustained weight loss for 2 or more years in individuals who are overweight or obese, on CVD risk factors, CVD events, and health and psychological outcomes?

- What percent of weight loss needs to be maintained at 2 or more years to be associated with health benefits?

Tables 9 and 10 show studies rated fair or good and studies rated poor, respectively. The studies include SRs and MAs and the Look AHEAD study.

Table A–10. CQ1 Studies Rated Fair or Good

Count	Citations	Quality Rating
1	Aucott, L; Poobalan, A; Smith, W, C, S; Avenell, A; Jung, R; Broom, J; Grant, A, M Weight loss in obese diabetic and non-diabetic individuals and long-term diabetes outcomes--a systematic review. *Diabetes, obesity & metabolism Mar 2004, 6 (2) : 85-94*	SR or MA Good

Count	Citations	Quality Rating
2	Aucott, Lorna; Poobalan, Amudha; Smith, W, Cairns, S; Avenell, Alison; Jung, Roland; Broom, John Effects of weight loss in overweight/obese individuals and long-term hypertension outcomes: a systematic review. *Hypertension Jun 2005, 45 (6) : 1035-41*	SR/MA Good
3	Avenell, A; Broom, J; Brown, T, J; Poobalan, A; Aucott, L; Stearns, S, C; Smith, W, C, S; Jung, R, T; Campbell, M, K; Grant, A, M Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health technology assessment (Winchester, England) May 2004, 8 (21) : iii-iv*	SR/MA Good
4	Avenell, A; Brown, T, J; McGee, M, A; Campbell, M, K; Grant, A, M; Broom, J; Jung, R, T; Smith, W, C, S What interventions should we add to weight reducing diets in adults with obesity? A systematic review of randomized controlled trials of adding drug therapy, exercise, behaviour therapy or combinations of these interventions. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association Aug 2004, 17 (4) : 293-316*	SR/MA Good
5	Avenell, A; Brown, T, J; McGee, M, A; Campbell, M, K; Grant, A, M; Broom, J; Jung, R, T; Smith, W, C, S What are the long-term benefits of weight reducing diets in adults? A systematic review of randomized controlled trials. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association Aug 2004, 17 (4) : 317-35*	SR/MA Fair
6	Douketis, J, D; Macie, C; Thabane, L; Williamson, D, F Systematic review of long-term weight loss studies in obese adults: clinical significance and applicability to clinical practice. *International journal of obesity (2005) Oct 2005, 29 (10) : 1153-67*	SR/MA Fair
7	Galani, Carmen; Schneider, Heinz Prevention and treatment of obesity with lifestyle interventions: review and meta-analysis. *International journal of public health Jan 2007, 52 (6) : 348-59*	SR/MA Fair
8	Horvath, Karl; Jeitler, Klaus; Siering, Ulrich; Stich, Anne, K; Skipka, Guido; Gratzer, Thomas, W; Siebenhofer, Andrea Long-term effects of weight-reducing interventions in hypertensive patients: systematic review and meta-analysis. *Archives of internal medicine Mar 2008, 168 (6) : 571-80*	SR/MA Good
9	Hutton, Brian; Fergusson, Dean Changes in body weight and serum lipid profile in obese patients treated with orlistat in addition to a hypocaloric diet: a systematic review of randomized clinical trials. *The American journal of clinical nutrition Dec 2004, 80 (6) : 1461-8*	SR/MA Fair
10	Johansson, K; Sundström, J; Neovius, K; Rössner, S; Neovius, M Long-term changes in blood pressure following orlistat and sibutramine treatment: a meta-analysis. *Obesity reviews : an official journal of the International Association for the Study of Obesity Nov 2010, 11 (11) : 777-91*	SR/MA Good

Count	Citations	Quality Rating
11	Look AHEAD Research Group; Pi-Sunyer, Xavier; Blackburn, George; Brancati, Frederick, L; Bray, George, A; Bright, Renee; Clark, Jeanne, M; Curtis, Jeffrey, M; Espeland, Mark, A; Foreyt, John, P; Graves, Kathryn; Haffner, Steven, M; Harrison, Barbara; Hill, James, O; Horton, Edward, S; Jakicic, John; Jeffery, Robert, W; Johnson, Karen, C; Kahn, Steven; Kelley, David, E; Kitabchi, Abbas, E; Knowler, William, C; Lewis, Cora, E; Maschak-Carey, Barbara, J; Montgomery, Brenda; Nathan, David, M; Patricio, Jennifer; Peters, Anne; Redmon, J, Bruce; Reeves, Rebecca, S; Ryan, Donna, H; Safford, Monika; Van Dorsten, Brent; Wadden, Thomas, A; Wagenknecht, Lynne; Wesche-Thobaben, Jacqueline; Wing, Rena, R; Yanovski, Susan, Z Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. *Diabetes care Jun 2007, 30 (6) : 1374-83*	Controlled intervention study Good
12	Look AHEAD Research Group; Wing, Rena, R Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: four-year results of the Look AHEAD trial. *Archives of internal medicine Sep 2010, 170 (17) : 1566-75*	Controlled intervention study Good
13	Norris, S, L; Zhang, X; Avenell, A; Gregg, E; Brown, T, J; Schmid, C, H; Lau, J Long-term non-pharmacologic weight loss interventions for adults with type 2 diabetes. *Cochrane database of systematic reviews (Online) Jan 2005, (2) : CD004095-*	SR/MA Fair
14	Norris, S, L; Zhang, X; Avenell, A; Gregg, E; Schmid, C, H; Lau, J Long-term non-pharmacological weight loss interventions for adults with prediabetes. *Cochrane database of systematic reviews (Online) Jan 2005, (2) : CD005270-*	SR/MA Good
15	Norris, S, L; Zhang, X; Avenell, A; Gregg, E; Schmid, C, H; Lau, J Pharmacotherapy for weight loss in adults with type 2 diabetes mellitus. *Cochrane database of systematic reviews (Online) Jan 2005, (1) : CD004096-*	SR/MA Good
16	Norris, Susan, L; Zhang, Xuanping; Avenell, Alison; Gregg, Edward; Bowman, Barbara; Serdula, Mary; Brown, Tamara, J; Schmid, Christopher, H; Lau, Joseph Long-term effectiveness of lifestyle and behavioral weight loss interventions in adults with type 2 diabetes: a meta-analysis. *The American journal of medicine Nov 2004, 117 (10) : 762-74*	SR/MA Fair
17	Padwal, R; Li, S, K; Lau, D, C, W Long-term pharmacotherapy for obesity and overweight. *Cochrane database of systematic reviews (Online) Jan 2004, (3) : CD004094-*	SR/MA Good
18	Padwal, R; Li, S, K; Lau, D, C, W Long-term pharmacotherapy for overweight and obesity: a systematic review and meta-analysis of randomized controlled trials. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Dec 2003, 27 (12) : 1437-46*	SR/MA Good
19	Pirozzo, S; Summerbell, C; Cameron, C; Glasziou, P Should we recommend low-fat diets for obesity? *Obesity reviews : an official journal of the International Association for the Study of Obesity May 2003, 4 (2) : 83-90*	SR/MA Good

Count	Citations	Quality Rating
20	Poobalan, A, S; Aucott, L, S; Smith, W, C, S; Avenell, A; Jung, R; Broom, J Long-term weight loss effects on all cause mortality in overweight/obese populations. *Obesity reviews : an official journal of the International Association for the Study of Obesity Nov 2007, 8 (6) : 503-13*	SR/MA Fair
21	Poobalan, A; Aucott, L; Smith, W, C, S; Avenell, A; Jung, R; Broom, J; Grant, A, M Effects of weight loss in overweight/obese individuals and long-term lipid outcomes--a systematic review. *Obesity reviews : an official journal of the International Association for the Study of Obesity Feb 2004, 5 (1) : 43-50*	SR/MA Fair
22	Rucker, Diana; Padwal, Raj; Li, Stephanie, K; Curioni, Cintia; Lau, David, C, W Long term pharmacotherapy for obesity and overweight: updated meta-analysis. *BMJ (Clinical research ed.) Dec 2007, 335 (7631) : 1194-9*	SR/MA Good
23	Shaw, K; Gennat, H; O'Rourke, P; Del Mar, C Exercise for overweight or obesity. *Cochrane database of systematic reviews (Online) Jan 2006, (4) : CD003817-*	SR/MA Good
24	Siebenhofer, Andrea; Horvath, Karl; Jeitler, Klaus; Berghold, Andrea; Stich, Anne, K; Matyas, Eva; Pignitter, Nicole; Siering, Ulrich Long-term effects of weight-reducing drugs in hypertensive patients. *Cochrane database of systematic reviews (Online) Jan 2009, (3) : CD007654-*	SR/MA Good
25	Thomas, D, E; Elliott, E, J; Baur, L Low glycaemic index or low glycaemic load diets for overweight and obesity. *Cochrane database of systematic reviews (Online) Jan 2007, (3) : CD005105-*	SR/MA Good
26	Tuah, Nik, Aa; Amiel, Cressida; Qureshi, Samrina; Car, Josip; Kaur, Balvinder; Majeed, Azeem Transtheoretical model for dietary and physical exercise modification in weight loss management for overweight and obese adults. *Cochrane database of systematic reviews (Online) Jan 2011, (10) : CD008066-*	SR/MA Good
27	Wing, Rena, R; Lang, Wei; Wadden, Thomas, A; Safford, Monika; Knowler, William, C; Bertoni, Alain, G; Hill, James, O; Brancati, Frederick, L; Peters, Anne; Wagenknecht, Lynne; the Look AHEAD Research Group Benefits of Modest Weight Loss in Improving Cardiovascular Risk Factors in Overweight and Obese Individuals With Type 2 Diabetes. *Diabetes care Jul 2011, 34 (7) : 1481-1486*	Controlled intervention study Fair
28	Witham, Miles, D; Avenell, Alison Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. *Age and ageing Mar 2010, 39 (2) : 176-84*	SR/MA Fair

Table A–11. CQ1 Studies Rated as Poor with Rationale

Count	Citations	Quality Rating	Rating Rationale
1	**Astrup, A;** Ryan, L; Grunwald, G, K; Storgaard, M; Saris, W; Melanson, E; Hill, J, O The role of dietary fat in body fatness: evidence from a preliminary meta-analysis of ad libitum low-fat dietary intervention studies. *The British journal of nutrition Mar 2000, 83 Suppl 1: S25-32*	SR/MA **Poor**	Comprehensive, systematic approach not used in literature search; titles, abstracts, and full-text articles not dually and independently reviewed; quality of each included study not rated independently by two or more reviewers using a standard method to appraise internal validity; publication bias and heterogeneity not assessed
2	**Aucott, L;** Gray, D; Rothnie, H; Thapa, M; Waweru, C Effects of lifestyle interventions and long-term weight loss on lipid outcomes - a systematic review. *Obesity reviews: an official journal of the International Association for the Study of Obesity May 2011, 12 (5) : e412-25*	SR/MA **Poor**	Quality of each included study not rated independently by two or more reviewers using a standard method to appraise internal validity; publication bias not assessed
3	**Aucott, Lorna;** Rothnie, Helen; McIntyre, Linda; Thapa, Mohan; Waweru, Charles; Gray, Denise Long-term weight loss from lifestyle intervention benefits blood pressure?: a systematic review. *Hypertension Oct 2009, 54 (4) : 756-62*	SR/MA **Poor**	Quality of each included study not rated independently by two or more reviewers using a standard method to appraise internal validity; publication bias not assessed
4	**Bales, Connie, W;** Buhr, Gwendolen Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. *Journal of the American Medical Directors Association Jun 2008, 9 (5):302-12*	SR/MA **Poor**	Titles, abstracts, and full-text articles not dually and independently reviewed; quality of each included study not rated independently by two or more reviewers using a standard method to appraise internal validity; publication bias not assessed
5	**Dyson, P, A** A review of low and reduced carbohydrate diets and weight loss in type 2 diabetes. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association Dec 2008, 21 (6) : 530-8*	SR/MA **Poor**	Titles, abstracts, and full-text articles not dually and independently reviewed; quality of each included study not rated independently by two or more reviewers using a standard method to appraise internal validity; publication bias not assessed

Count	Citations	Quality Rating	Rating Rationale
6	**Gillies, Clare, L; Abrams, Keith, R; Lambert, Paul, C; Cooper, Nicola, J; Sutton, Alex, J; Hsu, Ron, T; Khunti, Kamlesh** Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ (Clinical research ed.) Feb 2007, 334 (7588) : 299-	?????	???????
7	**Harrington, Mary;** Gibson, Sigrid; Cottrell, Richard, C A review and meta-analysis of the effect of weight loss on all-cause mortality risk. *Nutrition research reviews Jun 2009, 22 (1) : 93-108*	SR/MA **Poor**	Quality of each included study not rated independently by two or more reviewers using a standard method to appraise internal validity; publication bias not assessed
8	**Kim, Su, Hyun;** Lee, Young, Mee; Jee, Sun, Ha; Nam, Chung, Mo Effect of sibutramine on weight loss and blood pressure: a meta-analysis of controlled trials. *Obesity research Sep 2003, 11 (9) : 1116-23*	SR/MA **Poor**	Quality of each included study not rated independently by two or more reviewers using a standard method to appraise internal validity
9	**Laederach-Hofmann, K;** Messerli-Burgy, N; Meyer, K Long-term effects of non-surgical therapy for obesity on cardiovascular risk management: A weighted empirical review *Journal of Public Health Jan 2008, 16 (1) : 21-29*	SR/MA **Poor**	Titles, abstracts, and full-text articles not dually and independently reviewed; quality of each included study not rated independently by two or more reviewers using a standard method to appraise its internal validity; publication bias was not assessed
10	**Leung, Wilson, Y, S;** Thomas, G, Neil; Chan, Juliana, C, N; Tomlinson, Brian Weight management and current options in pharmacotherapy: orlistat and sibutramine. *Clinical therapeutics Jan 2003, 25 (1) : 58-80*	SR/MA **Poor**	Eligibility criteria for included and excluded studies not specified; titles, abstracts, and full-text articles not dually and independently reviewed; quality of each included study not rated independently by two or more reviewers using a standard method to appraise its internal validity; publication bias not assessed
11	**Mannucci, Edoardo;** Dicembrini, Ilaria; Rotella, Francesco; Rotella, Carlo, Maria Orlistat and sibutramine beyond weight loss. *Nutrition, metabolism, and cardiovascular diseases : NMCD Jun 2008, 18 (5) : 342-8*	SR/MA **Poor**	Titles, abstracts, and full-text articles not dually and independently reviewed; publication bias not assessed

Count	Citations	Quality Rating	Rating Rationale
12	**Selvin, Elizabeth;** Paynter, Nina, P; Erlinger, Thomas, P The effect of weight loss on C-reactive protein: a systematic review. *Archives of internal medicine Jan 2007, 167 (1) : 31-9*	SR/MA **Poor**	No quality assessment; quality of each included study not rated independently by two or more reviewers using a standard method to appraise its internal validity; publication bias not assessed
13	**Sharma, Arya, M;** Golay, Alain Effect of orlistat-induced weight loss on blood pressure and heart rate in obese patients with hypertension. *Journal of hypertension Sep 2002, 20 (9) : 1873-8*	SR/MA **Poor**	Quality of each included study not rated independently by two or more reviewers using a standard method to appraise its internal validity; publication bias not assessed
14	**Tsai, Adam, Gilden;** Wadden, Thomas, A The evolution of very-low-calorie diets: an update and meta-analysis. *Obesity (Silver Spring, Md.) Aug 2006, 14 (8) : 1283-93*	SR/MA **Poor**	Quality of each included study not rated independently by two or more reviewers using a standard method to appraise its internal validity; publication bias not assessed
15	**Walker, K, Z;** O'Dea, K; Gomez, M; Girgis, S; Colagiuri, R Diet and exercise in the prevention of diabetes. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association Aug 2010, 23 (4) : 344-52*	SR/MA **Poor**	Larger review from Diabetes Australia could not be found online; titles, abstracts, and full-text articles not dually and independently reviewed; quality of each included study not rated independently by two or more reviewers using a standard method to appraise its internal validity; included studies along with important characteristics and results of each study not listed; publication bias not assessed

Critical Question 2

a. Are the current cutpoint values for overweight (BMI 25.0 to 29.9 kg/m^2) and obesity (BMI ≥30 kg/m^2) compared with BMI 18.5 to 24.9 kg/m^2 associated with elevated CVD risk (defined below)? Are the WC cutpoints of >102 cm (M) and >88 cm (F) associated with elevated CVD risk (defined below)?

How do these cutpoints compare with other cutpoints in terms of elevated CVD risk?

- Fatal and non-fatal CHD, stroke, and CVD
- Overall mortality
- Incident type 2 diabetes mellitus
- Incident dyslipidemia
- Incident hypertension

b. Are differences across population subgroups in the relationships of BMI and WC cutpoints with CVD sufficiently large to warrant different cutpoints? If so, what should they be?

- Fatal and non-fatal CHD, stroke, and CVD
- Overall mortality
- Incident type 2 diabetes mellitus
- Incident dyslipidemia
- Incident hypertension

Groups being considered include:

- Age
- Sex (both M and F)
- Race/ethnicity (African American, Hispanic, Native American, Asian, Caucasian)

c. What are the associations between maintaining weight and weight gain with elevated CVD risk in normal weight, overweight, and obese adults?

Tables 11 and 12 show SR/MAs rated fair or good and those rated poor, respectively:

CQ2 initially involved studies and SRs/MAs. Due to resource constraints, the final evidence review involved SRs/MAs only.

Table A–12. CQ2 Studies Rated Fair or Good

Count	Citations	Quality Rating
1	Emerging Risk Factors Collaboration; Wormser, David; Kaptoge, Stephen; Di Angelantonio, Emanuele; Wood, Angela, M; Pennells, Lisa; Thompson, Alex; Sarwar, Nadeem; Kizer, Jorge, R; Lawlor, Debbie, A; Nordestgaard, Børge, G; Ridker, Paul; Salomaa, Veikko; Stevens, June; Woodward, Mark; Sattar, Naveed; Collins, Rory; Thompson, Simon, G; Whitlock, Gary; Danesh, John Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *Lancet Mar 2011, 377 (9771) : 1085-95* ttSearchEngine.ttFilter: 100	Fair SR/MA
2	Lenz, Matthias; Richter, Tanja; Mühlhauser, Ingrid The morbidity and mortality associated with overweight and obesity in adulthood: a systematic review. *Deutsches Ärzteblatt international Oct 2009, 106 (40) : 641-8* ttSearchEngine.filteredChildren: 100	Fair SR/MA
3	Prospective Studies Collaboration; Whitlock, Gary; Lewington, Sarah; Sherliker, Paul; Clarke, Robert; Emberson, Jonathan; Halsey, Jim; Qizilbash, Nawab; Collins, Rory; Peto, Richard Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet Mar 2009, 373 (9669) : 1083-96* ttRankEngine.ttRank: 1	Fair SR/MA

Table A–13. CQ2 Studies Rated as Poor with Rationale

Count	Citations	Quality Rating	Rating Rationale
1	**Abell, Jill, E;** Egan, Brent, M; Wilson, Peter, W, F; Lipsitz, Stuart; Woolson, Robert, F; Lackland, Daniel, T Age and race impact the association between BMI and CVD mortality in women. *Public health reports (Washington, D.C. : 1974) Jul 2007, 122 (4) : 507-12* ttRankEngine: 93	**Poor** SR/MA	No predefined and specified I/E criteria; no comprehensive and systematic literature search; no dual review of abstracts and full text articles for I/E criteria; no quality assessment of included studies; no assessment of publication bias

Count	Citations	Quality Rating	Rating Rationale
2	**Berrington de Gonzalez, Amy;** Hartge, Patricia; Cerhan, James, R; Flint, Alan, J; Hannan, Lindsay; MacInnis, Robert, J; Moore, Steven, C; Tobias, Geoffrey, S; Anton-Culver, Hoda; Freeman, Laura, Beane; Beeson, W, Lawrence; Clipp, Sandra, L; English, Dallas, R; Folsom, Aaron, R; Freedman, D, Michal; Giles, Graham; Hakansson, Niclas; Henderson, Katherine, D; Hoffman-Bolton, Judith; Hoppin, Jane, A; Koenig, Karen, L; Lee, I-Min; Linet, Martha, S; Park, Yikyung; Pocobelli, Gaia; Schatzkin, Arthur; Sesso, Howard, D; Weiderpass, Elisabete; Willcox, Bradley, J; Wolk, Alicja; Zeleniuch-Jacquotte, Anne; Willett, Walter, C; Thun, Michael, J Body-mass index and mortality among 1.46 million white adults. *The New England journal of medicine Dec 2010, 363 (23): 2211-9* ttSearchEngine.ttFilter: 100	**Poor** SR/MA	Dual review, individual quality assessment of included studies not reported; all studies pulled from National Cancer Institute Cohort Consortium Not a comprehensive search, so there is potential for bias
3	**Bogers, Rik, P;** Bemelmans, Wanda, J, E; Hoogenveen, Rudolf, T; Boshuizen, Hendriek, C; Woodward, Mark; Knekt, Paul; van Dam, Rob, M; Hu, Frank, B; Visscher, Tommy, L, S; Menotti, Alessandro; Thorpe, Roland, J; Jamrozik, Konrad; Calling, Susanna; Strand, Bjørn, Heine; Shipley, Martin, J; for the BMI-CHD Collaboration Investigators Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: a meta-analysis of 21 cohort studies including more than 300 000 persons. *Archives of internal medicine Sep 2007, 167 (16) : 1720-8* ttSearchEngine.ttQuery: 100	**Poor** SR/MA	Only 31 of 70 studies contributed data to this individual participant MA, and data from only 21 studies were used in the analysis; no dual review of abstracts and full- text articles for I/E criteria; no quality assessment of included studies; no assessment of publication bias; Individual participant data analyzed for only 21 of 70 studies found in literature search
4	**de Koning, Lawrence;** Merchant, Anwar, T; Pogue, Janice; Anand, Sonia, S Waist circumference and waist-to-hip ratio as predictors of cardiovascular events: meta-regression analysis of prospective studies. *European heart journal Apr 2007, 28 (7) : 850-6* ttSearchEngine.ttFilter: 100	**Poor** SR/MA	No quality assessment of included studies
5	**Guh, Daphne, P;** Zhang, Wei; Bansback, Nick; Amarsi, Zubin; Birmingham, C, Laird; Anis, Aslam, H The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC public health Jan 2009, 9 : 88-* ttSearchEngine.filteredChildren: 100	**Poor** SR/MA	Unclear if abstracts and full-text articles were dually reviewed for I/E criteria; no quality assessment of included studies

Count	Citations	Quality Rating	Rating Rationale
6	**Hartemink, Nienke;** Boshuizen, Hendriek, C; Nagelkerke, Nico, J, D; Jacobs, Monique, A, M; van Houwelingen, Hans, C Combining risk estimates from observational studies with different exposure cutpoints: a meta-analysis on body mass index and diabetes type 2. *American journal of epidemiology Jun 2006, 163 (11) : 1042-52* ttSearchEngine.filteredChildren: 100	**Poor** SR/MA	No dual review of abstracts and full- text articles for I/E criteria; no quality assessment of included studies
7	**Heiat, A;** Vaccarino, V; Krumholz, H, M An evidence-based assessment of federal guidelines for overweight and obesity as they apply to elderly persons. *Archives of internal medicine May 2001, 161 (9) : 1194-203* caSearchEngine: 61 cxSearchEngine: 17 ttRankEngine: 92	**Poor** SR/MA	Literature search limited in scope; no dual review of abstracts and full- text articles for I/E criteria; no quality assessment of included studies; no assessment of publication bias
8	**McGee, Daniel, L;** Diverse Populations Collaboration Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. *Annals of epidemiology Feb 2005, 15 (2) : 87-97* caSearchEngine: 73 cxSearchEngine: 18 ttRankEngine: 93	**Poor** SR/MA	Unclear how the 26 included studies were selected; no comprehensive and systematic literature search; no dual review of abstracts and full-text articles for I/E criteria; no quality assessment of included studies; no assessment of publication bias
9	**Owen, C, G;** Whincup, P, H; Orfei, L; Chou, Q-A; Rudnicka, A, R; Wathern, A, K; Kaye, S, J; Eriksson, J, G; Osmond, C; Cook, D, G Is body mass index before middle age related to coronary heart disease risk in later life? Evidence from observational studies. *International journal of obesity (2005) Aug 2009, 33 (8) : 866-77* ttSearchEngine.filteredChildren: 100	**Poor** SR/MA	No dual review of abstracts and full- text articles for I/E criteria; no quality assessment of included studies; no assessment of publication bias

Count	Citations	Quality Rating	Rating Rationale
10	**Pischon, T;** Boeing, H; Hoffmann, K; Bergmann, M; Schulze, M, B; Overvad, K; van der Schouw, Y, T; Spencer, E; Moons, K, G, M; Tjønneland, A; Halkjaer, J; Jensen, M, K; Stegger, J; Clavel-Chapelon, F; Boutron-Ruault, M-C; Chajes, V; Linseisen, J; Kaaks, R; Trichopoulou, A; Trichopoulos, D; Bamia, C; Sieri, S; Palli, D; Tumino, R; Vineis, P; Panico, S; Peeters, P, H, M; May, A, M; Bueno-de-Mesquita, H, B; van Duijnhoven, F, J, B; Hallmans, G; Weinehall, L; Manjer, J; Hedblad, B; Lund, E; Agudo, A; Arriola, L; Barricarte, A; Navarro, C; Martinez, C; Quirós, J, R; Key, T; Bingham, S; Khaw, K, T; Boffetta, P; Jenab, M; Ferrari, P; Riboli, E General and abdominal adiposity and risk of death in Europe. *The New England journal of medicine Nov 2008, 359 (20) : 2105-20* ttSearchEngine.ttQuery: 100	**Poor** SR/MA	Key SR/MA criteria were not met, such as adequate search strategy, independent title, abstract, etc.; review: independent appraisal of internal validity
11	**Vazquez, Gabriela;** Duval, Sue; Jacobs, David, R; Silventoinen, Karri Comparison of body mass index, waist circumference, and waist/hip ratio in predicting incident diabetes: a meta-analysis. *Epidemiologic reviews Jan 2007, 29 : 115-28* ttRankEngine.ttRank: 62	**Poor** SR/MA	No comprehensive and systematic literature search; no quality assessment of included studies
12	**Whitlock, Gary;** Lewington, Sarah; Mhurchu, Cliona, Ni Coronary heart disease and body mass index: a systematic review of the evidence from larger prospective cohort studies. *Seminars in vascular medicine Nov 2002, 2 (4) : 369-81* cxSearchEngine: 13 ttRankEngine: 92	**Poor** SR/MA	No dual review of abstracts and full- text articles for I/E criteria; no quality assessment of included studies; no assessment of publication bias

Critical Question 3

a. In overweight or obese adults, what is the comparative efficacy/effectiveness of diets of differing forms and structures (macronutrient content, carbohydrate and fat quality, nutrient density, amount of energy deficit, dietary pattern) or other dietary weight loss strategies (e.g., meal timing, portion controlled meal replacements) in achieving or maintaining weight loss?

b. During weight loss or weight maintenance after weight loss, what are the comparative health benefits or harms of the above diets and other dietary weight loss strategies?

Tables A-14 and A-15 show studies rated fair or good and studies rated poor, respectively:

Table A–14. CQ3 Studies Rated Fair or Good

Count	Citations	Quality Rating
1	**Ashley, J, M;** St Jeor, S, T; Schrage, J, P; Perumean-Chaney, S, E; Gilbertson, M, C; McCall, N, L; Bovee, V Weight control in the physician's office. *Archives of internal medicine Jul 2001, 161 (13) : 1599-604*	**Fair** Controlled intervention study
2	**Burke, Lora, E;** Hudson, Alana, G; Warziski, Melanie, T; Styn, Mindi, A; Music, Edvin; Elci, Okan, U; Sereika, Susan, M Effects of a vegetarian diet and treatment preference on biochemical and dietary variables in overweight and obese adults: a randomized clinical trial. *The American journal of clinical nutrition Sep 2007, 86 (3) : 588-96*	**Good** Controlled intervention study
3	**Burke, Lora, E;** Styn, Mindi, A; Steenkiste, Ann, R; Music, Edvin; Warziski, Melanie; Choo, Jina A randomized clinical trial testing treatment preference and two dietary options in behavioral weight management: preliminary results of the impact of diet at 6 months--PREFER study. *Obesity (Silver Spring, Md.) Nov 2006, 14 (11) : 2007-17*	**Fair** Controlled intervention study
4	**Due, A;** Toubro, S; Skov, A, R; Astrup, A Effect of normal-fat diets, either medium or high in protein, on body weight in overweight subjects: a randomised 1-year trial. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Oct 2004, 28 (10) : 1283-90*	**Fair** Controlled intervention study
5	**Due, A;** Toubro, S; Stender, S; Skov, A, R; Astrup, A The effect of diets high in protein or carbohydrate on inflammatory markers in overweight subjects. *Diabetes, obesity & metabolism May 2005, 7 (3) : 223-9*	**Fair** Controlled intervention study
6	**Ebbeling, Cara, B;** Leidig, Michael, M; Feldman, Henry, A; Lovesky, Margaret, M; Ludwig, David, S Effects of a low-glycemic load vs. low-fat diet in obese young adults: a randomized trial. *JAMA : the journal of the American Medical Association May 2007, 297 (19) : 2092-102*	**Fair** Controlled intervention study
7	**Esposito, Katherine;** Maiorino, Maria, Ida; Ciotola, Miryam; Di Palo, Carmen; Scognamiglio, Paola; Gicchino, Maurizio; Petrizzo, Michela; Saccomanno, Franco; Beneduce, Flora; Ceriello, Antonio; Giugliano, Dario Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial. *Annals of internal medicine Sep 2009, 151 (5) : 306-14*	**Good** Controlled intervention study
8	**Foster, Gary, D;** Wyatt, Holly, R; Hill, James, O; Makris, Angela, P; Rosenbaum, Diane, L; Brill, Carrie; Stein, Richard, I; Mohammed, B, Selma; Miller, Bernard; Rader, Daniel, J; Zemel, Babette; Wadden, Thomas, A; Tenhave, Thomas; Newcomb, Craig, W; Klein, Samuel Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. *Annals of internal medicine Aug 2010, 153 (3) : 147-57* ttSearchEngine.ttFilter: 100	**Fair** Controlled intervention study

Count	Citations	Quality Rating
9	**Frisch, Sabine;** Zittermann, Armin; Berthold, Heiner, K; Götting, Christian; Kuhn, Joachim; Kleesiek, Knut; Stehle, Peter; Körtke, Heinrich A randomized controlled trial on the efficacy of carbohydrate-reduced or fat-reduced diets in patients attending a telemedically guided weight loss program. *Cardiovascular diabetology Jan 2009, 8 : 36-*	**Fair** Controlled intervention study
10	**Lejeune, Manuela, P, G, M;** Kovacs, Eva, M, R; Westerterp-Plantenga, Margriet, S Additional protein intake limits weight regain after weight loss in humans. *The British journal of nutrition Feb 2005, 93 (2) : 281-9*	**Fair** Controlled intervention study
11	**McAuley, K, A;** Hopkins, C, M; Smith, K, J; McLay, R, T; Williams, S, M; Taylor, R, W; Mann, J, I Comparison of high-fat and high-protein diets with a high-carbohydrate diet in insulin-resistant obese women. *Diabetologia Jan 2005, 48 (1) : 8-16*	**Fair** Controlled intervention study
12	**Pittas, Anastassios, G;** Roberts, Susan, B; Das, Sai, Krupa; Gilhooly, Cheryl, H; Saltzman, Edward; Golden, Julie; Stark, Paul, C; Greenberg, Andrew, S The effects of the dietary glycemic load on type 2 diabetes risk factors during weight loss. *Obesity (Silver Spring, Md.) Dec 2006, 14 (12) : 2200-9*	**Fair** Controlled intervention study
13	**Poppitt, Sally, D;** Keogh, Geraldine, F; Prentice, Andrew, M; Williams, Desmond, E, M; Sonnemans, Heidi, M, W; Valk, Esther, E, J; Robinson, Elizabeth; Wareham, Nicholas, J Long-term effects of ad libitum low-fat, high-carbohydrate diets on body weight and serum lipids in overweight subjects with metabolic syndrome. *The American journal of clinical nutrition Jan 2002, 75 (1) : 11-20*	**Fair** Controlled intervention study
14	**Sacks, Frank, M;** Bray, George, A; Carey, Vincent, J; Smith, Steven, R; Ryan, Donna, H; Anton, Stephen, D; McManus, Katherine; Champagne, Catherine, M; Bishop, Louise, M; Laranjo, Nancy; Leboff, Meryl, S; Rood, Jennifer, C; de Jonge, Lilian; Greenway, Frank, L; Loria, Catherine, M; Obarzanek, Eva; Williamson, Donald, A Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *The New England journal of medicine Feb 2009, 360 (9) : 859-73*	**Good** Controlled intervention study
15	**Skov, A, R;** Toubro, S; Bülow, J; Krabbe, K; Parving, H, H; Astrup, A Changes in renal function during weight loss induced by high vs low-protein low-fat diets in overweight subjects. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Nov 1999, 23 (11) : 1170-7*	**Fair** Controlled intervention study
16	**Skov, A, R;** Toubro, S; Rønn, B; Holm, L; Astrup, A Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity May 1999, 23 (5) : 528-36*	**Fair** Controlled intervention study
17	**Skov, Annebeth, R;** Haulrik, Nikolaj; Toubro, Søren; Mølgaard, Christian; Astrup, Arne Effect of protein intake on bone mineralization during weight loss: a 6-month trial. *Obesity research Jun 2002, 10 (6) : 432-8*	**Fair** Controlled intervention study

Count	Citations	Quality Rating
18	**Thompson, Warren, G;** Rostad Holdman, Nicole; Janzow, Denise, J; Slezak, Jeffrey, M; Morris, Kristin, L; Zemel, Michael, B Effect of energy-reduced diets high in dairy products and fiber on weight loss in obese adults. *Obesity research Aug 2005, 13 (8) : 1344-53*	**Good** Controlled intervention study
19	**Torgerson, J, S;** Agren, L; Sjöström, L Effects on body weight of strict or liberal adherence to an initial period of VLCD treatment. A randomised, one-year clinical trial of obese subjects. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Feb 1999, 23 (2) : 190-7*	**Fair** Controlled intervention study
20	**Turner-McGrievy, Gabrielle, M;** Barnard, Neal, D; Scialli, Anthony, R A two-year randomized weight loss trial comparing a vegan diet to a more moderate low-fat diet. *Obesity (Silver Spring, Md.) Sep 2007, 15 (9) : 2276-81*	**Fair** Controlled intervention study
21	**Turner-McGrievy, Gabrielle, M;** Barnard, Neal, D; Scialli, Anthony, R; Lanou, Amy, J Effects of a low-fat vegan diet and a Step II diet on macro- and micronutrient intakes in overweight postmenopausal women. *Nutrition (Burbank, Los Angeles County, Calif.) Sep 2004, 20 (9) : 738-46*	**Fair** Controlled intervention study
22	**Wadden, Thomas, A;** Foster, Gary, D; Sarwer, David, B; Anderson, Drew, A; Gladis, Madeline; Sanderson, Rebecca, S; Letchak, R, V; Berkowitz, Robert, I; Phelan, Suzanne Dieting and the development of eating disorders in obese women: results of a randomized controlled trial. *The American journal of clinical nutrition Sep 2004, 80 (3) : 560-8*	**Fair** Controlled intervention study
23	**Wien, M, A;** Sabaté, J, M; Iklé, D, N; Cole, S, E; Kandeel, F, R Almonds vs complex carbohydrates in a weight reduction program. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Nov 2003, 27 (11) : 1365-72*	**Fair** Controlled intervention study

Table A–15. CQ3 Studies Rated Poor with Rationale

Count	Citations	Quality Rating	Rating Rationale
1	**Ashley, Judith, M;** Herzog, Holly; Clodfelter, Sharon; Bovee, Vicki; Schrage, Jon; Pritsos, Chris Nutrient adequacy during weight loss interventions: a randomized study in women comparing the dietary intake in a meal replacement group with a traditional food group. *Nutrition journal Jan 2007, 6 : 12-*	**Poor** Controlled intervention study	Completers analysis with 27% overall attrition (10/18/11)
2	**Bertéus Forslund, H;** Klingström, S; Hagberg, H; Löndahl, M; Torgerson, J, S; Lindroos, A, K Should snacks be recommended in obesity treatment? A 1-year randomized clinical trial. *European journal of clinical nutrition Nov 2008, 62 (11) : 1308-17*	**Poor** Controlled intervention study	Overall attrition greater than 30%; downgrade to poor following (10/20/11)
3	**Brehm, Bonnie, J;** Lattin, Barbara, L; Summer, Suzanne, S; Boback, Jane, A; Gilchrist, Gina, M; Jandacek, Ronald, J; D'Alessio, David, A One-year comparison of a high-monounsaturated fat diet	**Poor** Controlled intervention study	Differences at baseline, high attrition and differential attrition; lacks baseline data for

Count	Citations	Quality Rating	Rating Rationale
	with a high-carbohydrate diet in type 2 diabetes. *Diabetes care Feb 2009, 32 (2) : 215-20*		full sample
4	**Brehm, Bonnie, J;** Seeley, Randy, J; Daniels, Stephen, R; D'Alessio, David, A A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. *The Journal of clinical endocrinology and metabolism Apr 2003, 88 (4) : 1617-23*	**Poor** Controlled intervention study	Only completers data for baseline demographics; no ITT analysis; high attrition; cannot determine power
5	**Brinkworth, G, D;** Noakes, M; Keogh, J, B; Luscombe, N, D; Wittert, G, A; Clifton, P, M Long-term effects of a high-protein, low-carbohydrate diet on weight control and cardiovascular risk markers in obese hyperinsulinemic subjects. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity May 2004, 28 (5) : 661-70*	**Poor** Controlled intervention study	Small sample size; high dropout rate; low adherence to both diets; difficult to come to conclusion about results; 8/27/12 changed overall quality rating from fair to poor per follow-up; rationale: ITT analysis was not an ITT analysis-it was conducted on 43 completers to impute missing data; so it is really a completers analysis with attrition of at least 26%.
6	**Brinkworth, Grant, D;** Buckley, Jonathan, D; Noakes, Manny; Clifton, Peter, M; Wilson, Carlene, J Long-term effects of a very low-carbohydrate diet and a low-fat diet on mood and cognitive function. *Archives of internal medicine Nov 2009, 169 (20) : 1873-80*	**Poor** Controlled intervention study	Results data is for completers only and dropout rate was high; note: rated together with Brinkworth 2009 AJCN paper; (8/28/12) overall quality rating changed from fair to poor per follow-up; rationale: high attrition (41%)
7	**Brinkworth, Grant, D;** Noakes, Manny; Buckley, Jonathan, D; Keogh, Jennifer, B; Clifton, Peter, M Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. *The American journal of clinical nutrition Jul 2009, 90 (1) : 23-32*	**Poor** Controlled intervention study	Results data is for completers only and dropout rate was high; 8/27/12 overall quality rating changed from fair to poor per follow-up; rationale: high attrition (41%).
8	**Cardillo, S;** Seshadri, P; Iqbal, N The effects of a low-carbohydrate versus low-fat diet on adipocytokines in severely obese adults: three-year follow-up of a randomized trial. *European review for medical and pharmacological sciences May 2006, 10 (3) : 99-106*	**Poor** Controlled intervention study	High attrition rate; only drawback is a very high attrition, which is mitigated by the inclusion of chart weights; note: rated together with Samaha 2003 paper; high overall

Count	Citations	Quality Rating	Rating Rationale
			and differential attrition; downgraded to poor after consultation (10/18/11)
9	**Chao, D;** Espeland, M, A; Farmer, D; Register, T, C; Lenchik, L; Applegate, W, B; Ettinger, W, H Effect of voluntary weight loss on bone mineral density in older overweight women. *Journal of the American Geriatrics Society Jul 2000, 48 (7) : 753-9*	**Poor** Controlled intervention study	No ITT analysis; no data for withdrawals per group, completers' baseline demographic data; choose poor because internal validity was threatened; all participants were not randomized causing differential selection; method used to generate randomization not mentioned and ITT not captured
10	**Clifton, Peter, M;** Keogh, Jennifer, B; Noakes, Manny Long-term effects of a high-protein weight-loss diet. *The American journal of clinical nutrition Jan 2008, 87 (1) : 23-9*	**Poor** Controlled intervention study	No ITT analysis; high attrition; no power; baseline demographics reported for completers only; whole group was treated as one intervention group because of the convergence in diets;
11	**Dansinger, Michael, L;** Gleason, Joi, Augustin; Griffith, John, L; Selker, Harry, P; Schaefer, Ernst, J Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA : the journal of the American Medical Association Jan 2005, 293 (1) : 43-53*	**Poor** Controlled intervention study	8/27/12 overall quality rating changed from fair to poor per follow-up; rationale: high attrition (41.9%)
12	**Das, Sai, Krupa;** Gilhooly, Cheryl, H; Golden, Julie, K; Pittas, Anastassios, G; Fuss, Paul, J; Cheatham, Rachel, A; Tyler, Stephanie; Tsay, Michelle; McCrory, Megan, A; Lichtenstein, Alice, H; Dallal, Gerard, E; Dutta, Chhanda; Bhapkar, Manjushri, V; Delany, James, P; Saltzman, Edward; Roberts, Susan, B Long-term effects of 2 energy-restricted diets differing in glycemic load on dietary adherence, body composition, and metabolism in CALERIE: a 1-y randomized controlled trial. *The American journal of clinical nutrition Apr 2007, 85 (4) : 1023-30*	**Poor** Controlled intervention study	Presents 6 and 12 mos results using completers data for completers of 12 mos; at that point, overall attrition is >10% (14.7%) (9/6/11)
13	**Davis, Nichola, J;** Tomuta, Nora; Schechter, Clyde; Isasi, Carmen, R; Segal-Isaacson, C, J; Stein, Daniel; Zonszein, Joel; Wylie-Rosett, Judith Comparative study of the effects of a 1-year dietary intervention of a low-carbohydrate diet versus a low-fat diet on weight and glycemic control in type 2 diabetes.	**Poor** Controlled intervention study	Downgrade to poor; analyses at least for these 2 outcomes had dropouts >15%; dietary compliance data based on 65% of participants

Count	Citations	Quality Rating	Rating Rationale
	Diabetes care Jul 2009, 32 (7) : 1147-52		at 6 mos and 54% at 12 mos (9/01); authors attempted to control for the baseline body mass difference in analysis
14	**Ditschuneit, H, H;** Flechtner-Mors, M Value of structured meals for weight management: risk factors and long-term weight maintenance. *Obesity research Nov 2001, 9 Suppl 4 : 284S-289S*	**Poor** Controlled intervention Study	High attrition; no ITT analysis; no data for withdrawals per group; no power calculation;
15	**Ditschuneit, H, H;** Frier, H, I; Flechtner-Mors, M Lipoprotein responses to weight loss and weight maintenance in high-risk obese subjects. *European journal of clinical nutrition Mar 2002, 56 (3) : 264-70*	**Poor** Controlled intervention study	High attrition; no ITT analysis; a large number of patients withdrew midstudy, and reentered several months later
16	**Due, Anette;** Larsen, Thomas, M; Mu, Huiling; Hermansen, Kjeld; Stender, Steen; Astrup, Arne Comparison of 3 ad libitum diets for weight-loss maintenance, risk of cardiovascular disease, and diabetes: a 6-mo randomized, controlled trial. *The American journal of clinical nutrition Nov 2008, 88 (5) : 1232-41*	**Poor** Controlled intervention study	Overall attrition 20%; high differential attrition; downgrade to poor following consultation (10/18/11)
17	**Ebbeling, Cara, B;** Leidig, Michael, M; Sinclair, Kelly, B; Seger-Shippee, Linda, G; Feldman, Henry, A; Ludwig, David, S Effects of an ad libitum low-glycemic load diet on cardiovascular disease risk factors in obese young adults. *The American journal of clinical nutrition May 2005, 81 (5) : 976-82* ttSearchEngine.ttFilter: 100	**Poor** Controlled intervention study	High attrition; completers data; primary data analysis done only on those that completed study; dropout rate high for both groups
18	**Ello-Martin, Julia, A;** Roe, Liane, S; Ledikwe, Jenny, H; Beach, Amanda, M; Rolls, Barbara, J Dietary energy density in the treatment of obesity: a year-long trial comparing 2 weight-loss diets. *The American journal of clinical nutrition Jun 2007, 85 (6) : 1465-77*	**Poor** Controlled intervention study	High attrition; no ITT analysis
19	**Flechtner-Mors, M;** Ditschuneit, H, H; Johnson, T, D; Suchard, M, A; Adler, G Metabolic and weight loss effects of long-term dietary intervention in obese patients: four-year results. *Obesity research Aug 2000, 8 (5) : 399-402*	**Poor** Controlled intervention study	Note: This paper linked to Ditschuneit 2002; high attrition; no ITT analysis; large number of patients withdrew mid-study and reentered several months later
20	**Fleming, Richard, M** The effect of high-, moderate-, and low-fat diets on weight loss and cardiovascular disease risk factors. *Preventive cardiology Jan 2002, 5 (3) : 110-8* ttSearchEngine.ttFilter: 100	**Poor** Controlled intervention study	High attrition; completers data; ITT not captured
21	**Fontaine, Kevin, R;** Yang, Dongyan; Gadbury, Gary, L; Heshka, Stanley; Schwartz, Linda, G; Murugesan, Radha; Kraker, Jennifer, L; Heo, Moonseong; Heymsfield, Steven,	**Poor** Controlled intervention	Very high attrition; no data on attrition for treatment groups; no

Count	Citations	Quality Rating	Rating Rationale
	B; Allison, David, B Results of soy-based meal replacement formula on weight, anthropometry, serum lipids & blood pressure during a 40-week clinical weight loss trial. *Nutrition journal Nov 2003, 2 : 14-*	study	ITT analysis
22	**Harvey-Berino, J** The efficacy of dietary fat vs. total energy restriction for weight loss. *Obesity research May 1998, 6 (3) : 202-7*	**Poor** Controlled intervention study	Note: rated together with Harvey-Berino 1999
23	**Harvey-Berino, J** Calorie restriction is more effective for obesity treatment than dietary fat restriction. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine Jan 1999, 21 (1) : 35-9*	**Poor** Controlled intervention study	High dropout; no ITT analysis; no power calculations; baseline demographics presented only for completers
24	**Iqbal, N;** Seshadri, P; Stern, L; Loh, J; Kundu, S; Jafar, T; Samaha, F, F Serum resistin is not associated with obesity or insulin resistance in humans. *European review for medical and pharmacological sciences May 2005, 9 (3) : 161-5*	**Poor** Controlled intervention Study	High attrition rate; only drawback is a very high attrition, which is mitigated by inclusion of chart weights; note: rated together with Samaha 2003 paper; high overall/differential attrition; downgraded to poor after consultation (10/18/11)
25	**Keogh, Jennifer, B;** Clifton, Peter The effect of meal replacements high in glycomacropeptide on weight loss and markers of cardiovascular disease risk. *The American journal of clinical nutrition Jun 2008, 87 (6) : 1602-5*	**Poor** Controlled intervention study	High attrition; no ITT analysis; no data on adherence
26	**Lantz, H;** Peltonen, M; Agren, L; Torgerson, J, S Intermittent versus on-demand use of a very low calorie diet: a randomized 2-year clinical trial. *Journal of internal medicine Apr 2003, 253 (4) : 463-71*	**Poor** Controlled intervention study	Did not inform method of randomization; very high dropout rate. which affects internal validity of study; extremely high attrition; baseline demographic for completers only
27	**Layman, Donald, K;** Evans, Ellen, M; Erickson, Donna; Seyler, Jennifer; Weber, Judy; Bagshaw, Deborah; Griel, Amy; Psota, Tricia; Kris-Etherton, Penny A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *The Journal of nutrition Mar 2009, 139 (3) : 514-21*	**Poor** Controlled intervention study	High attrition; high differential attrition; no data on adherence; differences at baseline
28	**Leslie, W, S;** Lean, M, E, J; Baillie, H, M; Hankey, C, R Weight management: a comparison of existing dietary approaches in a work-site setting. *International journal of obesity and related metabolic*	**Poor** Controlled intervention study	High attrition; high differential attrition; no ITT analysis

Count	Citations	Quality Rating	Rating Rationale
	disorders : journal of the International Association for the Study of Obesity Nov 2002, 26 (11) : 1469-75		
29	**Li, Z;** Hong, K; Saltsman, P; DeShields, S; Bellman, M; Thames, G; Liu, Y; Wang, H-J; Elashoff, R; Heber, D Long-term efficacy of soy-based meal replacements vs an individualized diet plan in obese type II DM patients: relative effects on weight loss, metabolic parameters, and C-reactive protein. *European journal of clinical nutrition Mar 2005, 59 (3) : 411-8*	**Poor** Controlled intervention study	(8/27/12) overall quality rating changed from fair to poor per follow-up; rationale: they say ITT analysis but actually they dropped 20% after randomization so not an ITT analysis plus >10% attrition
30	**Maki, Kevin, C;** Rains, Tia, M; Kaden, Valerie, N; Raneri, Kathleen, R; Davidson, Michael, H Effects of a reduced-glycemic-load diet on body weight, body composition, and cardiovascular disease risk markers in overweight and obese adults. *The American journal of clinical nutrition Mar 2007, 85 (3) : 724-34*	**Poor** Controlled intervention study	Completers data reported; withdrawals: 23.3% vs. 16.3%; overall =19.8%; downgrade to poor following consultation (9/6/11)
31	**McAuley, K, A;** Smith, K, J; Taylor, R, W; McLay, R, T; Williams, S, M; Mann, J, I Long-term effects of popular dietary approaches on weight loss and features of insulin resistance. *International journal of obesity (2005) Feb 2006, 30 (2) : 342-9*	**Poor** Controlled intervention study	Completers analysis with an overall attrition rate of 20.8%; downgrade to poor following consultation (9/13/11)
32	**Morgan, L, M;** Griffin, B, A; Millward, D, J; DeLooy, A; Fox, K, R; Baic, S; Bonham, M, P; Wallace, J, M, W; MacDonald, I; Taylor, M, A; Truby, H Comparison of the effects of four commercially available weight-loss programmes on lipid-based cardiovascular risk factors. *Public health nutrition Jun 2009, 12 (6) : 799-807*	**Poor** Controlled intervention Study	High attrition; no data on differential attrition; no ITT analysis; no power calculation
33	**Noakes, Manny;** Foster, Paul, R; Keogh, Jennifer, B; Clifton, Peter, M Meal replacements are as effective as structured weight-loss diets for treating obesity in adults with features of metabolic syndrome. *The Journal of nutrition Aug 2004, 134 (8) : 1894-9*	**Poor** Controlled intervention study	No ITT analysis; high dropout rate; no power calculation; baseline data for completers only
34	**Pereira, Mark, A;** Swain, Janis; Goldfine, Allison, B; Rifai, Nader; Ludwig, David, S Effects of a low-glycemic load diet on resting energy expenditure and heart disease risk factors during weight loss. *JAMA : the journal of the American Medical Association Nov 2004, 292 (20) : 2482-90*	**Poor** Controlled intervention study	Completers only with overall withdrawals >20%; differential attrition 21.8%; downgraded to poor following consultation (9/6/11)
35	**Poston, W, S, C;** Haddock, C, K; Pinkston, M, M; Pace, P; Karakoc, N, D; Reeves, R, S; Foreyt, J, P Weight loss with meal replacement and meal replacement plus snacks: a randomized trial. *International journal of obesity (2005) Sep 2005, 29 (9) : 1107-14*	**Poor** Controlled intervention study	Confusing way of reporting attrition (within sample and differential); very high attrition rate; confusing way of reporting adherence; no power calculation

Count	Citations	Quality Rating	Rating Rationale
36	**Ricci, T, A;** Heymsfield, S, B; Pierson, R, N; Stahl, T; Chowdhury, H, A; Shapses, S, A Moderate energy restriction increases bone resorption in obese postmenopausal women. *The American journal of clinical nutrition Feb 2001, 73 (2) : 347-52*	**Poor** Controlled intervention study	No ITT analysis; baseline data for completers only; no data on attrition; five women were assigned to weight loss group on basis of their inability to lose weight for first 6 wks; objective of study was not to compare diet interventions
37	**Riedt, Claudia, S;** Cifuentes, Mariana; Stahl, Theodore; Chowdhury, Hasina, A; Schlussel, Yvette; Shapses, Sue, A Overweight postmenopausal women lose bone with moderate weight reduction and 1 g/day calcium intake. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research Mar 2005, 20 (3) : 455-63*	**Poor** Controlled intervention study	No ITT analysis; lack of clarity about total sample size; no power; no data on adherence
38	**Rolls, Barbara, J;** Roe, Liane, S; Beach, Amanda, M; Kris-Etherton, Penny, M Provision of foods differing in energy density affects long-term weight loss. *Obesity research Jun 2005, 13 (6) : 1052-60*	**Poor** Controlled intervention study	Downgraded to poor after discussion (lack of appropriate stat analysis for ITT analysis and high attrition) (11/30/11)
39	**Rothacker, D, Q;** Staniszewski, B, A; Ellis, P, K Liquid meal replacement vs traditional food: a potential model for women who cannot maintain eating habit change. *Journal of the American Dietetic Association Mar 2001, 101 (3) : 345-7*	**Poor** Controlled intervention study	Completers analysis; overall attrition at least 14% (10/18/11)
40	**Samaha, Frederick, F;** Iqbal, Nayyar; Seshadri, Prakash; Chicano, Kathryn, L; Daily, Denise, A; McGrory, Joyce; Williams, Terrence; Williams, Monica; Gracely, Edward, J; Stern, Linda A low-carbohydrate as compared with a low-fat diet in severe obesity. *The New England journal of medicine May 2003, 348 (21) : 2074-81*	**Poor** Controlled intervention study	Only drawback is a very high attrition, which is mitigated by inclusion of chart weights; high overall and differential attrition; downgraded to poor after consultation (10/18/11)
41	**Saris, W, H;** Astrup, A; Prentice, A, M; Zunft, H, J; Formiguera, X; Verboeket-van de Venne, W, P; Raben, A; Poppitt, S, D; Seppelt, B; Johnston, S; Vasilaras, T, H; Keogh, G, F Randomized controlled trial of changes in dietary carbohydrate/fat ratio and simple vs complex carbohydrates on body weight and blood lipids: the CARMEN study. The Carbohydrate Ratio Management in European National diets. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Oct 2000, 24 (10) : 1310-8*	**Poor** Controlled intervention study	Overall attrition 20.6% and completers only analysis; downgrade to poor following consultation (9/6/11)

Count	Citations	Quality Rating	Rating Rationale
42	**Seshadri, Prakash;** Iqbal, Nayyar; Stern, Linda; Williams, Monica; Chicano, Kathryn, L; Daily, Denise, A; McGrory, Joyce; Gracely, Edward, J; Rader, Daniel, J; Samaha, Frederick, F A randomized study comparing the effects of a low-carbohydrate diet and a conventional diet on lipoprotein subfractions and C-reactive protein levels in patients with severe obesity. *The American journal of medicine Sep 2004, 117 (6) : 398-405*	**Poor** Controlled intervention study	High attrition rate; only drawback is very high attrition, which is mitigated by inclusion of chart weights; note: rated together with Samaha 2003; high overall/differential attrition; downgraded to poor after consultation (10/18/11)
43	**Seshadri, Prakash;** Samaha, Frederick, F; Stern, Linda; Chicano, Kathryn, L; Daily, Denise, A; Iqbal, Nayyar Free fatty acids, insulin resistance, and corrected qt intervals in morbid obesity: effect of weight loss during 6 months with differing dietary interventions. *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists Jul 2005, 11 (4) : 234-9*	**Poor** Controlled intervention study	High attrition rate; only drawback is very high attrition, which is mitigated by inclusion of chart weights; note: rated together with Samaha 2003 paper; high overall/differential attrition; downgraded to poor after consultation (10/18/11)
44	**Stern, Linda;** Iqbal, Nayyar; Seshadri, Prakash; Chicano, Kathryn, L; Daily, Denise, A; McGrory, Joyce; Williams, Monica; Gracely, Edward, J; Samaha, Frederick, F The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Annals of internal medicine May 2004, 140 (10) : 778-85*	**Poor** Controlled intervention study	High attrition rate; only drawback is very high attrition, which is mitigated by inclusion of chart weights; note: rated together with Samaha 2003 paper; high overall/differential attrition; downgraded to poor following consultation (10/18/11)
45	**Swenson, Brian, R;** Saalwachter Schulman, Alison; Edwards, Melissa, J; Gross, Meredith, P; Hedrick, Traci, L; Weltman, Arthur, L; Northrup, C, Joe; Schirmer, Bruce, D; Sawyer, Robert, G The effect of a low-carbohydrate, high-protein diet on post laparoscopic gastric bypass weight loss: a prospective randomized trial. *The Journal of surgical research Oct 2007, 142 (2) : 308-13*	**Poor** Controlled intervention study	Very high attrition; modified ITT analysis that contains completers only; no power calculation
46	**Tanumihardjo, Sherry, A;** Valentine, Ashley, R; Zhang, Zhumin; Whigham, Leah, D; Lai, HuiChuan, J; Atkinson, Richard, L Strategies to increase vegetable or reduce energy and fat intake induce weight loss in adults. *Experimental biology and medicine (Maywood, N.J.) May 2009, 234 (5) : 542-52*	**Poor** Controlled intervention study	High attrition; baseline difference between groups; no data on adherence; no power calculation; while paper states ITT; method used seems to be for completers data and dropout rate is >50%
47	**Tapsell, L, C;** Batterham, M, J; Teuss, G; Tan, S-Y; Dalton, S; Quick, C, J; Gillen, L, J; Charlton, K, E	**Poor** Controlled	High attrition; no ITT analysis; differences

Count	Citations	Quality Rating	Rating Rationale
	Long-term effects of increased dietary polyunsaturated fat from walnuts on metabolic parameters in type II diabetes. *European journal of clinical nutrition Aug 2009, 63 (8) : 1008-15*	intervention study	between groups at baseline
48	**Tay, Jeannie;** Brinkworth, Grant, D; Noakes, Manny; Keogh, Jennifer; Clifton, Peter, M Metabolic effects of weight loss on a very-low-carbohydrate diet compared with an isocaloric high-carbohydrate diet in abdominally obese subjects. *Journal of the American College of Cardiology Jan 2008, 51 (1) : 59-67*	**Poor** Controlled intervention study	Changed assessment to poor, so that overall assessment can be noted as poor per correspondence (8/27/12); changed overall quality rating from fair to poor per follow-up (8/27/12); rationale: authors do not take into account the 9 post-randomization exclusions in addition to 21 withdrawals during treatment; 25.4% attrition and not true ITT analysis
49	**Thomson, Cynthia, A;** Rock, Cheryl, L; Giuliano, Anna, R; Newton, Tara, R; Cui, Haiyan; Reid, Phyllis, M; Green, Tina, L; Alberts, David, S; Women's Healthy Eating & Living Study Group Longitudinal changes in body weight and body composition among women previously treated for breast cancer consuming a high-vegetable, fruit and fiber, low-fat diet. *European journal of nutrition Feb 2005, 44 (1) : 18-25*	**Poor** Controlled intervention study	No ITT analysis; high attrition; no data on adherence; no power; potentially different background interventions
50	**Thorpe, Matthew, P;** Jacobson, Edward, H; Layman, Donald, K; He, Xuming; Kris-Etherton, Penny, M; Evans, Ellen, M A diet high in protein, dairy, and calcium attenuates bone loss over twelve months of weight loss and maintenance relative to a conventional high-carbohydrate diet in adults. *The Journal of nutrition Jun 2008, 138 (6) : 1096-100*	**Poor** Controlled intervention study	Extremely high attrition and differential attrition; no power; differences between treatment groups at baseline;
51	**Vázquez, C;** Montagna, C; Alcaraz, F; Balsa, J, A; Zamarrón, I; Arrieta, F; Botella-Carretero, J, I Meal replacement with a low-calorie diet formula in weight loss maintenance after weight loss induction with diet alone. *European journal of clinical nutrition Oct 2009, 63 (10) : 1226-32*	**Poor** Controlled intervention study	Significant difference in weight loss accrued during induction phase, indicating possible randomization failure or experimental aberration; patients should have been randomized following induction phase, stratified by initial weight loss.
52	**Wing, R, R;** Venditti, E; Jakicic, J, M; Polley, B, A; Lang, W Lifestyle intervention in overweight individuals with a family history of diabetes. *Diabetes care Mar 1998, 21 (3) : 350-9*	**Poor** Controlled intervention study	High differential attrition; no ITT analysis; no power calculation

Count	Citations	Quality Rating	Rating Rationale
53	**Zemel, Michael, B;** Richards, Joanna; Milstead, Anita; Campbell, Peter Effects of calcium and dairy on body composition and weight loss in African-American adults. *Obesity research Jul 2005, 13 (7) : 1218-25*	**Poor** Controlled intervention study	High attrition; no ITT analysis; no data on attrition for treatment groups; no power calculation.
54	**Zemel, Michael, B;** Thompson, Warren; Milstead, Anita; Morris, Kristin; Campbell, Peter Calcium and dairy acceleration of weight and fat loss during energy restriction in obese adults. *Obesity research Apr 2004, 12 (4) : 582-90*	**Poor** Controlled intervention study	High attrition; no ITT analysis; no power calculation; no data on adherence

Critical Question 4

a. Among overweight and obese adults, what is the efficacy/effectiveness of a comprehensive lifestyle intervention program (i.e., comprised of diet, physical activity, and behavior therapy) in facilitating weight loss or maintenance of lost weight?

b. What characteristics of delivering comprehensive lifestyle interventions (e.g., frequency and duration of treatment, individual vs. group sessions, onsite vs. phone/email contact) are associated with greater weight loss and weight loss maintenance?

Tables A-16 and A-17 show studies rated fair or good and studies rated poor, respectively.

Table A–16. CQ4 Studies Rated Fair or Good

Count	Citations	Quality Rating
1	Andersen, R, E; Wadden, T, A; Bartlett, S, J; Zemel, B; Verde, T, J; Franckowiak, S, C Effects of lifestyle activity vs structured aerobic exercise in obese women: a randomized trial. *JAMA : the journal of the American Medical Association Jan 1999, 281 (4) : 335-40*	Good Controlled intervention study
2	Appel, Lawrence, J; Clark, Jeanne, M; Yeh, Hsin-Chieh; Wang, Nae-Yuh; Coughlin, Janelle, W; Daumit, Gail; Miller, Edgar, R; Dalcin, Arlene; Jerome, Gerald, J; Geller, Steven; Noronha, Gary; Pozefsky, Thomas; Charleston, Jeanne; Reynolds, Jeffrey, B; Durkin, Nowella; Rubin, Richard, R; Louis, Thomas, A; Brancati, Frederick, L Comparative effectiveness of weight-loss interventions in clinical practice. *The New England journal of medicine Nov 2011, 365 (21) : 1959-68*	Good Controlled intervention study

Count	Citations	Quality Rating
3	Blumenthal, J, A; Sherwood, A; Gullette, E, C; Babyak, M; Waugh, R; Georgiades, A; Craighead, L, W; Tweedy, D; Feinglos, M; Appelbaum, M; Hayano, J; Hinderliter, A Exercise and weight loss reduce blood pressure in men and women with mild hypertension: effects on cardiovascular, metabolic, and hemodynamic functioning. *Archives of internal medicine Jul 2000, 160 (13) : 1947-58*	Fair Controlled intervention study
4	Borg, P; Kukkonen-Harjula, K; Fogelholm, M; Pasanen, M Effects of walking or resistance training on weight loss maintenance in obese, middle-aged men: a randomized trial. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity May 2002, 26 (5) : 676-83*	Fair Controlled intervention study
5	Byrne, Nuala, M; Meerkin, Jarrod, D; Laukkanen, Raija; Ross, Robert; Fogelholm, Mikael; Hills, Andrew, P Weight loss strategies for obese adults: personalized weight management program vs. standard care. *Obesity (Silver Spring, Md.) Oct 2006, 14 (10) : 1777-88*	Fair Controlled intervention study
6	Christian, James, G; Bessesen, Daniel, H; Byers, Tim, E; Christian, Kyle, K; Goldstein, Michael, G; Bock, Beth, C Clinic-based support to help overweight patients with type 2 diabetes increase physical activity and lose weight. *Archives of internal medicine Jan 2008, 168 (2) : 141-6*	Good Controlled intervention study
7	Cussler, Ellen, C; Teixeira, Pedro, J; Going, Scott, B; Houtkooper, Linda, B; Metcalfe, Lauve, L; Blew, Robert, M; Ricketts, Jennifer, R; Lohman, J'Fleur; Stanford, Vanessa, A; Lohman, Timothy, G Maintenance of weight loss in overweight middle-aged women through the Internet. *Obesity (Silver Spring, Md.) May 2008, 16 (5) : 1052-60*	Good Controlled intervention study
8	Dale, Kelly, S; McAuley, Kirsten, A; Taylor, Rachael, W; Williams, Sheila, M; Farmer, Victoria, L; Hansen, Paul; Vorgers, Sue, M; Chisholm, Alexandra, W; Mann, Jim, I Determining optimal approaches for weight maintenance: a randomized controlled trial. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne May 2009, 180 (10) : E39-46*	Good Controlled intervention study
9	Diabetes Prevention Program Research Group; Knowler, William, C; Fowler, Sarah, E; Hamman, Richard, F; Christophi, Costas, A; Hoffman, Heather, J; Brenneman, Anne, T; Brown-Friday, Janet, O; Goldberg, Ronald; Venditti, Elizabeth; Nathan, David, M 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet Nov 2009, 374 (9702) : 1677-86*	Fair Controlled intervention study
10	Eriksson, J; Lindström, J; Valle, T; Aunola, S; Hämäläinen, H; Ilanne-Parikka, P; Keinänen-Kiukaanniemi, S; Laakso, M; Lauhkonen, M; Lehto, P; Lehtonen, A; Louheranta, A; Mannelin, M; Martikkala, V; Rastas, M; Sundvall, J; Turpeinen, A; Viljanen, T; Uusitupa, M; Tuomilehto, J Prevention of Type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland. Study design and 1-year interim report on the feasibility of the lifestyle intervention programme. *Diabetologia Jul 1999, 42 (7) : 793-801*	Good Controlled intervention study

Count	Citations	Quality Rating
11	Esposito, Katherine; Giugliano, Francesco; Di Palo, Carmen; Giugliano, Giovanni; Marfella, Raffaele; D'Andrea, Francesco; D'Armiento, Massimo; Giugliano, Dario Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. *JAMA : the journal of the American Medical Association Jun 2004, 291 (24) : 2978-84*	Good Controlled intervention study
12	Esposito, Katherine; Pontillo, Alessandro; Di Palo, Carmen; Giugliano, Giovanni; Masella, Mariangela; Marfella, Raffaele; Giugliano, Dario Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. *JAMA : the journal of the American Medical Association Apr 2003, 289 (14) : 1799-804*	Good Controlled intervention study
13	Fitzgibbon, Marian, L; Stolley, Melinda, R; Schiffer, Linda; Sharp, Lisa, K; Singh, Vicky; Dyer, Alan Obesity reduction black intervention trial (ORBIT): 18-month results. *Obesity (Silver Spring, Md.) Dec 2010, 18 (12) : 2317-25*	Fair Controlled intervention study
14	Fogelholm, M; Kukkonen-Harjula, K; Nenonen, A; Pasanen, M Effects of walking training on weight maintenance after a very-low-energy diet in premenopausal obese women: a randomized controlled trial. *Archives of internal medicine Jul 2000, 160 (14) : 2177-84*	Fair Controlled intervention study
15	Foster, Gary, D; Borradaile, Kelley, E; Sanders, Mark, H; Millman, Richard; Zammit, Gary; Newman, Anne, B; Wadden, Thomas, A; Kelley, David; Wing, Rena, R; Pi-Sunyer, F, Xavier; Reboussin, David; Kuna, Samuel, T; Sleep AHEAD Research Group of Look AHEAD Research Group A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Archives of internal medicine Sep 2009, 169 (17) : 1619-26*	Fair Controlled intervention study
16	Gold, Beth, Casey; Burke, Susan; Pintauro, Stephen; Buzzell, Paul; Harvey-Berino, Jean Weight loss on the web: A pilot study comparing a structured behavioral intervention to a commercial program. *Obesity (Silver Spring, Md.) Jan 2007, 15 (1) : 155-64*	Fair Controlled intervention study
17	Greaves, Colin, J; Middlebrooke, Andrew; O'Loughlin, Lucy; Holland, Sandra; Piper, Jane; Steele, Anna; Gale, Tracy; Hammerton, Fenella; Daly, Mark Motivational interviewing for modifying diabetes risk: a randomised controlled trial. *The British journal of general practice : the journal of the Royal College of General Practitioners Aug 2008, 58 (553) : 535-40*	Good Controlled intervention study
18	Haapala, Irja; Barengo, Noël, C; Biggs, Simon; Surakka, Leena; Manninen, Pirjo Weight loss by mobile phone: a 1-year effectiveness study. *Public health nutrition Dec 2009, 12 (12) : 2382-91*	Fair Controlled intervention study
19	Harvey-Berino, Jean; Pintauro, Stephen; Buzzell, Paul; Gold, Elizabeth, Casey Effect of internet support on the long-term maintenance of weight loss. *Obesity research Feb 2004, 12 (2) : 320-9*	Fair Controlled intervention study

Count	Citations	Quality Rating
20	Harvey-Berino, Jean; West, Delia; Krukowski, Rebecca; Prewitt, Elaine; VanBiervliet, Alan; Ashikaga, Takamaru; Skelly, Joan Internet delivered behavioral obesity treatment. *Preventive medicine Aug 2010, 51 (2) : 123-8*	Good Controlled intervention study
21	Heshka, S; Greenway, F; Anderson, J, W; Atkinson, R, L; Hill, J, O; Phinney, S, D; Miller-Kovach, K; Xavier Pi-Sunyer, F Self-help weight loss versus a structured commercial program after 26 weeks: a randomized controlled study. *The American journal of medicine Sep 2000, 109 (4) : 282-7*	Good Controlled intervention study
22	Heshka, Stanley; Anderson, James, W; Atkinson, Richard, L; Greenway, Frank, L; Hill, James, O; Phinney, Stephen, D; Kolotkin, Ronette, L; Miller-Kovach, Karen; Pi-Sunyer, F, Xavier Weight loss with self-help compared with a structured commercial program: a randomized trial. *JAMA : the journal of the American Medical Association Apr 2003, 289 (14) : 1792-8*	Fair Controlled intervention study
23	Hunter, Christine, M; Peterson, Alan, L; Alvarez, Lisa, M; Poston, Walker, C; Brundige, Antoinette, R; Haddock, C, Keith; Van Brunt, David, L; Foreyt, John, P Weight management using the internet a randomized controlled trial. *American journal of preventive medicine Feb 2008, 34 (2) : 119-26*	Good Controlled intervention study
24	Jakicic, J, M; Winters, C; Lang, W; Wing, R, R Effects of intermittent exercise and use of home exercise equipment on adherence, weight loss, and fitness in overweight women: a randomized trial. *JAMA : the journal of the American Medical Association Oct 1999, 282 (16) : 1554-60*	Fair Controlled intervention study
25	Jakicic, John, M; Marcus, Bess, H; Gallagher, Kara, I; Napolitano, Melissa; Lang, Wei Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. *JAMA : the journal of the American Medical Association Sep 2003, 290 (10) : 1323-30*	Fair Controlled intervention study
26	Jakicic, John, M; Marcus, Bess, H; Lang, Wei; Janney, Carol Effect of exercise on 24-month weight loss maintenance in overweight women. *Archives of internal medicine Jul 2008, 168 (14) : 1550-9*	Fair Controlled intervention study
27	Jeffery, Robert, W; Wing, Rena, R; Sherwood, Nancy, E; Tate, Deborah, F Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *The American journal of clinical nutrition Oct 2003, 78 (4) : 684-9*	Fair Controlled intervention study
28	Kaukua, J; Pekkarinen, T; Sane, T; Mustajoki, P Health-related quality of life in WHO class II-III obese men losing weight with very-low-energy diet and behaviour modification: a randomised clinical trial. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Apr 2002, 26 (4) : 487-95*	Fair Controlled intervention study
29	Kaukua, Jarmo; Pekkarinen, Tuula; Sane, Timo; Mustajoki, Pertti Sex hormones and sexual function in obese men losing weight. *Obesity research Jun 2003, 11 (6) : 689-94*	Fair Controlled intervention study

Count	Citations	Quality Rating
30	Knowler, William, C; Barrett-Connor, Elizabeth; Fowler, Sarah, E; Hamman, Richard, F; Lachin, John, M; Walker, Elizabeth, A; Nathan, David, M; Diabetes Prevention Program Research Group Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England journal of medicine Feb 2002, 346 (6) : 393-403*	Good Controlled intervention study
31	Kulzer, Bernhard; Hermanns, Norbert; Gorges, Daniela; Schwarz, Peter; Haak, Thomas Prevention of diabetes self-management program (PREDIAS): effects on weight, metabolic risk factors, and behavioral outcomes. *Diabetes care Jul 2009, 32 (7) : 1143-6*	Fair Controlled intervention study
32	Kumanyika, Shiriki, K; Espeland, Mark, A; Bahnson, Judy, L; Bottom, Juliene, B; Charleston, Jeanne, B; Folmar, Steve; Wilson, Alan, C; Whelton, Paul, K; TONE Cooperative Research Group Ethnic comparison of weight loss in the Trial of Nonpharmacologic Interventions in the Elderly. *Obesity research Feb 2002, 10 (2) : 96-106*	Fair Controlled intervention study
33	Leermakers, E, A; Perri, M, G; Shigaki, C, L; Fuller, P, R Effects of exercise-focused versus weight-focused maintenance programs on the management of obesity. *Addictive behaviors Mar 1999, 24 (2) : 219-27*	Fair Controlled intervention study
34	Lindström, Jaana; Eriksson, Johan, G; Valle, Timo, T; Aunola, Sirkka; Cepaitis, Zygimantas; Hakumäki, Martti; Hämäläinen, Helena; Ilanne-Parikka, Pirjo; Keinänen-Kiukaanniemi, Sirkka; Laakso, Mauri; Louheranta, Anne; Mannelin, Marjo; Martikkala, Vesa; Moltchanov, Vladislav; Rastas, Merja; Salminen, Virpi; Sundvall, Jouko; Uusitupa, Matti; Tuomilehto, Jaakko Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish Diabetes Prevention Study: results from a randomized clinical trial. *Journal of the American Society of Nephrology : JASN Jul 2003, 14 (7 Suppl 2) : S108-13*	Good Controlled intervention study
35	Lindström, Jaana; Louheranta, Anne; Mannelin, Marjo; Rastas, Merja; Salminen, Virpi; Eriksson, Johan; Uusitupa, Matti; Tuomilehto, Jaakko; Finnish Diabetes Prevention Study Group The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. *Diabetes care Dec 2003, 26 (12) : 3230-6*	Good Controlled intervention study
36	Logue, Everett; Sutton, Karen; Jarjoura, David; Smucker, William; Baughman, Kristin; Capers, Cynthia Transtheoretical model-chronic disease care for obesity in primary care: a randomized trial. *Obesity research May 2005, 13 (5) : 917-27*	Fair Controlled intervention study
37	Look AHEAD Research Group; Pi-Sunyer, Xavier; Blackburn, George; Brancati, Frederick, L; Bray, George, A; Bright, Renee; Clark, Jeanne, M; Curtis, Jeffrey, M; Espeland, Mark, A; Foreyt, John, P; Graves, Kathryn; Haffner, Steven, M; Harrison, Barbara; Hill, James, O; Horton, Edward, S; Jakicic, John; Jeffery, Robert, W; Johnson, Karen, C; Kahn, Steven; Kelley, David, E; Kitabchi, Abbas, E; Knowler, William, C; Lewis, Cora, E; Maschak-Carey, Barbara, J; Montgomery, Brenda; Nathan, David, M; Patricio, Jennifer; Peters, Anne; Redmon, J, Bruce; Reeves, Rebecca, S; Ryan, Donna, H; Safford, Monika; Van Dorsten, Brent; Wadden, Thomas, A; Wagenknecht, Lynne; Wesche-Thobaben, Jacqueline;	Good Controlled intervention study

Count	Citations	Quality Rating
	Wing, Rena, R; Yanovski, Susan, Z Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. *Diabetes care Jun 2007, 30 (6) : 1374-83*	
38	Look AHEAD Research Group; Wadden, Thomas, A; West, Delia, Smith; Delahanty, Linda; Jakicic, John; Rejeski, Jack; Williamson, Don; Berkowitz, Robert, I; Kelley, David, E; Tomchee, Christine; Hill, James, O; Kumanyika, Shiriki The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity (Silver Spring, Md.) May 2006, 14 (5) : 737-52*	Good Controlled intervention study
39	Look AHEAD Research Group; Wing, Rena, R Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: four-year results of the Look AHEAD trial. *Archives of internal medicine Sep 2010, 170 (17) : 1566-75*	Good Controlled intervention study
40	Messier, Stephen, P; Loeser, Richard, F; Miller, Gary, D; Morgan, Timothy, M; Rejeski, W, Jack; Sevick, Mary, Ann; Ettinger, Walter, H; Pahor, Marco; Williamson, Jeff, D Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis and rheumatism May 2004, 50 (5) : 1501-10*	Good Controlled intervention study
41	Miller, G, D; Nicklas, B, J; Davis, C, C; Ambrosius, W, T; Loeser, R, F; Messier, S, P Is serum leptin related to physical function and is it modifiable through weight loss and exercise in older adults with knee osteoarthritis? *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Nov 2004, 28 (11) : 1383-90*	Good Controlled intervention study
42	Miller, Gary, D; Rejeski, W, Jack; Williamson, Jeff, D; Morgan, Timothy; Sevick, Mary, Ann; Loeser, Richard, F; Ettinger, Walt, H; Messier, Stephen, P; ADAPT Investigators The Arthritis, Diet and Activity Promotion Trial (ADAPT): design, rationale, and baseline results. *Controlled clinical trials Aug 2003, 24 (4) : 462-80*	Good Controlled intervention study
43	Morgan, Philip, J; Lubans, David, R; Collins, Clare, E; Warren, Janet, M; Callister, Robin The SHED-IT randomized controlled trial: evaluation of an Internet-based weight-loss program for men. *Obesity (Silver Spring, Md.) Nov 2009, 17 (11) : 2025-32*	Good Controlled intervention study
44	Nicklas, Barbara, J; Ambrosius, Walter; Messier, Stephen, P; Miller, Gary, D; Penninx, Brenda, W, J, H; Loeser, Richard, F; Palla, Shana; Bleecker, Eugene; Pahor, Marco Diet-induced weight loss, exercise, and chronic inflammation in older, obese adults: a randomized controlled clinical trial. *The American journal of clinical nutrition Apr 2004, 79 (4) : 544-51*	Fair Controlled intervention study
45	Perri, M, G; Nezu, A, M; McKelvey, W, F; Shermer, R, L; Renjilian, D, A; Viegener, B, J Relapse prevention training and problem-solving therapy in the long-term management of obesity. *Journal of consulting and clinical psychology Aug 2001, 69 (4) : 722-6*	Fair Controlled intervention study

Count	Citations	Quality Rating
46	Perri, Michael, G; Limacher, Marian, C; Durning, Patricia, E; Janicke, David, M; Lutes, Lesley, D; Bobroff, Linda, B; Dale, Martha, Sue; Daniels, Michael, J; Radcliff, Tiffany, A; Martin, A, Daniel Extended-care programs for weight management in rural communities: the treatment of obesity in underserved rural settings (TOURS) randomized trial. *Archives of internal medicine Nov 2008, 168 (21):2347-54*	Good Controlled intervention study
47	Rejeski, W, Jack; Focht, Brian, C; Messier, Steven, P; Morgan, Tim; Pahor, Marco; Penninx, Brenda Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health psychology: official journal of the Division of Health Psychology, American Psychological Association Sep 2002, 21 (5) : 419-26*	Good Controlled intervention study
48	Rock, Cheryl, L; Flatt, Shirley, W; Sherwood, Nancy, E; Karanja, Njeri; Pakiz, Bilge; Thomson, Cynthia, A Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. *JAMA : the journal of the American Medical Association Oct 2010, 304 (16) : 1803-10*	Good Controlled intervention study
49	Rock, Cheryl, L; Pakiz, Bilge; Flatt, Shirley, W; Quintana, Elizabeth, L Randomized trial of a multifaceted commercial weight loss program. *Obesity (Silver Spring, Md.) Apr 2007, 15 (4) : 939-49*	Fair Controlled intervention study
50	Stenius-Aarniala, B; Poussa, T; Kvarnström, J; Grönlund, E, L; Ylikahri, M; Mustajoki, P Immediate and long term effects of weight reduction in obese people with asthma: randomised controlled study. *BMJ (Clinical research ed.) Mar 2000, 320 (7238) : 827-32*	Fair Controlled intervention study
51	Stevens, V, J; Obarzanek, E; Cook, N, R; Lee, I, M; Appel, L, J; Smith West, D; Milas, N, C; Mattfeldt-Beman, M; Belden, L; Bragg, C; Millstone, M; Raczynski, J; Brewer, A; Singh, B; Cohen, J; Trials for the Hypertension Prevention Research Group Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. *Annals of internal medicine Jan 2001, 134 (1) : 1-11*	Good Controlled intervention study
52	Stolley, Melinda, R; Fitzgibbon, Marian, L; Schiffer, Linda; Sharp, Lisa, K; Singh, Vicky; Van Horn, Linda; Dyer, Alan Obesity reduction black intervention trial (ORBIT): six-month results. *Obesity (Silver Spring, Md.) Jan 2009, 17 (1) : 100-6*	Fair Controlled intervention study
53	Subak, Leslee, L; Wing, Rena; West, Delia, Smith; Franklin, Frank; Vittinghoff, Eric; Creasman, Jennifer, M; Richter, Holly, E; Myers, Deborah; Burgio, Kathryn, L; Gorin, Amy, A; Macer, Judith; Kusek, John, W; Grady, Deborah; PRIDE Investigators Weight loss to treat urinary incontinence in overweight and obese women. *The New England journal of medicine Jan 2009, 360 (5) : 481-90*	Good Controlled intervention study
54	Svetkey, Laura, P; Stevens, Victor, J; Brantley, Phillip, J; Appel, Lawrence, J; Hollis, Jack, F; Loria, Catherine, M; Vollmer, William, M; Gullion, Christina, M; Funk, Kristine; Smith, Patti; Samuel-Hodge, Carmen; Myers, Valerie; Lien, Lillian, F; Laferriere, Daniel; Kennedy, Betty; Jerome, Gerald, J; Heinith, Fran; Harsha, David, W; Evans, Pamela; Erlinger, Thomas, P; Dalcin, Arline, T; Coughlin,	Good Controlled intervention study

Count	Citations	Quality Rating
	Janelle; Charleston, Jeanne; Champagne, Catherine, M; Bauck, Alan; Ard, Jamy, D; Aicher, Kathleen; Weight Loss Maintenance Collaborative Research Group Comparison of strategies for sustaining weight loss: the weight loss maintenance randomized controlled trial. *JAMA : the journal of the American Medical Association Mar 2008, 299 (10): 1139-48*	
55	Tate, Deborah, F; Jackvony, Elizabeth, H; Wing, Rena, R Effects of Internet behavioral counseling on weight loss in adults at risk for type 2 diabetes: a randomized trial. *JAMA : the journal of the American Medical Association Apr 2003, 289 (14) : 1833-6*	Good Controlled intervention study
56	Tate, Deborah, F; Jackvony, Elizabeth, H; Wing, Rena, R A randomized trial comparing human e-mail counseling, computer-automated tailored counseling, and no counseling in an Internet weight loss program. *Archives of internal medicine Jan 2006, 166 (15) : 1620-5*	Good Controlled intervention study
57	Tate, Deborah, F; Jeffery, Robert, W; Sherwood, Nancy, E; Wing, Rena, R Long-term weight losses associated with prescription of higher physical activity goals. Are higher levels of physical activity protective against weight regain? *The American journal of clinical nutrition Apr 2007, 85 (4) : 954-9*	Fair Controlled intervention study
58	Teixeira, Pedro, J; Silva, Marlene, N; Coutinho, Sílvia, R; Palmeira, António, L; Mata, Jutta; Vieira, Paulo, N; Carraça, Eliana, V; Santos, Teresa, C; Sardinha, Luís, B Mediators of weight loss and weight loss maintenance in middle-aged women. *Obesity (Silver Spring, Md.) Apr 2010, 18 (4) : 725-35*	Fair Controlled intervention study
59	ter Bogt, Nancy, C, W; Bemelmans, Wanda, J, E; Beltman, Frank, W; Broer, Jan; Smit, Andries, J; van der Meer, Klaas Preventing weight gain: one-year results of a randomized lifestyle intervention. *American journal of preventive medicine Oct 2009, 37 (4) : 270-7*	Fair Controlled intervention study
60	Truby, Helen; Baic, Sue; deLooy, Anne; Fox, Kenneth, R; Livingstone, M, Barbara, E; Logan, Catherine, M; Macdonald, Ian, A; Morgan, Linda, M; Taylor, Moira, A; Millward, D, Joe Randomised controlled trial of four commercial weight loss programmes in the UK: initial findings from the BBC "diet trials". *BMJ (Clinical research ed.) Jun 2006, 332 (7553) : 1309-14*	Fair Controlled intervention study
61	Tuomilehto, J; Lindström, J; Eriksson, J, G; Valle, T, T; Hämäläinen, H; Ilanne-Parikka, P; Keinänen-Kiukaanniemi, S; Laakso, M; Louheranta, A; Rastas, M; Salminen, V; Uusitupa, M; Finnish Diabetes Prevention Study Group Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *The New England journal of medicine May 2001, 344 (18) : 1343-50*	Good Controlled intervention study
62	Uusitupa, M; Louheranta, A; Lindström, J; Valle, T; Sundvall, J; Eriksson, J; Tuomilehto, J The Finnish Diabetes Prevention Study. *The British journal of nutrition Mar 2000, 83 Suppl 1 : S137-42*	Good Controlled intervention study
63	Wadden, Thomas, A; Neiberg, Rebecca, H; Wing, Rena, R; Clark, Jeanne, M; Delahanty, Linda, M; Hill, James, O; Krakoff, Jonathan; Otto, Amy; Ryan, Donna, H; Vitolins, Mara, Z; Look AHEAD Research Group Four-year weight losses in the Look AHEAD study: factors associated with long-term success. *Obesity (Silver Spring, Md.) Oct 2011, 19 (10) : 1987-98*	Good Controlled intervention study

Count	Citations	Quality Rating
64	Wadden, Thomas, A; Volger, Sheri; Sarwer, David, B; Vetter, Marion, L; Tsai, Adam, G; Berkowitz, Robert, I; Kumanyika, Shiriki; Schmitz, Kathryn, H; Diewald, Lisa, K; Barg, Ronald; Chittams, Jesse; Moore, Reneé, H A two-year randomized trial of obesity treatment in primary care practice. *The New England journal of medicine Nov 2011, 365 (21) : 1969-79*	Good Controlled intervention study
65	Wadden, Thomas, A; West, Delia, S; Neiberg, Rebecca, H; Wing, Rena, R; Ryan, Donna, H; Johnson, Karen, C; Foreyt, John, P; Hill, James, O; Trence, Dace, L; Vitolins, Mara, Z; Look AHEAD Research Group One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity (Silver Spring, Md.) Apr 2009, 17 (4) : 713-22*	Fair Controlled intervention study
66	West, D, S; Gorin, A, A; Subak, L, L; Foster, G; Bragg, C; Hecht, J; Schembri, M; Wing, R, R; Program to Reduce Incontinence by Diet and Exercise (PRIDE) Research Group A motivation-focused weight loss maintenance program is an effective alternative to a skill-based approach. *International journal of obesity (2005) Feb 2011, 35 (2) : 259-69*	Good Controlled intervention study
67	West, Delia, S; Elaine Prewitt, T; Bursac, Zoran; Felix, Holly, C Weight loss of black, white, and Hispanic men and women in the Diabetes Prevention Program. *Obesity (Silver Spring, Md.) Jun 2008, 16 (6) : 1413-20*	Good Controlled intervention study
68	West, Delia, Smith; DiLillo, Vicki; Bursac, Zoran; Gore, Stacy, A; Greene, Paul, G Motivational interviewing improves weight loss in women with type 2 diabetes. *Diabetes care May 2007, 30 (5) : 1081-7*	Good Controlled intervention study
69	Whelton, P, K; Appel, L, J; Espeland, M, A; Applegate, W, B; Ettinger, W, H; Kostis, J, B; Kumanyika, S; Lacy, C, R; Johnson, K, C; Folmar, S; Cutler, J, A Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA : the journal of the American Medical Association Mar 1998, 279 (11) : 839-46*	Good Controlled intervention study
70	Wing, Rena, R; Tate, Deborah, F; Gorin, Amy, A; Raynor, Hollie, A; Fava, Joseph, L A self-regulation program for maintenance of weight loss. *The New England journal of medicine Oct 2006, 355 (15) : 1563-71*	Good Controlled intervention study
71	Wolf, Anne, M; Conaway, Mark, R; Crowther, Jayne, Q; Hazen, Kristen, Y; L Nadler, Jerry; Oneida, Beverly; Bovbjerg, Viktor, E; Improving Control with Activity and Nutrition (ICAN) Study Translating lifestyle intervention to practice in obese patients with type 2 diabetes: Improving Control with Activity and Nutrition (ICAN) study. *Diabetes care Jul 2004, 27 (7) : 1570-6*	Good Controlled intervention study
72	Womble, Leslie, G; Wadden, Thomas, A; McGuckin, Brian, G; Sargent, Stephanie, L; Rothman, Rebecca, A; Krauthamer-Ewing, E, Stephanie A randomized controlled trial of a commercial internet weight loss program. *Obesity research Jun 2004, 12 (6) : 1011-8*	Fair Controlled intervention study

Table A–17. CQ4 Studies Rated Poor with Rationale

Count	Citations	Quality Rating	Rating Rationale
1	Ames, Gretchen, E; Perri, Michael, G; Fox, Lesley, D; Fallon, Elizabeth, A; De Braganza, Ninoska; Murawski, Mary, E; Pafumi, Lauren; Hausenblas, Heather, A Changing weight-loss expectations: a randomized pilot study. *Eating behaviors Jun 2005, 6 (3) : 259-69*	Poor Controlled intervention study	High attrition; no information about group demographics at baseline and group attrition; no ITT analysis; no power calculation; small sample size; paper very vague and not similar to majority of studies reviewed to date.
2	Annunziato, Rachel, A; Timko, C, Alix; Crerand, Canice, E; Didie, Elizabeth, R; Bellace, Dara, L; Phelan, Suzanne; Kerzhnerman, Irina; Lowe, Michael, R A randomized trial examining differential meal replacement adherence in a weight loss maintenance program after one-year follow-up. *Eating behaviors Aug 2009, 10 (3) : 176-83*	Poor Controlled intervention study	Reported data for completers only; 31.7% attrition; fatal flaw
3	Ashley, J, M; St Jeor, S, T; Schrage, J, P; Perumean-Chaney, S, E; Gilbertson, M, C; McCall, N, L; Bovee, V Weight control in the physician's office. *Archives of internal medicine Jul 2001, 161 (13) : 1599-604*	Poor Controlled intervention study	High attrition; failure to report attrition, randomization details, and study power projections; most outcomes reported for completers only-35% attrition; fatal flaw
4	Ashley, J, M; St Jeor, S, T; Perumean-Chaney, S; Schrage, J; Bovee, V Meal replacements in weight intervention. *Obesity research Nov 2001, 9 Suppl 4 : 312S-320S*	Poor Controlled intervention study	High attrition, no ITT analysis; no information on baseline data for non-completers; randomization details absent; baseline data for completers only; no power calculation
5	Bacon, L; Keim, N, L; Van Loan, M, D; Derricote, M; Gale, B; Kazaks, A; Stern, J, S Evaluating a 'non-diet' wellness intervention for improvement of metabolic fitness, psychological well-being and eating and activity behaviors. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Jun 2002, 26 (6) : 854-65*	Poor Controlled intervention study	High attrition; high differential attrition and no ITT analysis introduce a significant potential for bias
6	Bacon, Linda; Stern, Judith, S; Van Loan, Marta, D; Keim, Nancy, L Size acceptance and intuitive eating improve health for obese, female chronic dieters. *Journal of the American Dietetic Association Jun 2005, 105 (6) : 929-36*	Poor Controlled intervention study	High differential attrition; baseline data not reported for all participants.
7	Befort, Christie, A; Donnelly, Joseph, E; Sullivan, Debra, K; Ellerbeck, Edward, F; Perri, Michael, G Group versus individual phone-based obesity treatment for rural women. *Eating behaviors Jan 2010, 11 (1) : 11-7*	Poor Controlled intervention study	Completers data only for weight change; not powered for effect size (pilot study); good pilot study but with no true control group: comparator groups

Count	Citations	Quality Rating	Rating Rationale
			inappropriate for this question (will not include)
8	Brochu, Martin; Malita, Mircea, Florin; Messier, Virginie; Doucet, Eric; Strychar, Irene; Lavoie, Jean-Marc; Prud'homme, Denis; Rabasa-Lhoret, Rémi Resistance training does not contribute to improving the metabolic profile after a 6-month weight loss program in overweight and obese postmenopausal women. *The Journal of clinical endocrinology and metabolism Sep 2009, 94 (9) : 3226-33*	Poor Controlled intervention study	High attrition; confusion about ITT analysis; low compliance with treatment
9	Burke, Valerie; Beilin, Lawrie, J; Cutt, Hayley, E; Mansour, Jacqueline; Williams, Amy; Mori, Trevor, A A lifestyle program for treated hypertensives improved health-related behaviors and cardiovascular risk factors, a randomized controlled trial. *Journal of clinical epidemiology Feb 2007, 60 (2) : 133-41*	Poor Controlled intervention study	10/10/12 Burke et. al 2007 reported only weight loss by arm in figure only; Burke 2005 J Hypertens was added because the weight loss data the group wanted was only reported in a figure in Burke 2007 (subsequently marked as a "related study"). However, the Burke 2005 study (the main study) was eventually rated as poor; therefore, Burke 2007 should be rated as poor. It was previously rated on its own because Burke 2005 was not included initially. 10/10/12 This citation was downgraded from good to poor based on history of Burke citations (see above).
10	Burke, Valerie; Beilin, Lawrie, J; Cutt, Hayley, E; Mansour, Jacqueline; Wilson, Amy; Mori, Trevor, A Effects of a lifestyle programme on ambulatory blood pressure and drug dosage in treated hypertensive patients: a randomized controlled trial. *Journal of hypertension Jun 2005, 23 (6) : 1241-9*	Poor Controlled intervention study	Completers only analysis; at 4 mos, attrition was 15.4%, and at 1 yr was 20.3%. According to the guidelines, studies containing completers only data must have an attrition rate of less than 10%; ITT analysis not used.
11	Burke, Valerie; Mori, Trevor, A; Giangiulio, Nella; Gillam, Helen, F; Beilin, Lawrie, J; Houghton, Stephen; Cutt, Hayley, E; Mansour, Jacqueline; Wilson, Amy An innovative program for changing health behaviours. *Asia Pacific journal of clinical nutrition Jan 2002, 11 Suppl 3 : S586-97*	Poor Controlled intervention study	No ITT analysis reported; high dropout rates; no information on dropout rates per treatment group; poor refers to both studies mentioned in paper
12	Carels, Robert, A; Darby, Lynn, A; Cacciapaglia, Holly, M; Douglass, Olivia, M Reducing cardiovascular risk factors in	Poor Controlled intervention	Differences between groups at baseline (8 kg); differences in hormone replacement

Count	Citations	Quality Rating	Rating Rationale
	postmenopausal women through a lifestyle change intervention. *Journal of women's health (2002) May 2004, 13 (4): 412-26*	study	therapy that could affect results; no ITT analysis; no power calculation
13	Carels, Robert, A; Darby, Lynn, A; Douglass, Olivia, M; Cacciapaglia, Holly, M; Rydin, Sofia Education on the glycemic index of foods fails to improve treatment outcomes in a behavioral weight loss program. *Eating behaviors Feb 2005, 6 (2) : 145-50*	Poor Controlled intervention study	No ITT analysis; high attrition; trial rated poor for presenting completers analysis in conjunction with 25% attrition; study does not report attrition per treatment group
14	Carels, Robert, A; Darby, Lynn; Cacciapaglia, Holly, M; Douglass, Olivia, M; Harper, Jessica; Kaplar, Mary, E; Konrad, Krista; Rydin, Sofia; Tonkin, Karin Applying a stepped-care approach to the treatment of obesity. *Journal of psychosomatic research Dec 2005, 59 (6) : 375-83*	Poor Controlled intervention study	No ITT analysis; no prespecified groups; differences among groups; trial had no attrition, but did not provide details of randomization methods or adherence data; convoluted analysis, completers only data; 15% attrition; fatal flaws
15	Carels, Robert, A; Darby, Lynn; Cacciapaglia, Holly, M; Konrad, Krista; Coit, Carissa; Harper, Jessica; Kaplar, Mary, E; Young, Kathleen; Baylen, Chelsea, A; Versland, Amelia Using motivational interviewing as a supplement to obesity treatment: a stepped-care approach. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association May 2007, 26 (3) : 369-74*	Poor Controlled intervention study	Failure to report randomization procedures, power, or ITT analysis; completers data only; attrition >10%
16	Carels, Robert, A; Konrad, Krista; Young, Kathleen, M; Darby, Lynn, A; Coit, Carissa; Clayton, Anna, Marie; Oemig, Carmen, K Taking control of your personal eating and exercise environment: a weight maintenance program. *Eating behaviors Apr 2008, 9 (2) : 228-37*	Poor Controlled intervention study	High attrition; no ITT analysis; no power calculation; lack of consistency in measuring outcomes; 25% attrition rate can affect external validity; internal validity threatened because food diaries and measures of physical activities were not recorded at follow-up period, which establishes an absence of cause and effect relationship
17	Chao, D; Espeland, M, A; Farmer, D; Register, T, C; Lenchik, L; Applegate, W, B; Ettinger, W, H Effect of voluntary weight loss on bone mineral density in older overweight women. *Journal of the American Geriatrics Society Jul 2000, 48 (7) : 753-9*	Poor Controlled intervention study	No ITT analysis; no data for withdrawals per group; completers baseline demographic data; rated poor because internal validity was threatened; not all participants were randomized, causing differential selection; method used to generate randomization not mentioned and ITT not captured.

Count	Citations	Quality Rating	Rating Rationale
18	Cheskin, Lawrence, J; Mitchell, Amy, M; Jhaveri, Ami, D; Mitola, Andrea, H; Davis, Lisa, M; Lewis, Rebecca, A; Yep, Mary, A; Lycan, Thomas, W Efficacy of meal replacements versus a standard food-based diet for weight loss in type 2 diabetes: a controlled clinical trial. *The Diabetes educator Jan 2008, 34 (1) : 118-27*	Poor Controlled intervention study	High attrition; high differential attrition; significant differences at baseline; very high attrition and differential attrition past 34 wks.
19	Cheyette, C. Weight No More: a randomised controlled trial for people with type 2 diabetes on insulin therapy. *Practical Diabetes International Jan 2007, 24 (9) : 450-6*	Poor Controlled intervention study	High attrition; high differential attrition; no ITT analysis; significant difference in weight between groups at baseline; randomization method may not have been adequate; large difference in baseline weights supports this conclusion
20	Daly, Robin, M; Dunstan, David, W; Owen, Neville; Jolley, Damien; Shaw, Jonathan, E; Zimmet, Paul, Z Does high-intensity resistance training maintain bone mass during moderate weight loss in older overweight adults with type 2 diabetes? *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA Dec 2005, 16 (12) : 1703-12*	Poor Controlled intervention study	Completers data only; no ITT analysis; attrition >10%
21	Del Corral, Pedro; Chandler-Laney, Paula, C; Casazza, Krista; Gower, Barbara, A; Hunter, Gary, R Effect of dietary adherence with or without exercise on weight loss: a mechanistic approach to a global problem. *The Journal of clinical endocrinology and metabolism May 2009, 94 (5) : 1602-7*	Poor Controlled intervention study	High attrition; high differential attrition; no ITT analysis; no power calculation
22	Ditschuneit, H, H; Flechtner-Mors, M; Johnson, T, D; Adler, G Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. *The American journal of clinical nutrition Feb 1999, 69 (2) : 198-204*	Poor Controlled intervention study	High attrition; no ITT analysis; no sample size calculation; rated fair for not following ITT analysis
23	Djuric, Zora; DiLaura, Nora, M; Jenkins, Isabella; Darga, Linda; Jen, Catherine, K-L; Mood, Darlene; Bradley, Ellen; Hryniuk, William, M Combining weight-loss counseling with the weight watchers plan for obese breast cancer survivors. *Obesity research Jul 2002, 10 (7) : 657-65*	Poor Controlled intervention study	Significant differences between groups at baseline; no ITT analysis; unclear dropout rate by group; no details about randomization increase risk of bias; failure of underlying randomization scheme makes potential for confounding extremely high

Count	Citations	Quality Rating	Rating Rationale
24	Dunstan, David, W; Daly, Robin, M; Owen, Neville; Jolley, Damien; De Courten, Maximilian; Shaw, Jonathan; Zimmet, Paul High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. *Diabetes care Oct 2002, 25 (10) : 1729-36*	Poor Controlled intervention study	No ITT analysis; no reporting of randomization details; reported data for completers only; attrition > 10%; fatal flaw
25	Ello-Martin, Julia, A; Roe, Liane, S; Ledikwe, Jenny, H; Beach, Amanda, M; Rolls, Barbara, J Dietary energy density in the treatment of obesity: a year-long trial comparing 2 weight-loss diets. *The American journal of clinical nutrition Jun 2007, 85 (6) : 1465-77*	Poor Controlled intervention study	High attrition; no ITT analysis
26	Ely, Andrea, C; Banitt, Angela; Befort, Christie; Hou, Qing; Rhode, Paula, C; Grund, Chrysanne; Greiner, Allen; Jeffries, Shawn; Ellerbeck, Edward Kansas primary care weighs in: a pilot randomized trial of a chronic care model program for obesity in 3 rural Kansas primary care practices. *The Journal of rural health : official journal of the American Rural Health Association and the National Rural Health Care Association Jan 2008, 24 (2) : 125-32*	Poor Controlled intervention study	High dropout rate; no ITT analysis; groups dissimilar at baseline regarding demographics
27	Fogelholm, M; Kukkonen-Harjula, K; Oja, P Eating control and physical activity as determinants of short-term weight maintenance after a very-low-calorie diet among obese women. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Feb 1999, 23 (2) : 203-10*	Poor Controlled intervention study	No ITT analysis; no data on randomization, differential attrition, adherence, or power
28	Frimel, Tiffany, N; Sinacore, David, R; Villareal, Dennis, T Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. *Medicine and science in sports and exercise Jul 2008, 40 (7) : 1213-9*	Poor Controlled intervention study	No ITT; no report of attrition; completers only analysis; downgraded to poor (6/11); fatal flaw
29	Goodrick, G, K; Poston, W, S; Kimball, K, T; Reeves, R, S; Foreyt, J, P Nondieting versus dieting treatment for overweight binge-eating women. *Journal of consulting and clinical psychology Apr 1998, 66 (2) : 363-8*	Poor Controlled intervention study	Outcomes not measured consistently (no 18 mo outcomes for control group); very low integrity of intervention due to therapists being invested in their philosophical views; poor adherence; no sample size calculation; ranked fair for not reporting randomization

Count	Citations	Quality Rating	Rating Rationale
			details and possible problems with treatment delivery.
30	Harvey-Berino, J Calorie restriction is more effective for obesity treatment than dietary fat restriction. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine Jan 1999, 21 (1) : 35-9*	Poor Controlled intervention study	High dropout; no ITT analysis; no power calculations; baseline demographics presented only for completers; does not report ITT analysis or sample size justification; baseline data incomplete.
31	Harvey-Berino, J; Pintauro, S; Buzzell, P; DiGiulio, M; Casey Gold, B; Moldovan, C; Ramirez, E Does using the Internet facilitate the maintenance of weight loss? *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Sep 2002, 26 (9) : 1254-60*	Poor Controlled intervention study	High overall attrition (24%); no ITT analysis; differences in group demographics; no power calculation; no prespecified groups; no details on randomization; downgraded from good for failure to present power calculations and omitting randomization details; only presents a completers analysis.
32	Harvey-Berino, Jean; Pintauro, Stephen, J; Gold, Elizabeth, Casey The feasibility of using Internet support for the maintenance of weight loss. *Behavior modification Jan 2002, 26 (1) : 103-16*	Poor Controlled intervention study	No ITT analysis, demographic data for treatment groups, or data on randomization; sample size may be too small to derive any clinically meaningful results
33	Jeffery, Robert, W; Levy, Rona, L; Langer, Shelby, L; Welsh, Ericka, M; Flood, Andrew, P; Jaeb, Melanie, A; Laqua, Patricia, S; Hotop, Annie, M; Finch, Emily, A A comparison of maintenance-tailored therapy (MTT) and standard behavior therapy (SBT) for the treatment of obesity. *Preventive medicine Nov 2009, 49 (5) : 384-9*	Poor Controlled intervention study	High dropout; no ITT analysis; no sample size calculation; completers analysis; high attrition
34	Jeffery, Robert, W; Linde, Jennifer, A; Finch, Emily, A; Rothman, Alexander, J; King, Christie, M A satisfaction enhancement intervention for long-term weight loss. *Obesity (Silver Spring, Md.) May 2006, 14 (5) : 863-9*	Poor Controlled intervention study	High attrition; no ITT analysis or data about adherence and randomization; omits baseline data; only 71% of subjects completed study and no power calculation given
35	Kennedy, Betty, M; Paeratakul, Sahasporn; Champagne, Catherine, M; Ryan, Donna, H; Harsha, David, W; McGee, Bernestine; Johnson, Glenda; Deyhim, Farzad; Forsythe, William; Bogle, Margaret, L; Lower Mississippi Delta Nutrition Intervention Research Initiative A pilot church-based weight loss program for African-American adults using church members	Poor Controlled intervention study	A pilot study lacking sample size justification; high differential attrition; no ITT analysis; no power calculation

Count	Citations	Quality Rating	Rating Rationale
	as health educators: a comparison of individual and group intervention. *Ethnicity & disease Jan 2005, 15 (3) : 373-8*		
36	Keränen, Anna-Maria; Savolainen, Markku, J; Reponen, Annakaisa, H; Kujari, Mona-Lisa; Lindeman, Sari, M; Bloigu, Risto, S; Laitinen, Jaana, H The effect of eating behavior on weight loss and maintenance during a lifestyle intervention. *Preventive medicine Aug 2009, 49 (1) : 32-8*	Poor Controlled intervention study	High attrition; no ITT analysis; no data on adherence
37	Kinnunen, Tarja, I; Pasanen, Matti; Aittasalo, Minna; Fogelholm, Mikael; Weiderpass, Elisabete; Luoto, Riitta Reducing postpartum weight retention--a pilot trial in primary health care. *Nutrition journal Jan 2007, 6 : 21-*	Poor Controlled intervention study	Not a randomized trial; no participant randomization, ITT analysis, or power calculation; completers baseline data
38	Kuller, Lewis, H; Kinzel, Laura, S; Pettee, Kelley, K; Kriska, Andrea, M; Simkin-Silverman, Laurey, R; Conroy, Molly, B; Averbach, Frani; Pappert, W, Scott; Johnson, B, Delia Lifestyle intervention and coronary heart disease risk factor changes over 18 months in postmenopausal women: the Women On the Move through Activity and Nutrition (WOMAN study) clinical trial. *Journal of women's health (2002) Oct 2006, 15 (8) : 962-74*	Poor Controlled intervention study	No ITT analysis, baseline data for treatment groups, background interventions such as hormone therapy and hypertension medications, reported power, and data on adherence; unclear how many were randomized to each group; paper largely focused on women's hormone therapy status.
39	Lantz, Helén; Peltonen, Markku; Agren, Liselotte; Torgerson, Jarl, S A dietary and behavioural programme for the treatment of obesity. A 4-year clinical trial and a long-term posttreatment follow-up. *Journal of internal medicine Sep 2003, 254 (3) : 272-9*	Poor Controlled intervention study	High attrition; downgraded for not presenting ITT analysis and high overall attrition; reported data for completers only; attrition >10%; fatal flaw
40	Lejeune, M, P, G, M; Van Aggel-Leijssen, D, P, C; Van Baak, M, A; Westerterp-Plantenga, M, S Effects of dietary restraint vs exercise during weight maintenance in obese men. *European journal of clinical nutrition Oct 2003, 57 (10) : 1338-44*	Poor Controlled intervention study	High attrition (22%); no ITT analysis or power calculations; baseline demographics only for completers; some potential for bias due to high attrition and lack of ITT
41	Lowe, Michael, R; Tappe, Karyn, A; Annunziato, Rachel, A; Riddell, Lynnette, J; Coletta, Maria, C; Crerand, Canice, E; Didie, Elizabeth, R; Ochner, Christopher, N; McKinney, Shortie The effect of training in reduced energy density eating and food self-monitoring accuracy on weight loss maintenance. *Obesity (Silver Spring, Md.) Sep 2008, 16 (9) : 2016-23*	Poor Controlled intervention study	Very high attrition; no power calculation; confusion about assessing outcomes and attrition

Count	Citations	Quality Rating	Rating Rationale
42	Martin, Pamela, D; Dutton, Gareth, R; Rhode, Paula, C; Horswell, Ronald, L; Ryan, Donna, H; Brantley, Phillip, J Weight loss maintenance following a primary care intervention for low-income minority women. *Obesity (Silver Spring, Md.) Nov 2008, 16 (11) : 2462-7*	Poor Controlled intervention study	Differential attrition rate 21% (fatal flaw); high attrition overall and significantly greater attrition among intervention participants
43	Mayer-Davis, Elizabeth, J; D'Antonio, Angela, M; Smith, Sharon, M; Kirkner, Gregory; Levin Martin, Sarah; Parra-Medina, Deborah; Schultz, Richard Pounds off with empowerment (POWER): a clinical trial of weight management strategies for black and white adults with diabetes who live in medically underserved rural communities. *American journal of public health Oct 2004, 94 (10) : 1736-42*	Poor Controlled intervention study	Downgraded for only presenting completers data; no ITT; high attrition; reported data for completers only; attrition >10%; fatal flaw
44	McConnon, Aine; Kirk, Sara, Fl; Cockroft, Jennie, E; Harvey, Emma, L; Greenwood, Darren, C; Thomas, James, D; Ransley, Joan, K; Bojke, Laura The Internet for weight control in an obese sample: results of a randomised controlled trial. *BMC health services research Jan 2007, 7 : 206-*	Poor Controlled intervention study	No ITT analysis; high overall and differential attrition; lack of clarity about groups at baseline
45	Melanson, Kathleen, J; Angelopoulos, Theodore, J; Nguyen, Von, T; Martini, Margaret; Zukley, Linda; Lowndes, Joshua; Dube, Thomas, J; Fiutem, Justin, J; Yount, Byron, W; Rippe, James, M Consumption of whole-grain cereals during weight loss: effects on dietary quality, dietary fiber, magnesium, vitamin B-6, and obesity. *Journal of the American Dietetic Association Sep 2006, 106 (9) : 1380-8*	Poor Controlled intervention study	High attrition; high differential attrition; incomplete ITT analysis
46	Melanson, Kathleen, J; Dell'Olio, Jessica; Carpenter, Michael, R; Angelopoulos, Theodore, J Changes in multiple health outcomes at 12 and 24 weeks resulting from 12 weeks of exercise counseling with or without dietary counseling in obese adults. *Nutrition (Burbank, Los Angeles County, Calif.) Oct 2004, 20 (10) : 849-56*	Poor Controlled intervention study	High attrition; no ITT analysis; lack of details about adherence to treatment
47	Melin, I; Karlström, B; Lappalainen, R; Berglund, L; Mohsen, R; Vessby, B A programme of behaviour modification and nutrition counselling in the treatment of obesity: a randomised 2-y clinical trial. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Sep 2003, 27 (9) : 1127-35*	Poor Controlled intervention study	No ITT analysis; high overall attrition (26%); no power calculation

Count	Citations	Quality Rating	Rating Rationale
48	Melin, I; Reynisdottir, S; Berglund, L; Zamfir, M; Karlström, B Conservative treatment of obesity in an academic obesity unit. Long-term outcome and drop-out. *Eating and weight disorders : EWD Mar 2006, 11 (1): 22-30*	Poor Controlled intervention study	High attrition; no ITT analysis; not similar interventions in treatment groups, which could affect outcomes; lack of randomization and placement of subjects in group 2 based on comorbidity, introduces serious potential for bias
49	Mensink, M; Feskens, E, J, M; Saris, W, H, M; De Bruin, T, W, A; Blaak, E, E Study on Lifestyle Intervention and Impaired Glucose Tolerance Maastricht (SLIM): preliminary results after one year. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Mar 2003, 27 (3) : 377-84*	Poor Controlled intervention study	Completers analysis only; 10.52% attrition; reported data for completers only; attrition >10%; fatal flaw
50	Mensink, Marco; Blaak, Ellen, E; Corpeleijn, Eefje; Saris, Wim, H; de Bruin, Tjerk, W; Feskens, Edith, J Lifestyle intervention according to general recommendations improves glucose tolerance. *Obesity research Dec 2003, 11 (12) : 1588-96*	Poor Controlled intervention study	Rated together with primary paper; completers only data; 19.2% attrition; fatal flaw
51	Micco, Nicci; Gold, Beth; Buzzell, Paul; Leonard, Heather; Pintauro, Stephen; Harvey-Berino, Jean Minimal in-person support as an adjunct to internet obesity treatment. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine Feb 2007, 33 (1) : 49-56*	Poor Controlled intervention study	High attrition; no attrition by treatment group; no power calculation
52	Miller, Gary, D; Nicklas, Barbara, J; Davis, Cralen; Loeser, Richard, F; Lenchik, Leon; Messier, Stephen, P Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. *Obesity (Silver Spring, Md.) Jul 2006, 14 (7) : 1219-30*	Poor Controlled intervention study	Lacked ITT analysis (completers only) and randomization details; reported data for completers only; attrition >10%; differential attrition >15%; fatal flaws
53	Miller, Gary, D; Nicklas, Barbara, J; Loeser, Richard, F Inflammatory biomarkers and physical function in older, obese adults with knee pain and self-reported osteoarthritis after intensive weight-loss therapy. *Journal of the American Geriatrics Society Apr 2008, 56 (4) : 644-51*	Poor Controlled intervention study	No ITT; completers data only; reported data for completers only; attrition >10%; fatal flaw
54	Minniti, A; Bissoli, L; Di Francesco, V; Fantin, F; Mandragona, R; Olivieri, M; Fontana, G; Rinaldi, C; Bosello, O; Zamboni, M Individual versus group therapy for obesity: comparison of dropout rate and treatment	Poor Controlled intervention study	Incomplete randomization; high attrition; extremely high differential attrition; no ITT analysis

Count	Citations	Quality Rating	Rating Rationale
	outcome. *Eating and weight disorders : EWD Dec 2007, 12 (4) : 161-7*		
55	Munsch, Simone; Biedert, Esther; Keller, Ulrich Evaluation of a lifestyle change programme for the treatment of obesity in general practice. *Swiss medical weekly Mar 2003, 133 (9-10) : 148-54*	Poor Controlled intervention study	High differential dropout; no ITT analysis; no power calculation; partial randomization; rated poor because author did not capture ITT and verify that no bias was present by mentioning randomization method or blinding; dropout rate not recorded, which threatens internal validity
56	Penn, Linda; White, Martin; Oldroyd, John; Walker, Mark; Alberti, K, George, M, M; Mathers, John, C Prevention of type 2 diabetes in adults with impaired glucose tolerance: the European Diabetes Prevention RCT in Newcastle upon Tyne, UK. *BMC public health Jan 2009, 9 : 342-*	Poor Controlled intervention study	Very high attrition; no ITT analysis; no power calculation; no data on adherence
57	Poston, W, S, C; Haddock, C, K; Pinkston, M, M; Pace, P; Reeves, R, S; Karakoc, N; Jones, P; Foreyt, J, P Evaluation of a primary care-oriented brief counselling intervention for obesity with and without orlistat. *Journal of internal medicine Oct 2006, 260 (4) : 388-98*	Poor Controlled intervention study	High attrition; high differential attrition; attrition comparable between drug groups
58	Prior, Steven, J; Joseph, Lyndon, J; Brandauer, Josef; Katzel, Leslie, I; Hagberg, James, M; Ryan, Alice, S Reduction in midthigh low-density muscle with aerobic exercise training and weight loss impacts glucose tolerance in older men. *The Journal of clinical endocrinology and metabolism Mar 2007, 92 (3) : 880-6*	Poor Controlled intervention study	Study is a post-hoc analysis of two previously published RCTs; no ITT analysis; high attrition; no details on randomization; high overall attrition and probably high differential attrition since 34 AEX and only 12 AEX + WL subjects completed
59	Pritchard, JE; Nowson, CA; Billington, T; Wark, JD Benefits of a year-long workplace weight loss program on cardiovascular risk factors. *Nutrition & Dietetics: Journal of the Dietitians Association of Australia Jan 2002, 59 (2) : 87-96*	Poor Controlled intervention study	Use of volunteers; missing baseline data for 18 participants; several sources of bias; first comparison of diet, exercise, and control groups was randomized through random numbers generator; for exercise + diet group, there was no randomization , (subjects were volunteers, this group was not assessed

Count	Citations	Quality Rating	Rating Rationale
			concurrently with other groups, and they followed the intervention in the "subsequent 12 mos;" use of volunteers introduced selection bias—this group may be more motivated to follow interventions; baseline values not collected for 18 subjects (about 1/3 of sample) and the *N*s in table 1 do not add up to the number of participants reported; moreover, there was a 17.4% differential dropout rate between diet and exercise groups
60	Racette, S, B; Weiss, E, P; Obert, K, A; Kohrt, W, M; Holloszy, J, O Modest lifestyle intervention and glucose tolerance in obese African Americans. *Obesity research Jun 2001, 9 (6) : 348-55*	Poor Controlled intervention study	No randomization; difference between groups; no ITT analysis; high attrition rate; high differential attrition; no power calculation
61	Ramirez, E, M; Rosen, J, C A comparison of weight control and weight control plus body image therapy for obese men and women. *Journal of consulting and clinical psychology Jun 2001, 69 (3) : 440-6*	Poor Controlled intervention study	No baseline demographics; high dropout rate; no ITT analysis; lacked randomization information; no reported baseline data
62	Renjilian, D, A; Perri, M, G; Nezu, A, M; McKelvey, W, F; Shermer, R, L; Anton, S, D Individual versus group therapy for obesity: effects of matching participants to their treatment preferences. *Journal of consulting and clinical psychology Aug 2001, 69 (4) : 717-21*	Poor Controlled intervention study	7/2011,study rated poor due to completer only data and high attrition
63	Riebe, Deborah; Blissmer, Bryan; Greene, Geoffrey; Caldwell, Marjorie; Ruggiero, Laurie; Stillwell, Kira, M; Nigg, Claudio, R Long-term maintenance of exercise and healthy eating behaviors in overweight adults. *Preventive medicine Jun 2005, 40 (6) : 769-78*	Poor Controlled intervention study	High dropout rate, from 190 to 104 after 24 mos; no data on baseline demographics, data on adherence, and power calculation
64	Sherwood, N, E; Jeffery, R, W; Pronk, N, P; Boucher, J, L; Hanson, A; Boyle, R; Brelje, K; Hase, K; Chen, V Mail and phone interventions for weight loss in a managed-care setting: weigh-to-be 2-year outcomes. *International journal of obesity (2005) Oct 2006, 30 (10) : 1565-73*	Poor Controlled intervention study	High attrition; groups not similar at baseline in terms of depression; except for adherence, all criteria met; author comments that adherence to intervention was acceptable; reported data for completers only; attrition >10%; fatal flaw

Count	Citations	Quality Rating	Rating Rationale
65	Tate, D, F; Wing, R, R; Winett, R, A Using Internet technology to deliver a behavioral weight loss program. *JAMA : the journal of the American Medical Association Mar 2001, 285 (9) : 1172-7*	Poor Controlled intervention study	Downgraded from good for failure to report randomization and blinding procedures; reporting of completers data only and high overall attrition high attrition; fatal flaw
66	Tuomilehto, Henri, P, I; Seppä, Juha, M; Partinen, Markku, M; Peltonen, Markku; Gylling, Helena; Tuomilehto, Jaakko, O, I; Vanninen, Esko, J; Kokkarinen, Jouko; Sahlman, Johanna, K; Martikainen, Tarja; Soini, Erkki, J, O; Randell, Jukka; Tukiainen, Hannu; Uusitupa, Matti; Kuopio Sleep Apnea Group Lifestyle intervention with weight reduction: first-line treatment in mild obstructive sleep apnea. *American journal of respiratory and critical care medicine Feb 2009, 179 (4) : 320-7*	Poor Controlled intervention study	Serious risk of bias due to population differences at baseline; confusion about ITT analysis; no data on adherence; significant differences in baseline covariates suggests flawed randomization
67	van Wier, Marieke, F; Ariëns, Geertje, A, M; Dekkers, J, Caroline; Hendriksen, Ingrid, J, M; Smid, Tjabe; van Mechelen, Willem Phone and e-mail counselling are effective for weight management in an overweight working population: a randomized controlled trial. *BMC public health Jan 2009, 9 : 6-*	Poor Controlled intervention study	High dropout rate; use of self-reported outcomes together with self-reported measures; Downgraded from good for high overall attrition and poor adherence to the intervention
68	Wadden, T, A; Vogt, R, A; Foster, G, D; Anderson, D, A Exercise and the maintenance of weight loss: 1-year follow-up of a controlled clinical trial. *Journal of consulting and clinical psychology Apr 1998, 66 (2) : 429-33*	Poor Controlled intervention study	Lacked ITT analysis; high attrition; reported data for completers only; attrition >10%; fatal flaw
69	Wang, Xuewen; Lyles, Mary, F; You, Tongjian; Berry, Michael, J; Rejeski, W, Jack; Nicklas, Barbara, J Weight regain is related to decreases in physical activity during weight loss. *Medicine and science in sports and exercise Oct 2008, 40 (10) : 1781-8*	Poor Controlled intervention study	Completers only data; 16% attrition; reported data for completers only; attrition >10%; fatal flaw
70	Wang, Xuewen; Miller, Gary, D; Messier, Stephen, P; Nicklas, Barbara, J Knee strength maintained despite loss of lean body mass during weight loss in older obese adults with knee osteoarthritis. *The journals of gerontology. Series A, Biological sciences and medical sciences Aug 2007, 62 (8) : 866-71*	Poor Controlled intervention study	Rated together with Miller et al., 2006; reported data for completers only; attrition >10%; differential attrition >15%; fatal flaws
71	Weinstock, R, S; Dai, H; Wadden, T, A Diet and exercise in the treatment of obesity: effects of 3 interventions on insulin resistance. *Archives of internal medicine Jan 1998, 158 (22) : 2477-83*	Poor Controlled intervention study	High attrition; no ITT analysis; rated together with Wadden, et al.,1997

Count	Citations	Quality Rating	Rating Rationale
72	Wing, R, R; Jeffery, R, W Benefits of recruiting participants with friends and increasing social support for weight loss and maintenance. *Journal of consulting and clinical psychology Feb 1999, 67 (1) : 132-8*	Poor Controlled intervention study	High differential attrition; failing to report power calculations and randomization procedures. High differential attrition; fatal flaw
73	Wing, R, R; Venditti, E; Jakicic, J, M; Polley, B, A; Lang, W Lifestyle intervention in overweight individuals with a family history of diabetes. *Diabetes care Mar 1998, 21 (3) : 350-9*	Poor Controlled intervention study	High differential attrition; no ITT analysis; no power calculation;
74	Wing, Rena, R; Jeffery, Robert, W Prescribed "breaks" as a means to disrupt weight control efforts. *Obesity research Feb 2003, 11 (2) : 287-91*	Poor Controlled intervention study	No demographics data; high attrition rate; high differential attrition; no explanation of questionnaires' validity; no ITT analysis

Critical Question 5

a. Efficacy

What are the long-term effects of the following surgical procedures on weight loss, weight loss maintenance, CV risk factors, related comorbidities, and mortality?

- LAGB
- Laparascopic RYGB
- Open RYGB
- Biliopancreatic bypass with or without duodenal switch
- SG

What are the long-term effects of the surgical procedures (listed above) in patients with different BMIs and comorbidities?

- BMI <35
- BMI of 35 to 40 with no comorbidities
- BMI ≥35 with comorbidities, and
- BMI ≥40 with no comorbidities

b. Predictors

What are the predictors associated with long-term effects of the following surgical procedures on weight loss, weight loss maintenance, CV risk factors, related comorbidities, and mortality?

- LAGB
- Laparascopic RYGB
- Open RYGB
- BPD with or without duodenal switch
- SG

What are the predictors associated with long-term effects of the surgical procedures (listed above) in patients with different BMIs and comorbidities?

- BMI <35
- BMI of 35 to 40 with no comorbidities
- BMI ≥35 with comorbidities, and
- BMI ≥40 with no comorbidities.

c. Complications

What are the short-term (less than 30 days) and long-term (30 days or more) complications of the following bariatric surgical procedures? What are the predictors associated with complications?

- LAGB
- Laparascopic RYGB
- Open RYGB
- BPD with or without duodenal switch
- SG

What are the complications of the surgical procedures (listed above) in patients with different BMIs and comorbidities?

- BMI <35
- BMI of 35 to 40 with no comorbidities
- BMI ≥35 with comorbidities, and
- BMI ≥40 with no comorbidities.

Tables A-18 and A-19 show studies rated fair or good and studies rated poor, respectively.

Table A–18. CQ5 Studies Rated Fair or Good

Count	Citations	Quality Rating
1	**Adami, Gian, Franco;** Papadia, Francesco; Carlini, Flavia; Murelli, Federica; Scopinaro, Nicola Effect of biliopancreatic diversion on hypertension in severely obese patients. *Hypertension research : official journal of the Japanese Society of Hypertension Feb 2005, 28 (2) : 119-23*	**Good** Before-after study
2	**Agaba, Emmanuel, Atta;** Shamseddeen, Hazem; Gentles, Charmaine, Victoria; Sasthakonar, Venketesh; Gellman, Larry; Gadaleta, Dominick Laparoscopic vs open gastric bypass in the management of morbid obesity: a 7-year retrospective study of 1,364 patients from a single center. *Obesity surgery Nov 2008, 18 (11) : 1359-63*	**Good** Cohort or cross-sectional study
3	**Angrisani, Luigi;** Lorenzo, Michele; Borrelli, Vincenzo Laparoscopic adjustable gastric banding versus Roux-en-Y gastric bypass: 5-year results of a prospective randomized trial. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery Mar 2007, 3 (2) : 127-32*	**Fair** Controlled intervention study
4	**Bessler, Marc;** Daud, Amna; Kim, Teresa; DiGiorgi, Mary Prospective randomized trial of banded versus nonbanded gastric bypass for the super obese: early results. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery Jul 2007, 3 (4) : 480-4*	**Good** Controlled intervention study
5	**Biertho, Laurent;** Steffen, Rudolf; Branson, Ruth; Potoczna, Natascha; Ricklin, Thomas; Piec, Grazyna; Horber, Fritz, F Management of failed adjustable gastric banding. *Surgery Jan 2005, 137 (1) : 33-41*	**Good** Case series study
6	**Dixon, John, B;** O'Brien, Paul, E; Playfair, Julie; Chapman, Leon; Schachter, Linda, M; Skinner, Stewart; Proietto, Joseph; Bailey, Michael; Anderson, Margaret Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *JAMA : the journal of the American Medical Association Jan 2008, 299 (3) : 316-23*	**Fair** Controlled intervention study
7	**Favretti, F;** Cadière, G, B; Segato, G; Himpens, J; De Luca, M; Busetto, L; De Marchi, F; Foletto, M; Caniato, D; Lise, M; Enzi, G Laparoscopic banding: selection and technique in 830 patients. *Obesity surgery Jun 2002, 12 (3) : 385-90*	**Good** Case series study
8	**Favretti, Franco;** Segato, Gianni; Ashton, David; Busetto, Luca; De Luca, Maurizio; Mazza, Marco; Ceoloni, Andrea; Banzato, Oscar; Calo, Elisa; Enzi, Giuliano Laparoscopic adjustable gastric banding in 1,791 consecutive obese patients:	**Good** Case series study

Count	Citations	Quality Rating
	12-year results. *Obesity surgery Feb 2007, 17 (2) : 168-75*	
9	**Grunstein, Ronald, R;** Stenlöf, Kaj; Hedner, Jan, A; Peltonen, Markku; Karason, Kristjan; Sjöström, Lars Two year reduction in sleep apnea symptoms and associated diabetes incidence after weight loss in severe obesity. *Sleep Jun 2007, 30 (6) : 703-10*	**Fair** Cohort or cross-sectional study
10	**Ikonomidis, Ignatios;** Mazarakis, Andreas; Papadopoulos, Costas; Patsouras, Nikolaos; Kalfarentzos, Fotis; Lekakis, John; Kremastinos, Dimitrios, T; Alexopoulos, Dimitrios Weight loss after bariatric surgery improves aortic elastic properties and left ventricular function in individuals with morbid obesity: a 3-year follow-up study. *Journal of hypertension Feb 2007, 25 (2) : 439-47*	**Fair** Case control study
11	**Karlsson, J;** Sjöström, L; Sullivan, M Swedish obese subjects (SOS)--an intervention study of obesity. Two-year follow-up of health-related quality of life (HRQL) and eating behavior after gastric surgery for severe obesity. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Feb 1998, 22 (2) : 113-26*	**Good** Case control study
12	**Karlsson, J;** Taft, C; Rydén, A; Sjöström, L; Sullivan, M Ten-year trends in health-related quality of life after surgical and conventional treatment for severe obesity: the SOS intervention study. *International journal of obesity (2005) Aug 2007, 31 (8) : 1248-61*	**Fair** Cohort or cross-sectional study
13	**Kehagias, Ioannis;** Karamanakos, Stavros, N; Argentou, Marianna; Kalfarentzos, Fotis Randomized clinical trial of laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy for the management of patients with BMI < 50 kg/m2. *Obesity surgery Nov 2011, 21 (11) : 1650-6*	**Good** Controlled intervention study
14	**Larrad-Jiménez, Alvaro;** Díaz-Guerra, Carlos, Sánchez-Cabezudo; de Cuadros Borrajo, Pedro; Lesmes, Irene, Bretón; Esteban, Basilio, Moreno Short-, mid- and long-term results of Larrad biliopancreatic diversion. *Obesity surgery Feb 2007, 17 (2) : 202-10*	**Fair** Case series study
15	**Longitudinal Assessment of Bariatric Surgery (LABS) Consortium;** Flum, David, Reed; Belle, Steven, H; King, Wendy, C; Wahed, Abdus, S; Berk, Paul; Chapman, William; Pories, Walter; Courcoulas, Anita; McCloskey, Carol; Mitchell, James; Patterson, Emma; Pomp, Alfons; Staten, Myrlene, A; Yanovski, Susan, Z; Thirlby, Richard; Wolfe, Bruce Perioperative safety in the longitudinal assessment of bariatric surgery. *The New England journal of medicine Jul 2009, 361 (5) : 445-54*	**Good** Cohort or cross-sectional study
16	**Lopez-Jimenez, Francisco;** Bhatia, Sundeep; Collazo-Clavell, Maria, L; Sarr, Michael, G; Somers, Virend, K Safety and efficacy of bariatric surgery in patients with coronary artery disease. *Mayo Clinic proceedings. Mayo Clinic Sep 2005, 80 (9) : 1157-62*	**Good** Case series study
17	**Marinari, Giuseppe, M;** Papadia, Francesco, S; Briatore, Lucia; Adami, Gianfranco; Scopinaro, Nicola Type 2 diabetes and weight loss following biliopancreatic diversion for obesity. *Obesity surgery Nov 2006, 16 (11) : 1440-4*	**Fair** Before-after study
18	**Mingrone, Geltrude;** Panunzi, Simona; De Gaetano, Andrea; Guidone, Caterina; Iaconelli, Amerigo; Leccesi, Laura; Nanni, Giuseppe; Pomp, Alfons; Castagneto,	**Good** Controlled

Count	Citations	Quality Rating
	Marco; Ghirlanda, Giovanni; Rubino, Francesco Bariatric surgery versus conventional medical therapy for type 2 diabetes. *The New England journal of medicine Apr 2012, 366 (17) : 1577-85*	intervention study
19	**Narbro, K;** Agren, G; Jonsson, E; Larsson, B; Näslund, I; Wedel, H; Sjöström, L Sick leave and disability pension before and after treatment for obesity: a report from the Swedish Obese Subjects (SOS) study. *International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity Jun 1999, 23 (6) : 619-24*	**Good** Case control study
20	**Naslund, Ingmar** Lessons from the Swedish Obese Subjects Study: The effects of surgically induced weight loss on obesity comorbidity. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery Mar 2005, 1 (2) : 140-4*	**Good** Case control study
21	**O'Brien, Paul, E;** Dixon, John, B; Laurie, Cheryl; Skinner, Stewart; Proietto, Joe; McNeil, John; Strauss, Boyd; Marks, Sharon; Schachter, Linda; Chapman, Leon; Anderson, Margaret Treatment of mild to moderate obesity with laparoscopic adjustable gastric banding or an intensive medical program: a randomized trial. *Annals of internal medicine May 2006, 144 (9) : 625-33*	**Good** Controlled intervention study
22	**Schauer, Philip, R;** Kashyap, Sangeeta, R; Wolski, Kathy; Brethauer, Stacy, A; Kirwan, John, P; Pothier, Claire, E; Thomas, Susan; Abood, Beth; Nissen, Steven, E; Bhatt, Deepak, L Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *The New England journal of medicine Apr 2012, 366 (17) : 1567-76*	**Good** Controlled intervention study
23	**Sekhar, N;** Torquati, A; Youssef, Y; Wright, J, K; Richards, W, O A comparison of 399 open and 568 laparoscopic gastric bypasses performed during a 4-year period. *Surgical endoscopy Apr 2007, 21 (4) : 665-8*	**Fair** Cohort or cross-sectional study
24	**Sjöström, C, D** Surgery as an intervention for obesity. Results from the Swedish obese subjects study. *Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society Aug 2003, 13 Suppl A : S22-6*	**Good** Case control study
25	**Sjöström, C, D;** Lissner, L; Wedel, H; Sjöström, L Reduction in incidence of diabetes, hypertension and lipid disturbances after intentional weight loss induced by bariatric surgery: the SOS Intervention Study. *Obesity research Sep 1999, 7 (5) : 477-84*	**Fair** Controlled intervention study
26	**Sjöström, C, D;** Peltonen, M; Sjöström, L Blood pressure and pulse pressure during long-term weight loss in the obese: the Swedish Obese Subjects (SOS) Intervention Study. *Obesity research Mar 2001, 9 (3) : 188-95*	**Good** Case control study
27	**Sjöström, C, D;** Peltonen, M; Wedel, H; Sjöström, L Differentiated long-term effects of intentional weight loss on diabetes and hypertension. *Hypertension Jul 2000, 36 (1) : 20-5*	**Good** Case control study
28	**Sjöström, L** Bariatric surgery and reduction in morbidity and mortality: experiences from the SOS study. *International journal of obesity (2005) Dec 2008, 32 Suppl 7 : S93-7*	**Good** Case control study

Count	Citations	Quality Rating
29	**Sjöström, Lars;** Gummesson, Anders; Sjöström, C, David; Narbro, Kristina; Peltonen, Markku; Wedel, Hans; Bengtsson, Calle; Bouchard, Claude; Carlsson, Björn; Dahlgren, Sven; Jacobson, Peter; Karason, Kristjan; Karlsson, Jan; Larsson, Bo; Lindroos, Anna-Karin; Lönroth, Hans; Näslund, Ingmar; Olbers, Torsten; Stenlöf, Kaj; Torgerson, Jarl; Carlsson, Lena, M, S; Swedish Obese Subjects Study Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial. *The lancet oncology Jul 2009, 10 (7) : 653-62*	**Good** Case control study
30	**Sjöström, Lars;** Lindroos, Anna-Karin; Peltonen, Markku; Torgerson, Jarl; Bouchard, Claude; Carlsson, Björn; Dahlgren, Sven; Larsson, Bo; Narbro, Kristina; Sjöström, Carl, David; Sullivan, Marianne; Wedel, Hans; Swedish Obese Subjects Study Scientific Group Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *The New England journal of medicine Dec 2004, 351 (26) : 2683-93*	**Good** Case control study
31	**Sjöström, Lars;** Narbro, Kristina; Sjöström, C, David; Karason, Kristjan; Larsson, Bo; Wedel, Hans; Lystig, Ted; Sullivan, Marianne; Bouchard, Claude; Carlsson, Björn; Bengtsson, Calle; Dahlgren, Sven; Gummesson, Anders; Jacobson, Peter; Karlsson, Jan; Lindroos, Anna-Karin; Lönroth, Hans; Näslund, Ingmar; Olbers, Torsten; Stenlöf, Kaj; Torgerson, Jarl; Agren, Göran; Carlsson, Lena, M, S; Swedish Obese Subjects Study Effects of bariatric surgery on mortality in Swedish obese subjects. *The New England journal of medicine Aug 2007, 357 (8) : 741-52*	**Good** Case control study
32	**Steffen, Rudolf;** Biertho, Laurent; Ricklin, Thomas; Piec, Gracyna; Horber, Fritz, F Laparoscopic Swedish adjustable gastric banding: a five-year prospective study. *Obesity surgery Jun 2003, 13 (3) : 404-11*	**Good** Case series study
33	**Wölnerhanssen, Bettina, K;** Peters, Thomas; Kern, Beatrice; Schötzau, Andy; Ackermann, Christoph; von Flüe, Markus; Peterli, Ralph Predictors of outcome in treatment of morbid obesity by laparoscopic adjustable gastric banding: results of a prospective study of 380 patients. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery Jul 2008, 4 (4) : 500-6*	**Fair** Before-after study
34	**Weber, Markus;** Müller, Markus, K; Bucher, Tanja; Wildi, Stefan; Dindo, Daniel; Horber, Fritz; Hauser, Rennward; Clavien, Pierre-Alain Laparoscopic gastric bypass is superior to laparoscopic gastric banding for treatment of morbid obesity. *Annals of surgery Dec 2004, 240 (6) : 975-82*	**Fair** Case control study
35	**Weiner, Rudolf, A;** Weiner, Sylvia; Pomhoff, Ingmar; Jacobi, Christoph; Makarewicz, Wojciech; Weigand, Gerhard Laparoscopic sleeve gastrectomy--influence of sleeve size and resected gastric volume. *Obesity surgery Oct 2007, 17 (10) : 1297-305*	**Fair** Cohort or cross-sectional study

Table A–19. CQ5 Studies Rated Poor with Rationale

Count	Citations	Quality Rating	Rating Rationale
1	**Alami, Ramzi, S;** Morton, John, M; Schuster, Rob; Lie, Jie; Sanchez, Barry, R; Peters, Anna; Curet, Myriam, J Is there a benefit to preoperative weight loss in	Poor Controlled intervention study	Completers only data; no ITT; attrition greater than 10%

Count	Citations	Quality Rating	Rating Rationale
	gastric bypass patients? A prospective randomized trial. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery Mar 2007, 3 (2) : 141-5*		
2	**Angrisani, L;** Di Lorenzo, N; Favretti, F; Furbetta, F; Iuppa, A; Doldi, S, B; Paganelli, M; Basso, N; Lucchese, M; Zappa, M; Lesti, G; Capizzi, F, D; Giardiello, C; Paganini, A; Di Cosmo, L; Veneziani, A; Lacitignola, S; Silecchia, G; Alkilani, M; Forestieri, P; Puglisi, F; Gardinazzi, A; Toppino, M; Campanile, F; Marzano, B; Bernante, P; Perrotta, G; Borrelli, V; Lorenzo, M; Italian Collaborative Study Group for LAP-BAND The Italian Group for LAP-BAND: predictive value of initial body mass index for weight loss after 5 years of follow-up. *Surgical endoscopy Oct 2004, 18 (10) : 1524-7*	**Poor** Cohort or cross-sectional study	No sample size justification reported; reports only data available at 5 yrs; reports lost to follow-up rate at 5 yrs as 155/573 (27%) and 381/573 present at 5 yrs (66.5%), a 33.5% lost to follow-up rate
3	**Anthone, Gary, J;** Lord, Reginald, V, N; DeMeester, Tom, R; Crookes, Peter, F The duodenal switch operation for the treatment of morbid obesity. *Annals of surgery Oct 2003, 238 (4) : 618-27*	**Poor** Cohort or cross-sectional study	Very high attrition (47% follow-up at 1 yr; 10% at 3 yrs; 7% at ≥5 yrs)
4	**Arceo-Olaiz, Ricardo;** España-Gómez, María, Nayví; Montalvo-Hernández, Jorge; Velázquez-Fernández, David; Pantoja, Juan, Pablo; Herrera, Miguel, F Maximal weight loss after banded and unbanded laparoscopic Roux-en-Y gastric bypass: a randomized controlled trial. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery Jul 2008, 4 (4) : 507-11*	**Poor** Controlled intervention study	Treatment assignment could have been predicted (randomization method used sealed envelopes); sample size determined arbitrarily
5	**Basdevant, Arnaud;** Paita, Michel; Rodde-Dunet, Marie-Héléne; Marty, Michel; Noguès, Françoise; Slim, Karem; Chevallier, Jean-Marc A nationwide survey on bariatric surgery in France: two years prospective follow-up. *Obesity surgery Jan 2007, 17 (1) : 39-44*	**Poor** Before-after study	No *p*-values reported; 11/21 note to downgrade rating to poor due to completers analysis and attrition >10% (12.2% at yr 1; 18% at yr 2)
6	**Brolin, R, E;** Bradley, L, J; Wilson, A, C; Cody, R, P Lipid risk profile and weight stability after gastric restrictive operations for morbid obesity. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract Sep 2000, 4 (5) : 464-9*	**Poor** Case series study	87% dropout at 24 mos (91 subjects available out of 651); high attrition
7	**Busetto, Luca;** Segato, Gianni; De Luca, Maurizio; De Marchi, Francesco; Foletto, Mirto; Vianello, Marinella; Valeri, Marzia; Favretti, Franco; Enzi, Giuliano Weight loss and postoperative complications in morbidly obese patients with binge eating disorder	**Poor** Before-after study	9/10/12 changed quality rating from fair to poor after consultation on 9/9/12; rationale for downgrade: no sample size justification; exposure measure not

Count	Citations	Quality Rating	Rating Rationale
	treated by laparoscopic adjustable gastric banding. *Obesity surgery Feb 2005, 15 (2) : 195-201*		clearly defined and of unclear validity and reliability; no assessment of varying levels of exposure; exposure measure not assessed more than one time; not reported if outcome assessors were blinded to exposure status of participants; percentage of participants lost to follow-up not reported; potential confounding variables not adjusted for statistically regarding their impact on relationship between exposure and outcome
8	**Choban, Patricia, S;** Flancbaum, Louis The effect of Roux limb lengths on outcome after Roux-en-Y gastric bypass: a prospective, randomized clinical trial. *Obesity surgery Aug 2002, 12 (4) : 540-5*	**Poor** Controlled intervention study	Differences between treatment groups at baseline; no ITT analysis; results given in figures only; unable to determine actual data values 11/30/11 downgrade
9	**Christou, Nicolas, V;** Look, Didier; Maclean, Lloyd, D Weight gain after short- and long-limb gastric bypass in patients followed for longer than 10 years. *Annals of surgery Nov 2006, 244 (5) : 734-40*	**Poor** Cohort or cross-sectional study	Completers only; attrition >10 % (17%)
10	**Gravante, Gianpiero;** Araco, Antonino; Araco, Francesco; Delogu, Daniela; De Lorenzo, Antonino; Cervelli, Valerio Laparoscopic adjustable gastric bandings: a prospective randomized study of 400 operations performed with 2 different devices. *Archives of surgery (Chicago, Ill. : 1960) Oct 2007, 142 (10) : 958-61*	**Poor** Controlled intervention study	11/21 note to downgrade rating to poor due to completers analysis and attrition greater than 10%
11	**Himpens, Jacques;** Dapri, Giovanni; Cadière, Guy, Bernard A prospective randomized study between laparoscopic gastric banding and laparoscopic isolated sleeve gastrectomy: results after 1 and 3 years. *Obesity surgery Nov 2006, 16 (11) : 1450-6*	**Poor** Controlled intervention study	No dropouts reported—unknown whether there were none; no data on randomization, sample size, methods, etc.; randomization method not described; sample size and study power unclear; blinding not reported
12	**Nguyen, N, T;** Goldman, C; Rosenquist, C, J; Arango, A; Cole, C, J; Lee, S, J; Wolfe, B, M Laparoscopic versus open gastric bypass: a randomized study of outcomes, quality of life, and costs. *Annals of surgery Sep 2001, 234 (3) : 279-89*	**Poor** Controlled intervention study	High differential attrition (fatal flaw); poor attrition

Count	Citations	Quality Rating	Rating Rationale
13	**Nguyen, Ninh, T;** Slone, Johnathan, A; Nguyen, Xuan-Mai, T; Hartman, Jaimee, S; Hoyt, David, B A prospective randomized trial of laparoscopic gastric bypass versus laparoscopic adjustable gastric banding for the treatment of morbid obesity: outcomes, quality of life, and costs. *Annals of surgery Oct 2009, 250 (4) : 631-41*	**Poor** Controlled intervention study	High risk of bias due to participants being able to change their procedures; subjects were allowed to withdraw prior to treatment; effectively a non-randomized trial; baseline differences support this conclusion
14	**Nickel, C;** Widermann, C; Harms, D; Leiberich, P, L; Tritt, K; Kettler, C; Lahmann, C; Rother, W, K; Loew, T, H; Nickel, M, K Patients with extreme obesity: change in mental symptoms three years after gastric banding. *International journal of psychiatry in medicine Jan 2005, 35 (2) : 109-22*	**Poor** Controlled intervention study	Study not randomized
15	**Nocca, D;** Krawczykowsky, D; Bomans, B; Noël, P; Picot, M, C; Blanc, P, M; de Seguin de Hons, C; Millat, B; Gagner, M; Monnier, L; Fabre, J, M A prospective multicenter study of 163 sleeve gastrectomies: results at 1 and 2 years. *Obesity surgery May 2008, 18 (5) : 560-5*	**Poor** Cohort or cross-sectional study	High attrition (74% follow-up at yr 1; 60% at yr 2)
16	**Parikh, M, S;** Fielding, G, A; Ren, C, J U.S. experience with 749 laparoscopic adjustable gastric bands: intermediate outcomes. *Surgical endoscopy Dec 2005, 19 (12) : 1631-5*	**Poor** Cohort or cross-sectional study	No data on statistical analyses reported; high attrition at 2 and 3 yrs
17	**Peeters, Anna;** O'Brien, Paul, E; Laurie, Cheryl; Anderson, Margaret; Wolfe, Rory; Flum, David; MacInnis, Robert, J; English, Dallas, R; Dixon, John Substantial intentional weight loss and mortality in the severely obese. *Annals of surgery Dec 2007, 246 (6) : 1028-33*	**Poor** Case control study	Matching technique questionable
18	**Pontiroli, Antonio, E;** Folli, Franco; Paganelli, Michele; Micheletto, Giancarlo; Pizzocri, Pierluigi; Vedani, Paola; Luisi, Francesca; Perego, Lucia; Morabito, Alberto; Bressani Doldi, Santo Laparoscopic gastric banding prevents type 2 diabetes and arterial hypertension and induces their remission in morbid obesity: a 4-year case-controlled study. *Diabetes care Nov 2005, 28 (11) : 2703-9*	**Poor** Case control study	Subjects not randomized to either a case or control; controls consisted of subjects who refused surgery, but agreed to be followed up; no sample size justification; target population not clearly defined; unclear whether adjusting for confounders was done
19	**Prachand, Vivek, N;** Davee, Roy, T; Alverdy, John, C Duodenal switch provides superior weight loss in the super-obese (BMI > or =50 kg/m2) compared with gastric bypass. *Annals of surgery Oct 2006, 244 (4) : 611-9*	**Poor** Cohort or cross-sectional study	High loss to follow-up at various endpoints; high differential loss to follow-up; high potential for selection bias (not randomized) High Attrition.
20	**Puzziferri, Nancy;** Austrheim-Smith, Iselin, T; Wolfe, Bruce, M; Wilson, Samuel, E; Nguyen,	**Poor** Controlled	High attrition; patients allowed to change treatment

Count	Citations	Quality Rating	Rating Rationale
	Ninh, T Three-year follow-up of a prospective randomized trial comparing laparoscopic versus open gastric bypass. *Annals of surgery Feb 2006, 243 (2) : 181-8*	intervention study	groups during study; no data on sample size power; high dropout rate
21	**Puzziferri, Nancy;** Nakonezny, Paul, A; Livingston, Edward, H; Carmody, Thomas, J; Provost, David, A; Rush, A, John Variations of weight loss following gastric bypass and gastric band. *Annals of surgery Aug 2008, 248 (2) : 233-42*	**Poor** Controlled intervention study	12.4% drop out (>10%); completers analysis only
22	**Rabkin, R, A** Distal gastric bypass/duodenal switch procedure, Roux-en-Y gastric bypass and biliopancreatic diversion in a community practice. *Obesity surgery Feb 1998, 8 (1) : 53-9*	**Poor** Case series study	Statistical methods not described; complication results reported for distal gastric group only (only 82% of this group); unable to draw comparisons with other groups
23	**Sampalis, John, S;** Sampalis, Fotini; Christou, Nicolas Impact of bariatric surgery on cardiovascular and musculoskeletal morbidity. *Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery Nov 2006, 2 (6) : 587-91*	**Poor** Case control study	Little detail on study and target populations (e.g., demographics); time frame for collection of controls (and whether controls were concurrent) unclear; validity/reliability of I/E criteria; questionable whether measures of exposure/risk were clearly defined and implemented consistently across all study participants
24	**Schowalter, Marion;** Benecke, Andrea; Lager, Caroline; Heimbucher, Johannes; Bueter, Marco; Thalheimer, Andreas; Fein, Martin; Richard, Matthias; Faller, Hermann Changes in depression following gastric banding: a 5- to 7-year prospective study. *Obesity surgery Mar 2008, 18 (3) : 314-20*	**Poor** Controlled intervention study	Completers analysis only; no ITT; attrition >10%; high dropout rate; no ITT analysis
25	**Simard, Barbara;** Turcotte, Hélène; Marceau, Picard; Biron, Simon; Hould, Frédéric, Simon; Lebel, Stéphane; Marceau, Simon; Boulet, Louis-Philippe Asthma and sleep apnea in patients with morbid obesity: outcome after bariatric surgery. *Obesity surgery Nov 2004, 14 (10) : 1381-8*	**Poor** Before-after study	Preoperative data self-reported; postoperative results reported for only 139 subjects (32%); High Attrition.
26	**Spivak, Hadar;** Hewitt, Mary, F; Onn, Amir; Half, Elizabeth, E Weight loss and improvement of obesity-related illness in 500 U.S. patients following laparoscopic adjustable gastric banding procedure. *American journal of surgery Jan 2005, 189 (1) : 27-32*	**Poor** Before-after study	Very high loss to follow-up, although authors report "Ninety percent of patients were available for 2- and 3-yr follow-up"; weight loss data reported for only 143, 80, and 29 at 12, 24, and 36

Count	Citations	Quality Rating	Rating Rationale
			mos, respectively; change in comorbidity and lab values reported for only 163 patients with 18 mos of follow-up (29%); poor attrition
27	**Suter, Michel;** Giusti, Vittorio; Worreth, Marc; Héraief, Eric; Calmes, Jean-Marie Laparoscopic gastric banding: a prospective, randomized study comparing the Lapband and the SAGB: early results. *Annals of surgery Jan 2005, 241 (1) : 55-62*	**Poor** Controlled intervention study	11/21 note to downgrade rating to poor due to completers analysis and attrition greater than 10% (fatal flaw)
28	**Weiner, R;** Blanco-Engert, R; Weiner, S; Matkowitz, R; Schaefer, L; Pomhoff, I Outcome after laparoscopic adjustable gastric banding - 8 years experience. *Obesity surgery Jun 2003, 13 (3) : 427-34*	**Poor** Case series study	Results report confusing; unclear for which group some outcomes are reported; some outcomes reported for one group and not other, without an explanation; follow-up only on first 100 patients
29	**Wittgrove, A, C;** Clark, G, W Laparoscopic gastric bypass, Roux-en-Y- 500 patients: technique and results, with 3-60 month follow-up. *Obesity surgery Jun 2000, 10 (3) : 233-9*	**Poor** Case series study	Follow-up from 3–60 mos; yet all data merged together; no mention of *n*'s or analyses used; data not clearly presented

[i] Nutrition professional: In the studies that form the evidence base for this recommendation, a registered dietitian usually delivered the dietary guidance; in most cases, the intervention was delivered in university nutrition departments or in hospital medical care settings where access to nutrition professionals was available

[ii] Trained Interventionist: In the studies reviewed, trained interventionists included mostly health professionals (e.g., registered dietitians, psychologists, exercise specialists, health counselors, or professionals in training) who adhered to formal protocols in weight management. In a few cases, lay persons were used as trained interventionists; they received instruction in weight management protocols (designed by health professionals) in programs that have been validated in high quality trials published in peer-reviewed journals.

[iii] Trained Interventionist: In the studies reviewed, trained interventionists included mostly health professionals (e.g., registered dietitians, psychologists, exercise specialists, health counselors, or professionals in training) who adhered to formal protocols in weight management. In a few cases, lay persons were used as trained interventionists; they received instruction in weight management protocols (designed by health professionals) in programs that have been validated in high quality trials published in peer-reviewed journals.

[iv] Trained Interventionist: In the studies reviewed, trained interventionists included mostly health professionals (e.g., registered dietitians, psychologists, exercise specialists, health counselors, or professionals in training) who adhered to formal protocols in weight management. In a few cases, lay persons were used as trained interventionists; they received instruction in weight management protocols (designed by health professionals) in programs that have been validated in high quality trials published in peer-reviewed journals.

Spreadsheets and Summary Tables

Critical Question 1

Diabetes Spreadsheet 1.1. Weight Loss From *Lifestyle* Interventions in Patients *With Diabetes* on Blood Glucose and HbA1c

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% (CI)	Fasting Glucose, mmol/L	HbA1c or Glycated Hg, %
Look AHEAD Wing, R et al. 2011 Wing, R et al. 2010 RCT of intensive lifestyle vs. diabetes support & education 4-yr follow-up Good	*N*: 5,145 4,999 in 1-yr follow-up 4,815 at 4-yr follow-up Age: 45–76 yrs BMI: ≥25: type 2 diabetes: 100%	At 1 yr Average kg of weight changes (±SD) by group: Gained ≥2%: +4.73 (3.0) Lost ≥2 to <5%: --3.48 (1.11) Lost ≥5% to <10%: -7.25 (2.07) Lost ≥10% to 15%: -12.13 (2.83) Lost ≥15%: -21.25 (7.05) Weight stable: gained 2% or lost <2%: 0.11 (1.16) Percent of sample by group: Gained ≥2%: 13% Lost ≥2 to <5%: 18% Lost ≥5% to <10%: 19% Lost ≥10% to 15%: 12% Lost ≥15%: 8% Referent: Weight Stable: Gained ≤2% to lost 2%: 25% at 4 yrs Weight change at 4 yrs, %: Intensive lifestyle: -6.15% (−6.39, −5.91) Diabetes support: -0.88% (−1.12, −0.64) Mean difference: -5.27 *p*<0.0001 Average effect across 4 yrs: -5.27%, *p*<0.0001	Change in glucose associated with % weight change at 1 yr: -14.32 ± 46.08 *p* <0.0001 Odds of achieving a 20 mg/dl decrease in glucose at 1 yr in those who: Gained ≥2%: OR: 0.35 (0.26 to 0.46) Gained 2% or lost <2% - stable: OR: 0.31 (0.24 to 0.39) Lost ≥2 to <5% OR: 0.54 (0.43 to 0.68) Referent: Lost ≥5% to <10%: 1 Lost ≥10% to 15%: OR: 1.25 (0.98 to 1.60) Lost ≥15%: OR: 2.44 (1.84 to 3.23) Odds of achieving significant improvement in glucose at 1 yr Gained ≥ 2%: OR: 1.13 (0.87 to 1.46) Stable: Lost ≥2 to <5% OR: 1.75 (1.40 to 2.19) Lost ≥5% to <10%: OR: 3.24 (2.57 to 4.09) Lost ≥10% to 15%: OR: 4.07 (3.09 to 5.36) Lost ≥15% OR: 7.92 (5.78–10.85) NR at 4 yrs	Change in HbA1c associated with % weight change at 1 yr: -0.39 ± 1.02 *p* <0.0001 Odds Ratio (95% CI) of achieving a 0.5% reduction in HbA1c at 1 yr in those who: Gained ≥2%: OR: 0.33 (0.25 to 0.43) Gained 2% or lost <2% - stable: OR: 0.28 (0.23–0.36) Lost ≥2 to <5%: OR: 0.51 (0.41–0.64) Referent: Lost ≥5% to <10%: 1 Lost ≥10% to 15%: OR: 2.85 (2.15, 3.78) Odds of achieving significant improvement in HbA1c at 1 yr Gained ≥2%: OR: 1.17 (0.91 to 1.50) Lost ≥2 to <5%: OR: 1.80 (1.44 to 2.24) Lost ≥5% to <10%: OR: 3.52 (2.81 to 4.40) Lost ≥10% to 15%: OR: 5.44 (4.15 to 7.13) At 4 yrs HbA1c change at 4 yrs, % Intensive lifestyle: -0.36% (−0.40, −0.33) Diabetes Support: -0.09% (−0.13, −0.06)

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% (CI)	Fasting Glucose, mmol/L	HbA1c or Glycated Hg, %
				Mean difference. 0.27 *p*<0.0001 Average effect across 4 yrs: -0.27%, *p*<0.0001
Norris, 2004 Norris, 2005 2004 MAs and 2005 Cochrane systematic review and MAs of non-pharmacological weight loss interventions for type 2 diabetes 22 RCTs, 9 vs. usual care Intervention: any duration (10 wks to 5 yrs) Follow-up: 1–5 yrs Fair	*N:* 4,659 (range: 20–2,205) 585 vs. usual care Age 18+ (mean 55 yrs) 2004: Baseline BMI: 33 2005: Any weight at baseline type 2 diabetes: 100%	Any intervention vs. usual care with 1 –2 yr follow-up, WMD kg random models (95% CI): 5 trials with HbA1C data as well: Weight change, mean kg (SD) Lifestyle/Control *Heller*: -5.5 (3.84)/-3(3.19) *n*=87; WMD -2.50 (-4.00 to -1.00) *Korhonen*: -4.66 (8.72)/-3.19(10.5) *n*=80; WMD: -1.47 (-5.70 to 2.76) *Trento*: -1.4 (8.98)/-1.1 (10), *n*=112; WMD: -0.30 (-3.82 to 3.22) *Uusitupa*: -0.62 (9.35)/2.09 (9.81) *n*=86; WMD: -2.71 (-6.76 to 1.34) *Zapotoczky*: -5.87 (11.11)/-1.88 (8.91) *n*=34; WMD: -3.99 (10.73–2.75)	Any intervention vs. usual care, WMD kg random models (95% CI): ≤2 yr follow-up 0.32 (-0.37 to 1.00) 3 trials, *n*=272 Korhonen Trento Uusitupa	Any intervention vs. usual care with 1–2 yr follow-up, WMD kg random models (95% CI): -0.67 (-1.44 to 0.10) 5 trials, *n*=381 Heller Korhonen Trento Uusitupa Zapotoczky

Spreadsheet 1.2. Weight Loss From *Lifestyle* Interventions in Persons *at Risk* for Developing Diabetes (Pre-Diabetes) on Risk of Converting to Type 2 Diabetes

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% CI)	Fasting Glucose, mmol/L	A1c or Glycated Hg	DM Incidence
Aucott 2004 Systematic review of weight loss on diabetes mellitus risk in obese persons w/ & w/o diabetes mellitus 2 lifestyle trials (*Wing*,	*N*: 418 Age: 18–70 yrs BMI >28	Tuomilehto, kg (SD) 3.5 (4.4) *n*=265 Wing ≥4.5 kg			Tuomilehto, *n*=265 Impaired glucose tolerance (IGT) Men 1. HR 0.46 (0.1–0.74) IGT Women

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% CI)	Fasting Glucose, mmol/L	A1c or Glycated Hg	DM Incidence
Tuomilehto) Follow-up of 2 plus yrs Good		*n*=153			HR 0.37 (0.21–0.82) Wing, *n*=153 IGT RR 0.74 (0.59–0.90)
Avenell 2004a and c Health Technology Assessment, and J Hum Nutr Diet paper Systematic review and meta-analysis of long-term effects of obesity treatments and health outcomes 84 RCTs, 3 IGT trials (Swinburn, (no intervention, 6 people at 1 worksite, lifestyle) Wing 98, Tuomilehto 2–24 mos of intervention, Follow-up: ≥52 wks Good	*N*: 4,353 Age: ≥18 BMI: ≥28 type 2 diabetes Varies by study	Tuomilehto, 2001, *n*=506 Lifestyle: -5.00 (4.00) Control: =1.00 (15.00) Wing, 1998, *n*=66 At 24 mos Lifestyle: -2.10 (7.60) Control: -0.30(4.50)			2 trials of IGT reporting on status at 2 yrs: Tuomilehto, 2001 Lifestyle: 3–5 kg loss at 2 yrs (SD: 4.4) *p*<0.05 Men: HR (95% CI): 0.46 (0.19 to 0.74) Women: HR (95% CI): 0.37 (0.21–0.82) Wing1998 Kg/% incidence Lifestyle: -5.50/30.3% Control: -0.30/7% Risk for IGT: RR (95% CI): 0.74 (0.59 –0.90) *p*<0.05 Risk for normal glucose: RR (95% CI): 0.70 (0.53–0.87)
Douketis, J 2005 Lifestyle: 3 RCTs with IGT arms and fasting blood glucose outcome data (Erickson, Tuomilehto, Diabetes Prevention Program (DPP) Research Group) Fair	*N*: 2,701 (with IGT) Age: Adults BMI ≥25	Erickson 91 Weight NR Tuomilehto 01 Weight NR DPP 02 Weight loss kg last observation carried forward (LOCF) (%) at 4 yrs Lifestyle: 5.0 (5) Control: 0.1 (NR) Between group differences not reported	Fasting blood glucose change from baseline at 24 mos, % Lifestyle: -0.2% Control: -0.05% No between group differences reported Completers Analysis (3% dropout) Fasting blood glucose change from baseline at 48 mos, % Lifestyle: -0.1 Control: +0/2 No between group test		"IGT or type 2 diabetes who received dietary/lifestyle and exercise counseling or usual care, counseling had 58–63% lower risk of type 2 diabetes" (Note: these are the trials cited: Eriksson 91, Tuomilehto 01, DPP 02, only DPP has fasting blood glucose and weight data)

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% CI)	Fasting Glucose, mmol/L	A1c or Glycated Hg	DM Incidence
Norris, 2005 MA of lifestyle weight loss interventions for adults with prediabetes 9 RCTs – 2 with weight and incidence data Intervention: 4 wks to 10 yrs Follow-up: 1-6 yrs Good	*N*: 5,956 Age: ≥18 yrs Any weight at baseline Pre-diabetes 100%	*DPP* – includes a metformin arm Weight change at 2.8 yrs, kg (95% CI) -5.5 (-5.7, -5.3) *Tuomilehto* Weight change at 2 yrs, WMD random effect, kg (95% CI) -2.70 (-3.55, -1.85) Lifestyle -3.5 (5.5) Control: -0.8 (4.4) Weight change at 1 yr Lifestyle -4.2 (5.1) Control: -0.8 (3.7) *Liao* Weight change at 2 yrs, WMD random effect, kg (95% CI) -2.50 [3.96, -1.04] -1.8 (2.69) 0.7 (3.23)			*DPP* Incidence Lifestyle: 4.8 Control 11.0 *Tuomilehto* Risk reduction from 2.7 kg weight loss at 2 yrs: 58% all person yrs accumulated *p*<0.001 Incidence at 2 yrs: Lifestyle: 3.2 Control: 7.8 *Liao* Risk reduction from 2.5 kg weight loss as 2 yrs: 51% Incidence at 2 yrs Lifestyle: 1.6 (1 person) Control: 3.2 (2 persons)

Spreadsheet 1.3. Intentional Weight Loss From Lifestyle Interventions in Patients With or Without Diabetes on Mortality

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% CI)	Fasting Glucose, mmol/L	A1c or Glycated Hg, %	DM Mortality	NOTES FROM RTI
Poobalan A, 2007 Aucott 2004 Systematic review assessing long-term effectiveness of weight loss on all-cause mortality in overweight and obese people	*N*: >6,500 Age: 18 to 70, mean 55–60 yrs BMI: ≥ 25 DM or NIDDM				Mortality in those with diabetes with intentional weight loss in 1 yr vs. weight stable, random effects model: HR: 0.75 (0.67–0.83)	

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% CI)	Fasting Glucose, mmol/L	A1c or Glycated Hg, %	DM Mortality	NOTES FROM RTI
8 studies (cohort and trials) ≥2 ys follow-up Fair, Good						

Spreadsheet 1.4a. Weight Loss From *Orlistat* Interventions in Patients *With Diabetes* on Blood Glucose and HbA1c

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% CI)	Fasting Glucose, mmol/L	A1c or Glycated Hg, %
Avenell 2004a and b Health Technology Assessment, and J Hum Nutr Diet paper Systematic review and meta-analysis of long-term effects of obesity treatments and health outcomes 84 RCTs, 8 RCTs with orlistat plus diet comparisons Note: Two possible trials 1) Hollander 98, type 2 diabetes; 2) Lindgärde 99/00, included elevated FBG or type 2 diabetes 2–24 mos of intervention, Follow-up: ≥52 wks Good	*N*: 4,353 Age: ≥18 BMI: ≥28 type 2 diabetes Varies by study	NR for diabetes subjects only	Fasting plasma glucose change at 12 mos, WMD (95% CI) -0.58 (-0.80 to -0.36) *Hollander 98* WMD -0.08 (-0.34 to -0.18) *Lindgärde 00* WMD -0.54(-0.81 to -0.27)	HbA1c change at 12 mos, WMD fixed effects % (95% CI) -0.27 % (0.38 to -0.15) *Hollander 98* WMD -0.47 (-0.71 to -0.23) *Lindgärde 00* WMD -0.20 (-0.33 to -0.07)
Norris, 2005c MA of pharmacotherapy for weight loss in adults with type 2 diabetes 8 Orlistat trials Any duration or length of follow-up, but ranged from 12–57 wks Good	*N*: 2,036 Age: 18+ yrs BMI: Overweight, no minimum BMI at baseline type 2 diabetes 100%	Pooled effects over all follow-up periods, kg (95% CI)s: ?? -2.0 (-1.3 to -2.8) 7 trials in MA (*Bloch, Hanefeld, Hollander, Kelley, Kelley, Miles, Wang*) Weight loss WMD random effects, kg (95% CI): -2.12 (-2.82 to -1.25) 7 trials in MA (*Bloch, Hanefeld, Hollander, Kelley, Kelley, Miles, Wang*)	Fasting glucose WMD random effects, mmol/l (95% CI): -0.82 (-1.14, -0.50) 8 trials (*Bloch, Hanefeld, Hollander, Kelley, Kelley, Lindgärde, Miles, Wang*)	Pooled effects for follow-up between 24 and 57 wks, % (95% CI): -0.5% (-0.3 to -0.6) 7 trials in MA (*Hanefeld, Hollander, Kelley, Kelley, Miles, Urdgarde, Wang*) GHb WMD random effects, % (95% CI): -0.45 (-0.58, -0.31) 7 trials (*Hanefeld, Hollander, Kelley, Kelley, Lindgärde, Miles, Wang*)

Spreadsheet 1.4b. Weight Loss From *Orlistat* Interventions in Patients *at Risk* for Diabetes on Blood Glucose and HbA1c

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change, WMD kg (95% CI)	Fasting Glucose, mmol/L	A1c or Glycated Hg, %
No reviews with trials that specifically were in subjects with IGT				

Spreadsheet 1.5. Effect of Weight Loss on Serum Lipids

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
Lifestyle Interventions							
Avenell 2004a and c HTA systematic review and meta-analysis of different components of lifestyle interventions 84 in review, 19 RCTs of lifestyle vs. control Follow-up: mean or median of 52 wks post-randomization Good	*N*: 734 Age: Mean or median of ≥18 yrs BMI Mean or median of ≥28	Diet vs. control, WMD, kg (95% CI): At 12 mos *ODES*–5.10 (–6.68 to –3.52) *Wood '88*–7.80 (–9.38 to –6.22) *Wood '91a*–5.40 (–7.93 to –2.87) *Wood '91b*–6.80 (–9.13 to –4.47) Diet and exercise vs. control WMD, kg (95% CI): At 12 mos -4.78 (-5.41 to -4.16) *p* <0.00001 4 trials *n=774* *FDPS* –3.40 (–4.18 to –2.62) *ODES* –6.70 (–8.11 to –5.29) *Wood '91a* –6.40 (–8.69 to –4.11) *Wood 91b* –10.40 (–12.73 to –8.07) Diet and behavior vs.	Diet vs. control, WMD, mmol/L (95% CI): At 12 mos -0.21 (-034 to -0.08) *p*=0.05 4 trials *n*=329 *ODES* *Wood'88* *Wood'91a* *Wood'91b* Diet and exercise vs. control WMD, mmol/L (95% CI) At 12 mos -0.13 (-0.23 to -0.03) *p*=0.01 4 trials *n*=774 *FDPS* *ODES* *Wood '91a* *Wood'91b* Diet and behavior vs. control, WMD	Diet vs. control, WMD, mmol/L (95% CI): At 12 mos -0.13 (-0.26 to 0.00) *p=0.05* *4* trials *n*=329 *ODES* *Wood'88* *Wood'91a* *Wood'91b* Diet and exercise vs. control WMD, mmol/L (95% CI) At 12 mos -0.20 (-0.34 to 0.06) *p*=0.005 3 trials *n*=268 *ODES* *Wood '91a* *Wood'91b* Diet and behavior vs. control, WMD mmol/L (95% CI) At 12 or 24 mos *Only one study: Wing so*	Diet vs. control, WMD, mmol/L (95% CI): At 12 mos 0.06 (0.03–0.09) *p*=0.05 4 trials *n*=327 *ODES* *Wood'88* *Wood'91a* *Wood'91b* Diet and exercise vs. control WMD mmol/L (95% CI) At 12 mos 0.06 (0.04 –0.08) p<0.00001 4 trials *n*=774 *FDPS* *ODES* *Wood '91a* *Wood'91b* Diet and behavior vs. control, WMD mmol/L (95% CI)	Diet vs. control, WMD, mmol/L (95% CI): At 12 mos -0.19 (-0.31 to -0.06) *p*=0.05 4 trials *n*=329 *ODES* *Wood* *Wood* *Wood* Diet and exercise vs. control, mmol/L (95% CI) At 12 mos -0.23 (-0.31 to -0.15) p<0.00001 4 trials *n*=772 *FDPS* *ODES* *Wood '91a* *Wood'91b* Diet and behavior vs. control, WMD mmol/L (95% CI)	

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
		control WMD kg (95 CI) At 12 mos -7.21 (-8.68 to -5.75) 3 trials *Hakala* –12.00 (–15.44 to –8.56) *Karvetti*–6.60 (–8.57 to –4.63) *Wing 88* –5.20 (–8.07 to 2.33) Diet, exercise, and behavior therapy vs. control WMD Kg (95%CI): At 12 mos *Laitenen* –2.80 (–4.23 to –1.37) *Lindahl* –4.90 (–5.96 to –3.84) *Narayan* 1.70 (–0.94 to 4.34) *Jalkenen* –4.00 (–7.65 to –0.35) *Wing* –7.10 (–10.94 to –3.26) At 24 mos *Laitenen* 1.68 –2.20 (–6.81 to 2.41) Laitenen 1.99 –3.70 (–7.93 to 0.53 *Wing* 3.25 –2.20 (–5.51 to 1.11)	mmol/L (95% CI) At 12 mos 0.13 (0.34 to 0.08) 4 trials *n*=330 *Hakala* *Karvetti* *Karvetti* *Wing* Diet, exercise, and behavior therapy vs. control WMD mmol/L (95%CI): At 12 mos -0.14 (-0.27 to -0.01) 6 trials *Laitenen* *Lindahl* *Jalkenen* *Narayan* *Wing* At 24 mos -0.04 (-0.29 to 0.22) 2 trials *Laitenen* *Wing*	*not included here* Diet, exercise and behavior vs. control, WMD mmol/L (95% CI) At 12 mos *Only one study: Wing so not included here*	At 12 mos 0.11 (0.06–0.17) 4 trials *n*=330 *Hakala* *Karvetti* *Karvetti* *Wing* Diet, exercise, and behavior therapy vs. control WMD mmol/L (95%CI): At 12 mos 0.06 (0.01–0.12) 3 trials *Laitenen* *Jalkenen* *Wing* At 24 mos 0.02 (-0.06 –0.11) 2 trials *Laitenen* *Wing*	At 12 mos -0.58 (-0.98 to -0.17) 2 trials *n*=141 *Hakala* *Wing* Diet, exercise, and behavior therapy vs. control WMD mmol/L (95%CI): At 12 mos -0.17 (-0.32 to -0.02) 4 trials *Laitenen* *Lindahl* *Jalkenen* *Wing* At 24 mos -0.36 (-0.70 to -0.01) 2 trials *Laitenen* *Wing*	
Poobalan 2004 Avenell 2004c - focusing on long -term weight loss and lipids 13 studies; 1 RCT, 3 Observational (excluded 5 surgical studies and 1 metformin	2. *N*: 4,765 Wing: 202 Kaufman: 104 Sjostrom: 1,827 Age: 18–70 BMI	Weight change, kg (SE) Lifestyle 3 trials: *Wing '98* Weight cyclers Gainers: 10.30 (2.36) Stable: 3.00 (1.36) Large cycler: -2.10 (1.17) Small cycler: -2.60 (1.26)	TC change, mmol/L (SE) Lifestyle 3 trials: *Wing '98* Weight cyclers Gainers: 0.33 (0.28) Stable: 0.14 (0.22) Large cycler: -34 (0.19) Small cycler: 0.11		HDL change, mmol/L (SE) Lifestyle 2 trials: *Wing '98* Weight cyclers Gainers: -0.06 (0.07) Stable: 0.00 (0.06) Large cycler: -0.01 (0.05) Small cycler: -0.07 (0.06	Triglyceride change, mmol/L (SE) Lifestyle 2 trials: *Wing '98* Weight cyclers Gainers: 0.93 (0.40) Stable: 0.18 (0.31) Large cycler: -0.01 (0.27) Small cycler: 0.33 (0.29)	NOTE: Data presented does not give the between group *p* values; the correlations reported below are for all of the nonsurgical studies and not all meet our criterion

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
study, 2 lifestyle not compared to usual care, 2 orlistat trials) Follow-up: ≥2 yrs Fair	≥28 kg/m2	Partial cycler: -9.70 (1.69) Small success: -5.90 (2.92) Large success: -12.60 (2.63) 2 observ: *Kaufman* -2.20 (0.40) *Sjostrom* Women: -1.44 (0.40) Men: -2.7 (0.56)	(0.20) Partial cycler: -0.4 (0.20) Small success: 0.11 (0.41) Large success: --0.23 (0.29) 2 observ: *Kaufman* R=0.24; *p*=0.01 *N*=80 *Sjostrom* Women: -0.01 (0.06) Men: -0.26 (0.09)		Partial cycler: 0.10 (0.06) Small success: 0.17 (0.11) Large success: 0.09 (0.08) 1 observ: *Sjostrom* Women: -0.18 (0.04) Men: 0.00 (0.09)	Partial cycler: -0.38 (0.29) Small success: -0.10 (0.58) Large success: -0.29 (0.41) 1 observ: *Sjostrom* Women: -0.33 (0.06) Men: -0.31 (0.19)	Correlation with weight change =0.798 (*p*<0.001). Adjusted R-square=0.798 Correlation with weight change =0.903 (*p*<0.001). Adjusted R-square=0.804 Prospective studies and trials with 2-yr follow-up data in nonsurgical trials and 5 yr follow-up data in surgical studies. SUMMARY DATA NOT PRESENTED SEPARATELY FOR NON-SURGICAL STUDIES. For every 10 kg reduction in body weight there is a 0.23 mmol/L decrease in total cholesterol Correlation with weight change = -.0308 (ns). Correlation with weight change =0.828 (*p*<0.001). Adjusted R-square=0.672
Shaw 2006 Cochrane SR and	*N*: 3,476	WMD weight loss, kg (95%CI): -2.03 (-2.82 to -1.23)	TC change, mmol/L (95% CI): -0.03 (-0.09 to -0.15)		HDL change, mmol/L (95% CI): 0.06 (0.03 to 0.09)	WMD triglyceride change, mmol/L (95% CI):	

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
MA of exercise for overweight and obesity 41 RCTs, 12 exercise trials vs., no txt Follow-up: 3 –12 mos Loss to follow-up: <15% - inclusion criteria Good	Age: Adults BMI: Obese overweight	2 trials *n*=270 *Stefanik* *Wood*	3 trials *n*=348 *p*=0.65 *Hellenius* *Stefanik* *Wood*		3 trials *n*=348 *Hellenius* *Stefanik* *Wood*	-0.18 (-0.31 to -0.05) *p*<0.01 3 trials *n*=348 *Hellenius* *Stefanik* *Wood*	
Galani 2007 Systematic Review with Meta-Analysis of lifestyle interventions in overweight and obese 13 prevention RCTs; 17 treatment RCTs Follow-up: ≥1 year Fair	*N*: 3,566 Age: ≥18 yrs BMI: overweight and obese	Overweight WMD Lifestyle Intervention vs. Standard Care, kg (95% CI): -2.19 (-2.81 to -1.57) 11 studies *Burke* *Carr* *Dyson* *He* *Kastarinen* *Ketola* *Liao* *Mensink* *Simkin-Silverman* *Stefanick- female* *Stefanick –male* *Trento* Obese WMD Lifestyle Intervention vs. Standard Care, kg (95% CI): -3.49 (-4.70 to -2.27) 12 studies DPP Esposito Harvey Berino Jeffrey	Overweight WMD Lifestyle Intervention vs. Standard Care, mmol/L (95% CI): -0.26 (-0.41 to -0.12) 7 studies Obese WMD Lifestyle Intervention vs. Standard Care, mmol/L (95% CI): -0.14 (-0.24 to -0.03) 5 studies	Overweight WMD Lifestyle Intervention vs. Standard Care, mmol/L (95% CI): -0.16 (-0.28 to -0.03) 5 studies Obese: NR	Overweight WMD Lifestyle Intervention vs. Standard Care, mmol/L (95% CI): 0.01 (-0.22 to 0.04) (ns) 7 studies Obese WMD Lifestyle Intervention vs. Standard Care, mmol/L (95% CI): 0.04 (0.004–0.08) 4 studies	Overweight WMD Lifestyle Intervention vs. Standard Care, mmol/L (95% CI): -0.23 (-0.38 to -0.08) 7 studies Obese WMD Lifestyle Intervention vs. Standard Care, mmol/L (95% CI): -0.15 (-0.27 to -0.04) 4 studies	NOTE: Not directly tied to weight loss—Different number of studies in the different meta-analyses

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
		Lindhal Messier Moore Narayan Sbrocco Stevens Tate Wylie Rosset Whelton Wing Wolf Yeh					
Witham 2010 Systematic review and meta-analysis of long-term weight loss 9 trials targeting diet, physical activity, and mixed approaches 1 yr outcomes Fair	*N*: 1,954 Age: mean ≥60 BMI ≥30 kg/m2	WMD, kg (95% CI) *PATH (post menopausal)*-1.40 (-2.43, -0.37) *Toobert (post menopausal, CHD)*-1.90(-3.72, -0.09) *Mengham, (DM)* 0.80 (-2.20, 3.80) *Glasgow (DM)* -0.24 (-2.15, 1.67)	At 1 yr TC change, mmol/L (95% CI): -0.36 (-0.75 to 0.04) *p* =0.08 4 studies *n*=424 *PATH (post menopausal)* *Toobert (post menopausal, CHD)* *Mengham, (DM)* *Glasgow (DM)*	At 1 yr WMD LDL change, mmol/L (95% CI): -0.04 (-0.25 to 0.18) *p*=0.74 2 studies *Toobert (post menopausal, CHD)* *Frank (post menopausal)*	At 1 yr WMD HDL change, mmol/L (95% CI): 0.04 (-0.04 to 0.12) *p*=0.37 2 studies *Toobert (post menopausal, CHD)* *Frank (post menopausal)*	At 1 yr WMD Triglyceride change, mmol/L (95% CI): 0.44 (-0.55 to 1.43) *p*=0.39 2 studies *Toobert (post menopausal, CHD)* *Frank (post menopausal)*	NOTE: Not directly tied to weight loss—different number of studies in the different meta-analysis, but the bigger problem is the different populations being grouped together
Orlistat Interventions							
Avenell 2004a and b HTA, JHND Journal article Health Technology Assessment 8 orlistat RCT's Duration: 1+ yrs Good	*N*: 4,533 of orlistat trials Ages: ≥18 yrs BMI mean or median >28 kg/m2	WMD orlistat vs. placebo weight loss at 12 mos, kg (95% CI): *Broom* –3.50 (–4.79 to –2.21) *Davidson –2.95 (–4.45 to –1.45)* *Finer* –1.98 (–3.73 to –0.23) *Hauptman* –3.99 (–5.31 to –2.67) *Hollander*– 2.41 (–3.54 to –1.28) *Lindägrde* –1.30 (–2.69 to 0.09) *Rossner*–2.90 (–4.30 to –1.50)	WMD orlistat vs. placebo TC, mmol/L (95% CI): At 12 mos -0.34 (-0.41 to -0.27) 7 trials *Broom* *Finer* *Hauptman* *Hollander* *Lindgärde* *Rossner* *Sjostrom* At 24 mos -0.21 (-0.34 to -0.09) 3 trials	WMD orlistat vs. placebo LDL, mmol/L (95% CI): At 12 mos -0.29 (-0.34 to -0.24) 7 trials *Broom* *Finer* *Hauptman* *Hollander* *Lindgärde* *Rossner* *Sjostrom* At 24 mos -0.22 (-0.31 to -0.13) 3 trials *Davidson*	WMD orlistat vs. placebo HDL, mmol/L (95% CI): At 12 mos -0.03 (-0.01 to -0.05) 6 trials *Same as cholesterol minus Broom* At 24 mos -0.03 (0 to -0.07) 3 trials *Davidson* *Hauptman* *Rossner*	WMD orlistat vs. placebo Triglyceride, mmol/L (95% CI): At 12 mos -0.03 (-0.04 to -0.10) 6 trials *Same as cholesterol minus Finer* At 24 mos -0.04 (-0.07 to 0.15) 3 trials *Davidson* *Hauptman* *Rossner*	NOTE: Different number of studies in the different MAs From Pooblan 2004: For every 10 kg reduction in body weight there is a 0.23 mmol/L decrease in total cholesterol

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
		Sjostrom–4.20 (–5.35 to –3.05) At 2 yrs 2 trials *Hauptman*–3.56 (–4.79 to –2.33) *Rossner*–2.92 (–4.21 to –1.63) *Data for Davidson from Pooblan 2004* *Davidson* Orlistat: -7.60 (0.20) Placebo: -4.00 (0.50)	*Davidson* *Hauptman* *Rossner*	*Hauptman* *Rossner*			
Norris, 2005c MA of *pharmacotherapy* for weight loss in adults with type 2 diabetes 8 Orlistat trials Any duration or length of follow-up, but ranged from 12–57 wks Good	*N*: 2,036 Age: 18+ yrs BMI: Overweight, no minimum BMI at baseline type 2 diabetes 100%	WMD weight changes for orlistat vs. placebo, random effects, kg (95% CI): *Bloch* -0.80 (-1.97, 0.7) *Hanefeld* -1.90 (-2.96, -0.84) *Hollander* -1.88 (-3.38, -0.38) *Kelley 02* -2.62 (-6.08, 0.84) *Kelley 04-0.70 (-4.44, -3.04)* *Miles-2.90 (-3.73, -2.07)* *Wang* -4.00 (-7.19, -0.81)	WMD TC changes, orlistat vs. placebo random effects, mmol/L (95% CI): -0.41 (-0.52 to -0.30) 6 trials *Bloch* *Hanefeld* *Hollander* *Kelley* *Miles* *Wang*	WMD LDL changes, orlistat vs. placebo random effects, mmol/L (95% CI): -0.32 (-0.43 to -0.21) 6 trials *Hanefeld* *Hollander* *Kelley 02* *Kelley 04* *Miles* *Wang*	Not estimable	WMD Triglyceride changes, orlistat vs. placebo random effects, mmol/L (95% CI): -0.23 (-0.40 to -0.05) 6 trials *Bloch* *Hollander* *Kelley 02* *Kelley 04* *Miles* *Wang*	NOTE: Different number of studies in the different meta-analyses, authors don't report which ones are included in other than kg weight loss
Rucker 2007 Updated Cochrane SR and MA of pharmaco-therapy + diet weight loss trials 30 studies (16 orlistat) Duration: 1+ yrs	*N*: 10,631 of orlistat trials Ages: ≥18 yrs BMI ≥30 or ≥27 kg/m2 with one or more obesity related comorbidities	WMD Orlistat vs. placebo Weight loss in all populations, kg (95% CI): -2.87 (-3.21 to -2.53) 14 studies *Bakris* *Berne* *Broom* *Davidson*	WMD Orlistat vs. placebo Total cholesterol change, mmol/L (95% CI): 0.32 (-0.37 to -0.28) 13 studies *n*=5,206 Orlistat: significantly reduced cholesterol (data not presented)	WMD Orlistat vs. placebo LDL, mmol/L (95% CI): -0.26 (-0.30 to -0.22) 13 studies *n*=5,206	WMD Orlistat vs. placebo HDL change, mmol/L (95% CI): -0.03 (-0.04 to -0.02) 11 studies *n*=4,152	WMD Orlistat vs. placebo Triglyceride change, mmol/L (95% CI): -0.03 (-0.12 to -0.07) 11 studies *n*=4,456	NOTE: Different number of studies in the different meta-analyses, authors don't report which ones are included in other than kg weight loss Not clear at what time interval

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
Good		*Derosa* *Finer* *Hauptman* *Hollander* *Kelly* *Krempf* *Lindgärde* *Miles* *Rossner* *Sjostrom* *Swinburn* *XENDOS* % weight loss, % (95% CI): -2.93% (-3.35 to -2.50) 13 studies ≥5% weight loss, % (95% CI) 0.21 (0.18 to 0.24) 14 trials ≥10% weight loss, % (95% CI) 0.12 (0.09 –0.14) 13 trials					outcomes were used for the MA: 4 trials were 2-yr weight maintenance trials: *Davidson, Hauptman, Rossner, Sjostrom* "Therefore, in contrast to our previous version of this review (Padwal 2003), we analysed separately published weight loss and weight maintenance trials together." ITT with LOCF
DIABETES SUBJECTS							
Look AHEAD Wing 2010 Wing 2011 RCT of intensive lifestyle vs. diabetes support & education 4-yr averaged outcome (Wing 2010) 1-yr outcomes (Wing 2011) Good	*N*: 5,145 Age: Adults age 45–75, BMI ≥25 type 2 diabetes 100% With and without hypertension Placebo subtracted −5.27 % (−5.61 to −4.93)	Over 4 yrs Mean difference of % initial weight of intensive vs. diabetes support at 4 yrs, %: −5.27 *p*<0.001 At 1 yr, % weight loss, % (SD): -4.77 (7.57) *p*<0.0001 At 1 yr, % weight loss by weight loss groups, % (SD): Gained >2% (13% of subjects) +4.73 (3.0) Referent	NR	Over 4 yrs Mean difference of LDL mg/dl: +1.57 *p*<0.009 At 1 yr, 10 mg/dl decrease in LDL by weight loss groups, Odds (95% CI): Gained >2% 1.17 (0.95–1.45) Referent: Weight Stable, Gained ≤2% to lost <2%: 1.0 Lost >2 to <5% : 1.05 (0.86–1.29) Lost >5 to <10%:	Over 4 yrs Mean difference of HDL mg/dl: +1.70 *p*<0.0001 At 1 yr, 5 mg/dl increase in HDL by weight loss groups, Odds (95% CI): Gained >2% 0.88 (0.71–1.11) Referent: Weight Stable, Gained ≤2% to lost <2%: 1.0 Lost >2 to <5% : 1.13 (0.93–1.39) Lost >5 to <10%:	Over 4 yrs Mean difference of Triglycerides, mg/dl: -5.81 *P* =0.0006 At 1 yr, 40 mg/dl decrease in Triglycerides by weight loss groups, Odds (95% CI): Gained >2% 0.80 (0.60–1.06) Referent: Weight Stable, Gained ≤2% to lost <2%: 1.0 Lost >2 to <5% : 1.46 (1.14–1.87)	Between group mean differences were adjusted for baseline medication use

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
	(*p*<0.001)	Weight Stable Gained ≤2% to lost <2% (25% of subjects): -0.11 (1.16) Lost >2 to <5% (18% of subjects) -3.4 (1.11) Lost >5 to <10% (19% of subjects) -7.25 (2.07) Lost >10 to 15% (12% of subjects) -12.13 (2.83) Lost >15% (8% of subjects) -21.25 (7.05)		1.34 (1.09–1.64) Lost >10 to 15%: 1.26 (0.98–1.62) Lost >15%: 1.34 (1.02–1.78) At 1 yr, 10 mg/dl decrease in LDL in those not on medications by weight loss groups, Odds (95% CI): Gained >2% 1.39 (0.9 to 1.99) Referent: Weight Stable, Gained ≤2% to lost <2%: 1.0 Lost >2 to <5% : 0.97 (0.69–1.36) Lost >5 to <10%: 1.41 (1.00–2.00) Lost >10 to 15%: 1.28 (0.83–1.96) Lost >15%: 1.52 (0.96–2.41)	1.69 (1.37–2.07) Lost >10–15%: 2.30 (1.80 to 2.93) Lost >15%: 4.34 (3.30-5.72) At 1 yr, 5 mg/dl increase in HDL in those not on medications by weight loss groups, Odds (95% CI): Gained >2% 0.79 (0.5 to 1.15) Referent: Weight Stable, Gained ≤2% to lost <2%: 1.0 Lost >2 to <5% : 0.99 (0.71–1.39) Lost >5 to <10%: 1.52 (1.08–2.15) Lost >10 to 15%: 2.54 (1.68–3.82) Lost >15%: 5.27 (3.36–8.27)	Lost >5 to <10%: 2.20 (1.71–2.83) Lost >10 to 15%: 3.99 (2.97 to 5.35) Lost >15%: 7.18 (5.19 to 9.93)	
Thomas 2006 – Cochrane SR and MA of exercise vs. no exercise for type 2 diabetes 14 trials Duration: 8 wks to 12 mos Good	*N*: 377 Age: No criteria, but no included study involved children BMI: Inclusion criteria not reported type 2 diabetes 100%	At 1 yr, weight change, WMD kg (95% CI) *Maiorana* 0.0 (-12.20, 12.20) *Mourier* -0.40 (-12.22, 11.42) *Ronnemaa* -0.10 (-12.81, 12.61) *Tessier* 3.50 (-6.68, 13.68) *Wing 88b*-1.60 (-16.89, 13.69) NOTE: No weight loss data for Raz	At 1 yr, WMD TC change, mmol/L (95% CI): -0.11 (-0.41 to +0.18) 5 studies *n*=139 *Maiorana* *Mourier* *Raz* *Ronnemaa* *Wing 88b*	At 1 yr, WMD LDL change, mmol/L (95% CI): -0.12 (-0.29 to +0.53) 3 studies *n*=73 *Maiorana* *Mourier* *Ronnemaa*	At 1 yr, WMD HDL change, mmol/L (95% CI): -0.02 (-0.10 to +0.06) 5 studies *n*=139 *Maiorana* *Mourier* *Raz* *Ronnemaa* *Wing 88b*	At 1 yr, WMD Triglyceride change, mmol/L (95% CI): -0.25 (-0.48 to -0.02) 5 studies *n*=139 *Maiorana* *Mourier* *Raz* *Ronnemaa* *Wing 88b*	NOTE: Not directly tied to weight loss—Different number of studies in the different meta-analyses
Hutton 2004 SR and MA to assess orlistat effect on weight	3. *N*: 2,679 Age:	WMD kg, (95% CI) -2.50 (-2.97 to -2.02) 4 trials *n*=1,480 *Hollander*	WMD orlistat vs. placebo, mmol/L (95% CI): -0.37 (-0.47, -0.26)	WMD orlistat vs. placebo, mmol/L (95% CI): -0.25 (-0.25, -0.15)	WMD orlistat vs. placebo, mmol/L (95% CI): -0.03 (-0.05, -0.01)	WMD orlistat vs. placebo, mmol/L (95% CI): -0.20 (-0.35, -0.05)	NOTE: Different number of studies in the different MA, authors don't

Author, Year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	Total Cholesterol	LDL	HLDL	Triglycerides	Notes
loss and lipids 28 RCTs NR Fair	adults BMI: >25 type 2 diabetes 100%	*Hanefled* *Kelley* *Miles*	*p*≤0.05 4 trials *n*=1,729 NR	*p*≤0.05 4 trials *n*=1,729 NR	*p*≤0.05 4 trials *n*=1,729 NR	*p*≤0.05 4 trials *n*=1,729 NR	report which ones are included in other than kg weight loss
Norris, 2004 Norris, 2005a and b MA and Cochrane SR and MA of non-pharmacological weight loss interventions for type 2 diabetes 22 RCTs, 9 vs. usual care Intervention: any duration (10 wks to 5 yrs) Follow-up: 1–5 yrs Fair	N 4,659 for SR 585 vs. usual care Age 18+ (mean 55 yrs) BMI: 2003: 33 2005: Any weight at baseline type 2 diabetes: 100%	Any intervention vs. usual care with 1–2 yr follow-up, WMD kg random models (95% CI): *Pissarek* -5.80 (-10.40, -1.20) *Zapotoczky* -3.99 (-10.73, 2.75) *Trento* -0.30 (-3.82, 3.33) *Uusitupa* -2.71 (-6.76, 1.34)	Any intervention vs. usual care with 1–2 yr follow-up, WMD random models, mmol/L (95% CI): -0.13 (-0.41 to 0.15) 4 trials, *n*=344 *Pissarek* *Trento* *Zapotoczky* *Uusitupa*		Any intervention vs. usual care with 1–2 yr follow-up, WMD random models, mmol/L (95% CI): -0.09 (-0.05 to 0.23) 3 trials, *n*=226 *Trento* *Zapotoczky* *Uusitupa*	Any intervention vs. usual care with 1–2 yr follow-up, WMD random models, mmol/L (95% CI): -0.36 (-0.58 to 0.14) 4 trials, *n*=344 *Pissarek* *Trento* *Zapotoczky* *Uusitupa*	NOTE: Different number of studies in the different MAs, authors don't report which ones are included in other than kg weight loss
Norris, 2005 MA of *pharmacotherapy* for weight loss in adults with type 2 diabetes 8 Orlistat trials Any duration or length of follow-up, but ranged from 12 to 57 wks Good	*N*: 2,036 Age: 18+ yrs BMI: Overweight, no minimum BMI at baseline type 2 diabetes 100%	WMD weight changes for orlistat vs. placebo, random effects, kg (95% CI): *Bloch* -0.80 (-1.97, 0.7) *Hanefeld* -1.90 (-2.96, -0.84) *Hollander* -1.88 (-3.38, -0.38) *Kelley 02* -2.62 (-6.08, 0.84) *Kelley 04-0.70 (-4.44, -3.04)* *Miles-2.90 (-3.73, -2.07)* *Wang* -4.00 (-7.19, -0.81)	WMD total cholesterol changes, orlistat vs. placebo random effects, mmol/L (95% CI): -0.41 (-0.52 to -0.30) 6 trials *Bloch* *Hanefeld* *Hollander* *Kelley* *Miles* *Wang* Note: Does not include Hanefeld	WMD LDL changes, orlistat vs. placebo random effects, mmol/L (95% CI): -0.32 (-0.43 to -0.21) 6 trials *Hanefeld* *Hollander* *Kelley 02* *Kelley 04* *Miles* *Wang* Note: Does not include Bloch	Not estimable	WMD Triglyceride changes, orlistat vs. placebo random effects, mmol/L (95% CI): -0.23 (-0.40 to -0.05) 6 trials *Bloch* *Hollander* *Kelley 02* *Kelley 04* *Miles* *Wang* Note: Does not include Hanefeld	NOTE: Different number of studies in the different MA, authors don't report which ones are included in other than kg weight loss ALSO IN ORLISTAT SECTION

Spreadsheet 1.6. Weight Loss and Hypertension Risk

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	SBP, mm Hg	DBP, mm Hg	Notes
ORLISTAT TRIALS: ALL SUBJECTS and SUBGROUPS (DM only or HTN only)					
ALL SUBJECTS (NB Subgroups HTN or DM only)					
Avenell 2004b Health Technology Assessment of treatments for obesity and implications for health improvement 8 orlistat RCTs provided with dietary intervention compared to placebo plus diet Duration: 2 yrs Good	*N*: 4,533 of orlistat trials Ages: >18 yrs BMI mean or median >28 kg/m2 All Subjects were 'high risk': may have had DM (1 study), CVD risk (3 studies), or other risk factors	WMD orlistat vs. placebo weight loss at 12 mos, kg range (95% CI) 7 trials Broom–3.50 (–4.79 to –2.21) Davidson–2.95 (–4.45 to –1.45) Hauptman–3.99 (–5.31 to –2.67) Hollander–2.41 (–3.54 to –1.28) Lindgärde–1.30 (–2.69 to 0.09) Rossner–2.90 (–4.30 to –1.50) Sjostrom–4.20 (–5.35 to –3.05) At 2 yrs, all subjects hypertensiion only -3.26 (- 4.15 to -2.37) 2 trials *(n*=899) Hauptman Rossner	WMD orlistat vs. placebo SBP, mmHg (95% CI): At 12 mos (Tbl. 5) -2.02 (-2.87 to -1.17) 7 trials (*n*=3677) Broom Davidson Hauptman Hollander Lindgärde Rossner Sjostrom At 24 mos (Tbl. 5) -1.42 (-3.08 to 0.24) [NS] 2 studies (*n*=899) Hauptman Rossner	WMD orlistat vs. placebo DBP, mmHg (95% CI): At 12 mos (Tbl. 5) -1.64 (-2.20 to -1.09) 7 trials (*n*=3667) Broom Davidson Hauptman Hollander Lindgärde Rossner Sjostrom At 24 mos (Tbl. 5) -1.20 (-2.28 to -0.11) 2 studies (*n*=899) Hauptman Rossner	Avenell: Clear definitions: weight maintenance trials were excluded; this helps edit other SRA, M\HTA Fig. 17,18 For both lifestyle and pharmacotherapy interventions: "A weight loss of 10 kg was associated with a fall in …DBP of 3.6 mmHg. A weight loss of 10% was associated with a fall in SBP of 6.1 mmHg."
Rucker 2007 Padwal 2004 Updated Cochrane systematic review and meta-analysis of pharmacotherapy + diet weight loss trials 30 studies (16 orlistat) Duration: 1+ yrs Good	*N*: 10,631 of orlistat trials Ages: >18 yrs BMI >30 or >27 kg/m2 with one or more obesity related comorbidities	WMD Orlistat vs. placebo Weight loss mean differences, kg (95% CI): [Same for whether 12 or 13 trials] Lowest: -1.00 (-3.39, 1.39) Derosa Highest: -4.20 (-6.69, -1.71) Sjostrum Padwall 2004 Analysis	WMD Orlistat vs. placebo SBP, mmHg (95% CI): -1.52 (-2.19 to -0.86) 13 studies (*n*=6,965)	WMD Orlistat vs. placebo DBP, mmHg (95% CI): -1.38 (-2.03 to -0.74) 12 studies (*n*=8,322) Bakris 2002 Berne 2004 Broom 2002 Davidson 1999 Derosa 2003 Hauptman 2000 Kelley 2002	DM sub-group analyses is only weight loss (kg or %); weight loss data are not tied to blood pressure

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	SBP, mm Hg	DBP, mm Hg	Notes
		1.3 Krempf 2003 Hollander 1998 Bakris 2002 Berne 2004 Broom 2002 Davidson 1999 Derosa 2003 Hauptman 2000 Kelley 2002 Lindgarde 2000 Miles 2002 Rossner 2000 Sjostrom 1998 Swinburn 2005 XENDOS WMD weight loss, % (95% CI): [Range same for whether 12 or 13 trials] Lowest: -1.30 (-2.40, -0.20) Lindgarde Highest: -4.10 (-5.14, -3.06) Sjostrum Padwall 2004 Analysis 1.3 ≥5% weight loss, % risk diff. (95% CI) [Same for whether 12 or 13 trials] Lowest: 0.13 (0.03, 0.23) Lindgarde Highest: 0.35 (0.24, 0.46) Berne Padwall 2004, Analysis 1.3 ≥10% weight loss, % risk difference (95% CI) [Same for whether 12 or 13 trials] Lowest: 0.04 (-0.03, 0.12) Lindgärde		Lindgarde 2000 Rossner 2000 Sjostrom 1998 Swinburn 2005 XENDOS	

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	SBP, mm Hg	DBP, mm Hg	Notes
		Highest: 0.21 (0.15, 0.28) Sjostrom Padwall 2004, Analysis 1.3			
Johansson et al., 2009 Systematic review and meta-analysis of blood pressure outcomes after weight loss by drug treatment 12 trials of orlistat (combined with diet, PA, surgery as well as head to head); 3 in subjects with diabetes All 12-mo duration Good	*N*: 5,540 orlistat trials Age: Mean age ranged between 42–59 yrs BMI: 31.9–38.9. 8 orlistat studies only recruited patients with 'high risk': type 2 diabetes, hypertension, hypercholesterolemia or one or more CVD risk factors (HTN, dyslipidemia, DM, or impaired glucose tolerance); one study only included patients with HTN. Mean baseline SBP ranged from 119 to 153 mmHg, and mean DBP from 69 to 98 mmHg	WMD weight loss at 12 mos, kg (95% CI): Non-diabetics Appendix 4 -2.82 (-3.51, -2.13) *p*<0.001 9 trials (*n*=5542) In Diabetics Fig. 2 -2.79 (-3.31, -2.26) 3 studies (*n*=1,259) *Berne:* -3.05 (-4.54, -1.56) *Kelley: -2.62 (-3.38, -1.86)* *Miles:* -2.90 (-3.73, -2.07)	WMD SBP change at 1yr, mmHg (95% CI): Non-diabetics Fig. 2 -2.19 (-3.09, -1.29) 9 trials (*n*=4,281) In Diabetics: Fig. 2 -0.93 (-2.56, 0.70) NS 3 studies (*n*=1,259) *Berne* *Kelley* *Miles*	WMD DBP change at 1 yr, mmHg (95% CI): Non-diabetics Fig. 2 -1.62 (-2.43, -0.81) 9 trials In Diabetics Fig. 2 -1.03 (-2.39, 0.34) NS 2 studies *Kelley* *Berne*	Attrition: 0 to 61% "Compared to patients without diabetes, diabetic patients treated with orlistat experienced smaller and non-significant changes in systolic and DBP."
DIABETES SUBJECTS					
Norris, 2005 Meta-analysis of pharmacotherapy for weight loss in adults with type 2 DM 8 Orlistat trials Any duration or length of follow-up, but ranged from 12 to 57 wks. Any combined	*N*: 2,036 Age: 18+ yrs BMI: Overweight, no minimum BMI at baseline type 2 diabetes	WMD weight changes for orlistat vs. placebo, kg (95% CI): Bloch -0.80 [-1.97 to 0.37)] Kelley 02 -2.62 [-6.08, 0.84] Kelley 04 -0.70 [-4.44, 3.04] Miles -0.70 [-4.44, 3.04]	WMD SBP changes, orlistat vs. placebo random effects, mmHg (95% CI): -2.99 (-6.29 to 0.32) 5 trials Bloch Kelley 02 Kelley 04 Miles Wang	WMD SBP changes, orlistat vs. placebo random effects, mmHg (95% CI): -4.21 (-7.82 to -0.61) 4 trials Bloch Kelley 02 Kelley 04 Wang Appendix 7.22	"Modest weight loss may have health benefits…the weight loss demonstrated in this review is equivalent to weight changes shown to be effective in management and prevention of hypertension in high-risk individuals."

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	SBP, mm Hg	DBP, mm Hg	Notes
intervention as defined above. Good	100%	Wang -4.00 [-7.19, -0.81] Appendix 7.14	Appendix 7.21		
HYPERTENSION SUBJECTS					
Aucott 2005 Meta-analysis of Health Technology Assessment of treatments for obesity and implications for health improvement 11 orlistat RCTs provided with dietary intervention compared to placebo plus diet Duration: 2 yrs Good	*N*: 489 in orlistat trials Ages: ≥18 yrs BMI: mean or median >28 kg/m^2 All had hypertension: *Hauptman, Rossner*	At 2 yrs, hypertensive subjects [Aucott] WMD kg (SD) 2 trials *Hauptman* Orlistat: -5.16 (0.78) Placebo: -1.54 (0.58) *Rossner* Orlistat: -7.60 (1.35) Placebo: -4.30 (0.63)	At 2 yrs, hypertensive subjects WMD, mm Hg (SE) 2 trials *Hauptman* Orlistat: 0.0 (1.67) Placebo: 3.00 (2.52) *Rossner* Orlistat: -6.10 (1.94) Placebo: -5.10 (2.10)	At 2 yrs, hypertensive subjects WMD, mm Hg (SE) 2 trials *Hauptman* Orlistat: -1.00 (1.67) Placebo: 1.00 (1.82) *Rossner* Orlistat: -2.60 (1.19) Placebo: -2.70 (1.26)	"DBP changes are related to weight changes (labeled in the plots) up to 3 yrs, after which the relationship breaks down and blood pressure appears to creep up with time. This time effect is also reflected to some extent in the SBP results." …meta regression analysis to estimate that a mean weight loss of 10 kg decreased SBP (SBP) by 6 mm Hg and DBP by 4.6. Models for DPB were more stable, whereas those for SBP were less reliable. Table 7 a 1 kg change in weight leads to a -0.252 change in DBP (p<.01); A 1 kg change in weight leads to a -2.32 change in sbp (p<.01)
Siebenhofer 2009 Horvath 2008 Cochrane systematic review and meta-analysis of weight loss pharmacotherapy vs. placebo in those with HTN 4 trials (Head-to-Head, no other intervention component reported) Intervention: ≥24 wks Follow-up: 6 –48 mos Good	*N*: 3,132 of orlistat trials Ages: ≥18 yrs BMI NR All had essential HTN (baseline SBP of ≥140 mmHg and/or a DBP of ≥90 mmHg or patients on antihypertensive treatment	WMD orlistat vs. placebo weight change, kg (95% CI): -3.73 (-4.65 to -2.80) 4 studies *n*=1,080 *Bakris* *Cocco* *Guy-Grand* *XENDOS* *Fig 4.* [Appendix 1.3]	WMD orlistat vs. placebo change in SBP, mmHg (95% CI): -2.46 (-4.01 to -0.90) 4 trials *n*=1,058 *Bakris* *Cocco* *Guy-Grand* *XENDOS* *Fig. 2* [Appendix 1.1]	WMD orlistat vs. placebo change in DBP, mmHg (95% CI): -1.92 (-2.99 to -0.85) 4 trials *n*=1,058 *Bakris* *Cocco* *Guy-Grand* *XENDOS* *Fig 3* [Appendix 1.1]	*The authors note that a weight loss of 4 kg is needed to achieve a 2.5 mm HG by orlistat and suggested that diet may be more effective in lowering BP (weight loss and changes in diet quality that may influence BP).* *Note: High dropout and risk of bias in studies*

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	SBP, mm Hg	DBP, mm Hg	Notes
LIFESTYLE TRIALS: ALL SUBECTS and SUBGROUPS (DIABETES SUBJECTS)					
ALL SUBJECTS					
Avenell 2004c Health Technology Assessment of treatments for obesity and implications for health improvement RCTs comparing exercise combined with diet or BT Duration: up to 24 mos Good	2 studies ODES (*n*=219) only 21 women WOOD (*n*=264 men and women) 1 study Pavlou (*n*=160 men only) 2 studies Wing, (*n*=30) 1988 (*n*=154) 1998 type 2 diabetes only More females than males Ages: ≥18 yrs BMI: mean or median >28 kg/m^2 Subjects: could have DM (1 study), CVD risk (3 studies), or other RF	Diet and exercise 12 mos -1.95 (-3.22 to -0.68) 18 mos -7.63 (-10.33 to =4.92) 1 study Diet, Exercise, BT 12 mos (Wing 1988) -3.02 (-494 to -1.11) 24 mos (Wing 1998) -2.16 (-4.2 to -0.12)	-0.03 (-1.99 to +1.93) -8.90 (-13.65 to -4.15) -4.20 (-10.02 to +1.62) -4.0 (-10.06 to +2.06)	-1.14 (-2.56 to +0.29) -12.10 (-15.20 to -9.0) -4.40 (-8.98 to +0.18) -3.2 (-7.66 to +1.26)	Exercise or diet alone, combined diet and exercise vs. control/usual care 12 mos (up to 7 trials depending on outcome) Exercise compared to diet and BT 12 and 24 mos (2 trials) in DM subjects. Avenell: Clear definitions: weight maintenance trials were excluded; this helps edit other systematic reasoning assessment, MA.\Health Technology Assessment Fig. 17,18 Reported here are results on lifestyle intervention for weight reduction (diet w/ and w/o physical activity, behavioral strategies; physical activity alone). For both lifestyle and pharmacotherapy interventions: "A weight loss of 10 kg was associated with a fall in …DBP of 3.6 mmHg. A weight loss of 10% was associated with a fall in SBP of 6.1 mmHg."
Aucott 2005 Meta-analysis of Health Technology Assessment of treatments for obesity and implications for health improvement 2 RCTs and 2 prospective trials Duration: up to 5 yrs Good	*N*: 670 Ages: >18 yrs BMI mean or median >28 kg/m^2	Weight difference, kg (SE) Kauffman, 1992: -2.20* Sjostrom, 1999: Men: -1.44 Women: -2.7 Wing 1995 Large cyclers:-2.1 Small cyclers:+2.60 Partial cyclers:-9.70 Small success: -5.9 Large success: -12.6 Wing 1998: Diet + Behavioral therapy (BT): -2.1 Exercise + BT: 1.0 Diet, Ex + BT: -2.5	SBP difference, mmHg (SE) Kauffman, 1992: correlation =0.2 Sjostrom, 1999: Men: -6.03 (1.15) Women: -3.66 (1.40) Wing 1995 Large cyclers:-3.1 Small cyclers: +0.4 Partial cyclers:-10.00 Small success: -4.6 Large success: -2.5 Wing 1998: Diet + BT: 0.8 Exercise + BT: +0.9 Diet, Ex + BT: -4.8	DBP difference, mmHg (SE) Sjostrom, 1999: Men: -5.00 (0.76) Women: -2.94 (0.86) Wing 1995 Large cyclers:-2.2 Small cyclers: +5.0 Partial cyclers:-5.1 Small success: -2.4 Large success: -4.1 Wing 1998: Diet + BT: +3.0 Exercise + BT: +2.0 Diet, Ex + BT: -0.20	

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	SBP, mm Hg	DBP, mm Hg	Notes
DIABETES SUBJECTS					
Look AHEAD Pi-Sunyer 2007 Wing 2010 Wing 2011 RCT of intensive lifestyle vs. diabetes support & education 4 yr averaged outcome (Wing 2010) 1 yr outcomes (Wing 2011) Comprehensive lifestyle: low-fat diet (<30%), 120–1550 kcal, 15+% protein; 75 minutes physical activity, behavioral strategies (goal setting, self-monitoring, problem solving). Registered dietician, Physical activity specialists, behavioral counselors Good	*N*: 5,145 Age: Adults age 45–75, BMI: ≥ 25 overweight and obese type 2 diabetes 100% W and w/o hypertension	At 4 yrs Mean difference (MD) of % initial weight of intensive vs. diabetes support, % of initial weight: −5.27 *p*<0.001 At 1 yr Mean % loss of initial weight, % (SD): Intensive: 8.6 (6.9) diabetes support: 0.7 (4.8) *p*<0.001 % weight loss by weight loss groups, % (SD): Gained >2% (13% of subjects) +4.73 (3.0) Referent Weight Stable Gained ≤2% to lost <2% (25% of subjects): -0.11 (1.16) Lost >2 to <5% (18% of subjects) -3.4 (1.11) Lost >5 to <10% (19% of subjects) -7.25 (2.07) Lost >10 to 15% (12% of subjects) -12.13 (2.83) Lost >15% (8% of subjects) -21.25 (7.05)	At 4 yrs MD of SBP change of intensive vs. diabetes support, mmHg: −2.36 (−3.03 to −1.70) *p*< 0.001 At 1 yr Change in SBP, mmHg (SD): Intensive: -6.8 (0.4) Diabetes Support: -2.8 (0.3) *p*<0.001 ODDS of improved blood pressure at 1 yr 5 mm Hg decrease in SBP by weight loss groups, odds (95% CI): Gained >2% 0.86 (0.70–1.06) Referent: Weight Stable, Gained ≤ 2% to lost <2%: 1.0 Lost >2 to <5%: 1.24 (1.02–1.50) Lost >5 to <10%: 1.56 (1.27–1.91) Lost >10 to 15%: 2.29 (1.79–2.93) Lost >15%: 2.65 (2.00–3.50)	At 4 yrs MD of DBP change of intensive vs. diabetes support, mmHg (95% CI): −0.43 (−0.77 to −0.10) P < 0.012 At 1 yr Change in DBP, mmHg (SD): Intensive: -3.0 (0.2) Diabetes Support: -1.8 (0.2) *p*< 0.001 Odds of improved blood pressure at 1 yr 5 mm Hg decrease in DBP by weight loss groups, odds (95% CI): Gained >2% (13%) 1.03 (0.83–1.28) Referent: Weight Stable, Gained ≤2% to lost <2%: 1.0 Lost >2 to <5% : 1.24 (1.02–1.50) 1.05 (.86-1.28) Lost >5 to <10%: 1.48 (1.20–1.82) Lost >10 to 15%: 1.48 (1.20–1.82) 1.64 (1.25-2.06) Lost >15%: 2.39 (1.81–3.16)	Between group mean differences were adjusted for baseline medication use Fewer ILI patients continued or initiated hypertension medication use at 1-4 yr follow-up; 85% vs. 92.7% at 4 yrs. (Table 2) Intensive vs. diabetes support at 4 yrs, change in use of antihypertensive drugs (SD): Intensive: -0.1 (0.6) Diabetes Support: 2.2 (0.6) *p*=0.02

Author, year, Study Design, No. of Studies, Duration Quality Rating	Population Characteristics	Weight Change	SBP, mm Hg	DBP, mm Hg	Notes
Norris, 2004 Norris, 2005 Cochrane SR & MA of non-pharmacological weight loss trials for type 2 diabetes 22 RCTs, 9 vs. usual care (Diet [1200-–500 or VLCD], physical activity, BT by registered dietician, nurse educators, physical activity specialist) Intervention: 10 wks to 5 yrs Followup: 1–5 yrs Fair	*N*: 4,659 for SR 585 vs. usual care Age: ≥ 18 (mean 55 yrs) BMI: 33 but could include those of normal weight as well as overweight and obese [Norris 2005: Any weight at baseline, (one study under 22] type 2 diabetes: 100%	Any intervention vs. usual care with 1–2 yr follow-up, WMD kg (95% CI): *Uusitupa:* -2.71 (-6.76, 1.34) *Zapotoczky:* -3.99 (-10.73, 2.75) [Norris 2005, 3.11 Appendix]	SBP change for any intervention vs. usual care with 1–2 yr follow-up, WMD kg random models (95% CI): -1.85 (-6.41, 270) 2 trials, *n*=114 *Uusitupa* *Zapotoczky*	DBP change for any intervention versus usual care with 1–2 yr follow-up, WMD kg random models (95% CI): 0.0 (-2.49 to 2.49) 2 trials, *n*=114 *Uusitupa* *Zapotoczky*	Between group difference: 1 and -4 mmHg
SUBJECTS WITH HYPERTENSION					
Horvath et al., 2008 SR & MA of diet, drug & surgical inter-ventions for weight loss in hypertension subjects 4 dietary intervention studies reported here only (pharmacological interventions – see Siebenhofer above) Lifestyle: 6–36 mos Good	*N*: 2219 diet Age: mean 45–66 BMI: NR Hypertension 100%	Diet intervention WMD weight change in diet vs. placebo, kg (95% CI): *Croft:* -6.30 (–9.96 to –2.64) *TAIM* -5.40 (–6.65 to –4.15) *ODES* - NR	Diet intervention WMD SBP change, mmHg (95% CI): -6.26 (-9.82 to -2.70) 2 studies *Croft* *ODES*	Diet intervention WMD DBP change, mmHg (95% CI): -3.41 (-5.55 to -1.27) 3 studies *Croft* *ODES* *TAIM*	Issues with inadequate randomization and lack of blinding *The authors note that a weight loss of 4 kg is needed to achieve a 6 mm HG reduction in SBP by diet and a 2.5 mm HG by orlistat suggesting that diet is more effective in lowering blood pressure.* *Table 1 weight loss (n=832)* *SBP (n=202)* *DBP (n=731)*

Critical Question 2

Spreadsheet 2.1. Study Descriptives

	Author, Journal, Year	Type	Number and types of studies / participants included	Inclusion / exclusion criteria	Age	Sex	Race/ ethnicity	Countries	Adjustment factors	Quality rating & reasons if rating was poor
1	Abell PH, Reports 2007	Pooled	2,843 women from Black Pooling Project	Included all participants from the Evans County Heart Study, Charleston Heart Study, NHANES I and NHANES III	<30 to >70	F	Black, White	US	age, smoking	Poor No predefined and specified I/E criteria No comprehensive and systematic literature search No dual review of abstracts and full-text articles for I/E criteria No quality assessment of included studies No assessment of publication bias
2	Bogers, Arch Intern Med 2007	Pooled	21 cohorts	Cohort studies presenting RR with multiple adjustments for age, sex, physical activity, and smoking, with and without simultaneous adjustment for blood pressure and cholesterol levels	20–94 yr	M, F	Mainly White	Australia, Finland, Italy, Sweden, US, Norway, Scotland, Netherland, England, Ireland, entire Britain	age, sex, smoking, physical activity	Poor No dual review of abstracts and full-text articles for I/E criteria No quality assessment of included studies No assessment of publication bias Individual participant data analyzed for only 21 of 70 studies found in the literature search
3	DeGonzalez, NEJM 2010	Pooled	1.46 million white adults from NCI cohorts	<u>Cohorts included:</u> >5 yrs follow-up >1000 deaths among non-Hispanic Whites Baseline year in 1970 or later Ascertained height, weight, and smoking status at baseline <u>Participants included:</u>	19–84	M, F	White	US, Sweden, Australia, Norway	age as time metric adjusted for alcohol, education, marital status, physical activity *Note: restricted analysis to never smokers*	Poor No comprehensive and systematic literature search No dual review of included studies for I/E No quality assessment of included studies No assessment of publication bias

	Author, Journal, Year	Type	Number and types of studies / participants included	Inclusion / exclusion criteria	Age	Sex	Race/ ethnicity	Countries	Adjustment factors	Quality rating & reasons if rating was poor
				non-Hispanic white <84 yrs 1 yr follow-up Information on height or weight BMI between 15 and 50 kg/m^2						
4	De Koning, Eur Heart J 2007	Meta-analysis	15 cohort studies; 258,114 participants	Inclusion: English language prospective cohort studies or RCTs that reported RR for incidence CVD Reported sex-stratified RR in at least three quantiles of WC Exclusion: All participants had existing metabolic risk factor or diagnosis or suspected CVD	Mean: 57 yr	M, F	White, Black, Asian	Sweden, US, Britain, Finland, China	Stratified by sex; Adjusted for age, cohort year, drug treatment (if RCT), confounders (e.g., smoking) but not mediators (e.g., diabetes, dyslipidaemia);	Poor No quality assessment of included studies
5	Hartemink, AJE 2006	Meta-analysis	31	Inclusion: Prospective cohort studies on the relation between BMI or overweight and type 2 diabetes Studies had a follow-up period of at least 4 yrs Studies that consisted of at least 80% Caucasians Exclusion: Clinical trials and other intervention studies aiming to reduce obesity	NA	No.	At least 80% Caucasians	Studies from Europe, US, and Asia	Somewhat different covariates were adjusted in different original studies	Poor No dual review of abstracts and full-text articles for I/E criteria No quality assessment of included studies Diagnosis of diabetes varied in different studies; most used self-reported diabetes

	Author, Journal, Year	Type	Number and types of studies / participants included	Inclusion / exclusion criteria	Age	Sex	Race/ ethnicity	Countries	Adjustment factors	Quality rating & reasons if rating was poor
				Cross-sectional studies and case-control studies Publications from 1979 or earlier Studies presenting only results that were adjusted for change in BMI						
6	Heiat, Arch Int Med, 2001	Systematic Review	13	Inclusion: Studies that included only, or presented separate data analyses for, subjects 65 yrs or older Studies that performed age adjustment Studies that included at least 100 subjects Studies with at least 3 yrs of follow-up Studies with all-cause and/or CV mortality and/or CHD events as end points Studies that restricted, stratified, or adjusted for smoking and health at baseline Studies that selected nonhospitalized subjects at the time of enrollment Exclusion: Studies that used weight and did not	65+	M, F	NR	United States, Finland, Italy, Netherlands	Results presented as "adjusted for potential weight-related CVD factors" controlled for at least one of the following: serum cholesterol level, serum glucose level, systolic, diastolic, or mean arterial blood pressure, and history of diabetes, dyslipidemia, or high blood pressure.	Poor • Literature search limited in scope • No dual review of abstracts and full-text of articles for I/E • No quality assessment of included studies • No assessment of publication bias

	Author, Journal, Year	Type	Number and types of studies / participants included	Inclusion / exclusion criteria	Age	Sex	Race/ ethnicity	Countries	Adjustment factors	Quality rating & reasons if rating was poor
				adjust for height (BMI) Studies based on specific populations of diseased individuals						
7	Lenz, Dtsch Arztebl Int 2009	Systematic review	27 meta-analyses & 15 cohort studies	Studies excluded: Case control studies Cross-sectional studies MA that include case-control or cohort studies Studies on children, adolescents, or high risk groups Studies investigating surrogate parameters (e.g., blood pressure)	18–75	M, F	White	Germany	Differed by study	Fair
8	McGee, Ann Epidemiol 2005	Pooled	26 RCTs and cohort studies; 388,622 individuals	Studies of the Diverse Population Collaboration	NA	M, F	White, Black, Hispanic (according to countries included)	US, Iceland, Israel, Norway, Puerto Rico, Scotland, Yugoslavia, Denmark	age, smoking	Poor No comprehensive and systematic literature search No dual review of abstracts and full-text articles for I/E criteria No quality assessment of included studies No assessment of publication bias
9	Owen, Int J Obes 2009	Systematic review	15 cohort studies	Exclusion: Studies adjusting for body weight or BMI at another age Not in English Studies with Outcomes including, but not exclusively based on CHD were excluded Not considering CHD	BMI at ages 2–30 yr	M, F	Mainly White (according to countries included)	Denmark, Finland, Norway, Sweden, US, UK, Netherland, Scotland,	MA was based on unadjusted or (where available) age-adjusted and (where appropriate) age-gender adjusted associations	Poor No dual review of abstracts and full-text articles for I/E criteria No quality assessment of included studies No assessment of publication bias

	Author, Journal, Year	Type	Number and types of studies / participants included	Inclusion / exclusion criteria	Age	Sex	Race/ ethnicity	Countries	Adjustment factors	Quality rating & reasons if rating was poor
				as an outcome						
10	Pischon, NEJM, 2008	Pooled study	359,387 participants from 23 centers in 10 European countries	Inclusion: General population residing in a given geographic area in 10 European countries participating in the EPIC study Exclusion: Participants who withdrew from the study and for whom there was no follow-up on vital status Cohort in Umea, Sweden due to incompatible information on leisure time activities Subject for whom data on height or weight was missing, including all participants from the Norwegian cohorts (37,205), 52,872 participants from the French cohorts, and 8,451 from other cohorts Participants with missing questionnaire data (1,441) Participants with extreme values, including 7,659 in the top or bottom 1% of the cohort for ratio of energy intake to estimated energy	25–70	M, F	NR	Denmark, France, Germany, Greece, Italy, the Netherlands, Norway, Spain, Sweden, and the United Kingdom	Age, smoking status, education level, alcohol consumption, physical activity, height Models for WC and waist-to-hip ratio were also adjusted for BMI	Poor No comprehensive and systematic literature search No dual review of abstracts and full-text articles for I/E criteria No quality assessment of included studies No assessment of publication bias

	Author, Journal, Year	Type	Number and types of studies / participants included	Inclusion / exclusion criteria	Age	Sex	Race/ ethnicity	Countries	Adjustment factors	Quality rating & reasons if rating was poor
				requirements Participants who reported a history of cancer, heart disease, or stroke at baseline (25,155)						
11	Vazquez, Epidemiol Rev 2007	Meta-analysis	32	Inclusion: Diabetes as the outcome At least one indicator of abdominal obesity as the exposure or as a confounding factor Follow-up study	20–80	4 studies on men, 3 on women, and 25 on both	Multiple	Europe (9 studies), US (12 studies), Asia (4 studies), and other populations (7 studies)	Somewhat different covariates were adjusted in different original studies Diagnosis of diabetes varied in different studies; most used self-reported diabetes	Poor No comprehensive and systematic literature search No quality assessment of included studies
12	Whitlock, Semin Vasc Med 2002	Review/ meta-analysis	80 studies from 46 cohorts	Exclusion: No English-language abstract Participants were selected on the basis of a positive disease history Studies that did not report RR or data from which these could be calculated	25–89 y	M, F	Mainly White (according to countries included)	US, Britain, Canada, Finland, Sweden, Netherlands, Italy, Greece, Yugoslavia	Differed by study but did not include estimates that were adjusted for intermediate factors	Poor No dual review of abstracts and full-text articles for I/E criteria No quality assessment of included studies No assessment of publication bias
13	Whitlock (Prospective Studies Collaboration) Lancet 2009	Pooled meta-analysis that combines individual data from all 57 studies	57 cohort studies; 894,576 participants	Inclusion: Prospective cohort studies with more than 5,000 person yrs of follow-up in which data on age, sex, blood pressure, and blood cholesterol had all been recorded on enrolment and in subsequent follow-up,	35–89 y (46±11)	61% male; 39% female	White	92% Western Europe Israel, the US, or Australia; 8% Japan	Age at risk (in 5-year groups), sex, baseline smoking, study	Fair

	Author, Journal, Year	Type	Number and types of studies / participants included	Inclusion / exclusion criteria	Age	Sex	Race/ ethnicity	Countries	Adjustment factors	Quality rating & reasons if rating was poor
				the cause and date of death had been routinely sought for all individual participants Excluded: Subjects with missing data on age, sex, or BMI BMI <15 kg/m^2 or ≥50 kg/m^2 Baseline history of heart disease or stroke No follow-up in the age range 35–89 yr						
14	Wormser (Emerging risk factors collaboration), Lancet 2011	Pooled	58 cohort studies; 221,934 participants	Participants were not selected on the basis of having previous vascular disease Concomitant information for weight, height, high cholesterol and WC at baseline Cause-specific mortality or vascular morbidity, or both were recorded by use of well-defined criteria At least 1 yr of follow-up Studies with fewer than 10 cases participants with BMI ≥20	Mean: 58 yr	M, F	White, Non-White (did not state specifics about other ethnicities)	US, Italy, Greece, Australia, UK, Denmark, Spain, Finland, Israel, Sweden, Japan, Netherlands, Germany, Canada, France, Ireland, Turkey, Norway	Age, sex, smoking	Fair

Spreadsheet 2.2.1a. Combined Fatal and Non-Fatal CHD—Results for BMI

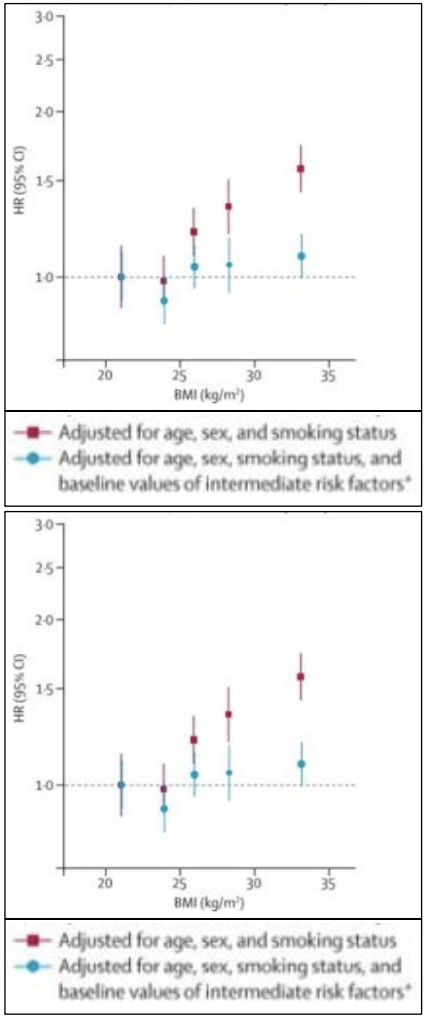
	Author, Journal, Year	Measured (all, ≥85% or <85%)	BMI cutpoints / standardized continuous BMI	Results	Notes
2	Bogers, Arch Intern Med 2007	<85%	5 kg/m^2	Studies with measured BMI: RR=1.27 (1.21–1.33)	
10	Owen, Int J Obes 2009	All	1 SD (2.5 kg/m^2)	RR=1.19 (1.11–1.29)	MA was based on unadjusted or (where available) age-adjusted and (where appropriate) age-gender adjusted associations Here are only the results for 18–30 yr olds presented.
13	Whitlock, Semin Vasc Med 2002	Not specific (at least 3 studies used self-report)	2 kg/m^2	Fatal & non-fatal CHD: RR=1.13 Non-fatal CHD: RR=1.15 Studies with measured BMI: RR=1.12	
15	Wormser (Emerging risk factors collaboration), Lancet 2011	≥85% of participants (192,029 out of 221,934 participants)	<18.5 18.5-24.9 25.0-29.9 + normal WC 25.0-29.9 + high WC 30.0-34.9 + normal WC 30.0-34.9 + high WC 35.0-39.9 ≥40 1SD (4.56 kg/m^2)	HR=1.70 (1.42–2.05) HR=1.00 (0.91–1.10) – reference HR=1.25 (1.18–1.33) HR=1.46 (1.33–.61) HR=1.77 (1.51–2.09) HR=1.82 (1.71–1.95) HR=2.21 (1.93–2.54) HR=2.98 (2.47–3.60) <u>Overall:</u> random effects: HR=1.29 (1.22–1.37) fixed effect: HR=1.25 (1.21–1.28) Female: HR=1.24 (1.14–1.35) Male: HR=1.26 (1.18–1.34) p for interaction: 0.643	

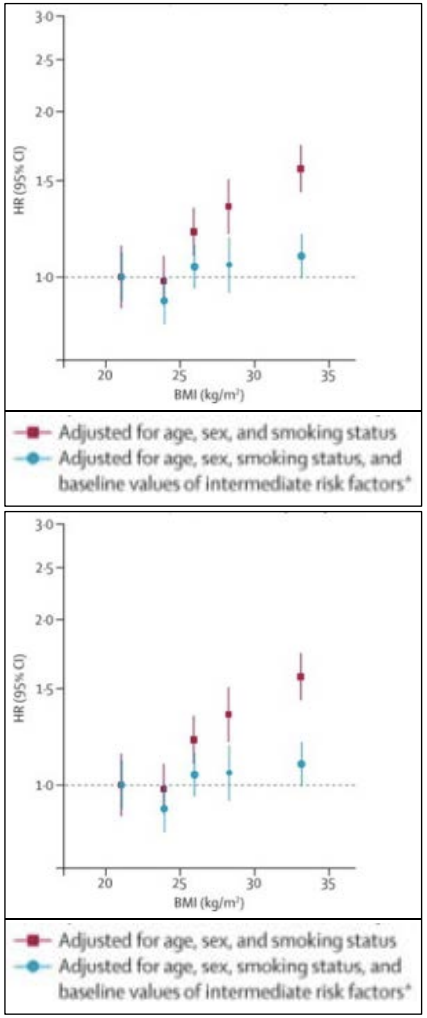
Spreadsheet 2.2.1b. Fatal CHD—Results for BMI

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
9	McGee, Ann Epidemiol 2005	All	18.5–4.9 25.0–29.9 ≥30 18.5–24.9 25.0–29.9 ≥30	Women REF 1.097 (1.001–1.201) 1.624 (1.459–1.806) Men REF 1.159 (1.088–1.235) 1.508 (1.362–1.670)	Used for overall statement since results for men and women are similar.
13	Whitlock, Semin Vasc Med 2002	Not specific (at least 3 studies used self-report)	2 kg/m2	Weighted average RR: Fatal CHD: 1.15	
14	Whitlock (Prospective Studies Collaboration), Lancet 2009	≥85% (54 out of 57 studies)	5 kg/m2	Overall: HR=1.39 (1.34–1.44) Men: HR=1.42 (1.35–1.48) Women: HR=1.35 (1.28–1.43) Heterogeneity: *p*=0.2 Stratified by BMI: 15-25 kg/m2: HR=1.22 (1.13–1.32) 25-50 kg/m2: HR=1.39 (1.34–1.44)	

Spreadsheet 2.2.2a. Combined Fatal and Non-Fatal Stroke—Results for BMI

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Continuous / categorical BMI	Results	Notes
15	Wormser (Emerging Risk Factor Collaboration), Lancet 2011	≥85% of participants (192,029 out of 221,934 participants)	1SD (4.56 kg/m^2)	Overall: RR=1.20 (1.12–1.28)	

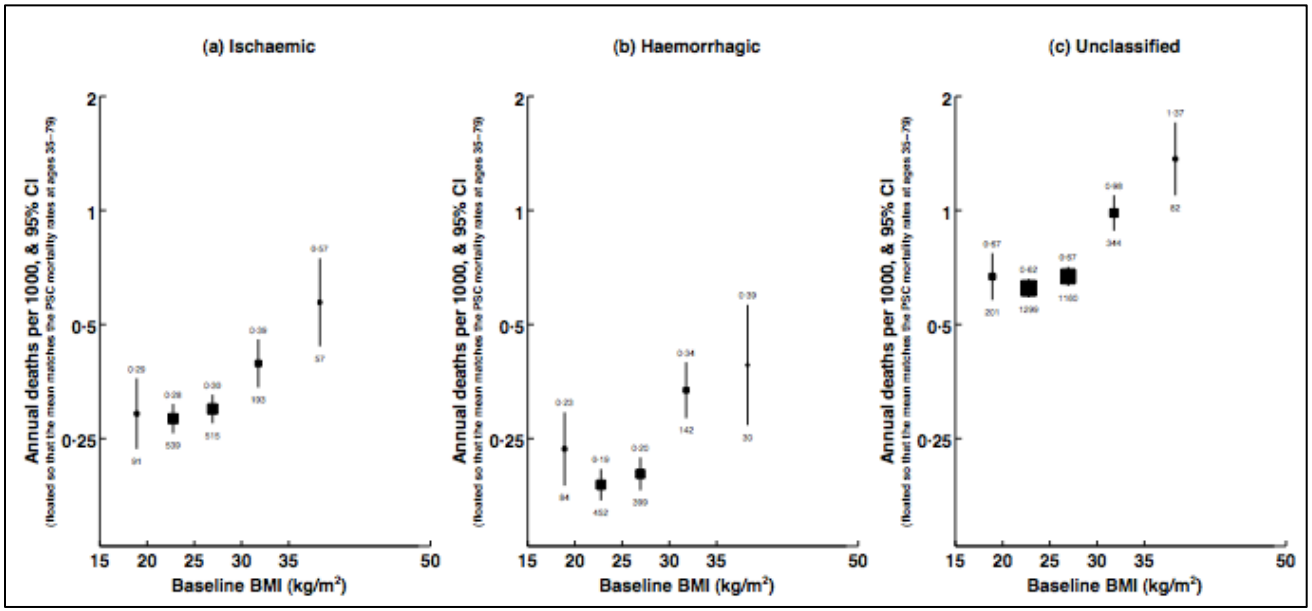
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Continuous / categorical BMI	Results	Notes
					

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Continuous / categorical BMI	Results	Notes
					

Spreadsheet 2.2.2b. Fatal Stroke—Results for BMI

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Continuous / categorical BMI	Results	Notes
14	Whitlock (Prospective Studies Collaborative), 2009	≥85% (54 out of 57 studies)	5 kg/m^2	In BMI 25–50: Overall: RR=1.39 (1.31–1.48) 15–25 kg/m^2: RR=0·92 (0·82–1·03) 25–50 kg/m^2: RR=1.39 (1.10–1.48) Ischaemic: RR=1·38 (1·23–1·56) Haemorrhagic: RR=1·53 (1·32–1·78) Subarachnoid: RR=1·19 (0·94–1·52) Unclassified: RR=1·40 (1·28–1·53) Overall stroke - Never smokers: 15-25 kg/m^2: RR=0·98 (0·78-1·23) 25-50 kg/m^2: RR=1.38 (1.25-1.52)	

Webfigure 4: Stroke subtype mortality vs. BMI in the range 15-50 kg/m^2 (excluding the first 5 years of follow-up)



Spreadsheet 2.2.3a. Combined Fatal and Non-Fatal CVD—Results for BMI

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
15	Wormser (Emerging risk factors collaboration), Lancet 2011	≥85% of participants (192,029 out of 221,934 participants)	1SD (4.56 kg/m^2)	HR=1.23 (1.17–1.29)	

Spreadsheet 2.2.3b. Fatal CVD—Results for BMI

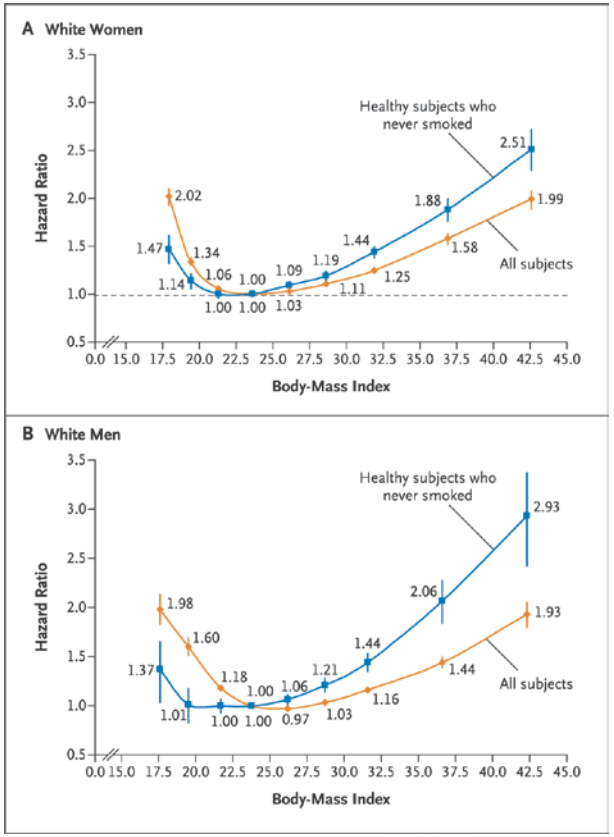
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
1	Abell PH, Reports 2007	All	18.5–24.9 25.0–29.9 ≥30.0 18.5–24.9 25.0–29.9 ≥30.0 18.5–24.9 25.0–29.9 ≥30.0 18.5–24.9 25.0–29.9 ≥30.0	White women, <60 yrs REF RR=1.28 (0.99–1.67) RR=2.49 (1.91–3.22) Black women, <60 yrs REF RR=1.12 (0.79–1.58) RR=1.46 (1.07–2.01) White women, ≥60 yrs REF RR=0.98 (0.85–1.12) RR=1.44 (1.25–1.65) Black women, ≥60 yrs REF RR=0.86 (0.65–1.13) RR=1.18 (0.90–1.55)	
9	McGee, Ann Epidemiol 2005	All	18.5–24.9 25.0–29.9 ≥30 18.5–24.9 25.0–29.9 ≥30	Women REF RR=1.029 (0.948–1.116) RR=1.529 (1.381–1.692) Men REF RR=1.096 (1.034–1.163) RR=1.453 (1.327–1.590)	
8	Lenz, Dtsch Arztebl Int 2009	This one study measured BMI (Bender J ClinEpi 2006)	36–39.9 ≥40.0 36–39.9 ≥40.0	Women SMR=1.51 (1.2–1.9) SMR=2.77 (2.3–3.3) Men SMR=2.24 (1.6–3.1) SMR=4.36 (3.2–5.8)	SMR … standardized mortality ratio The overall German population was used as a reference.

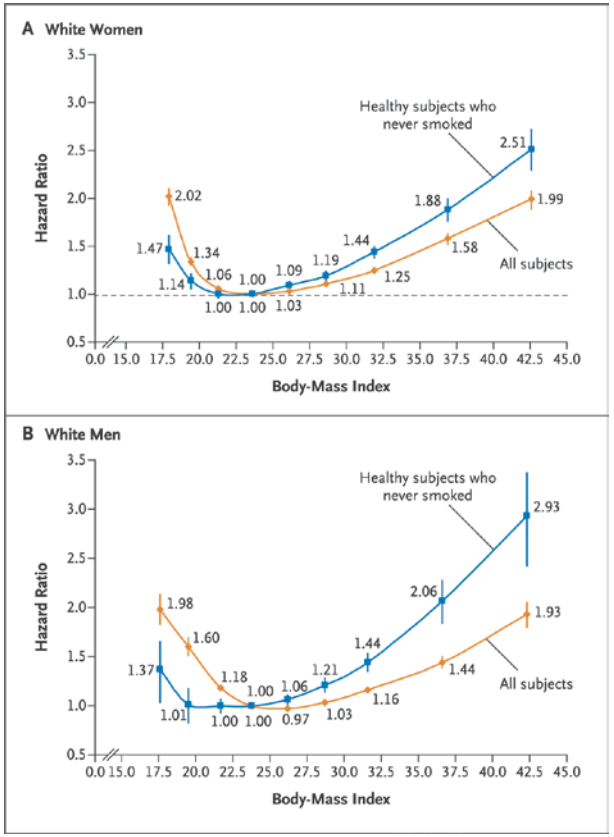
Spreadsheet 2.2.4. Incident Diabetes—Results for BMI

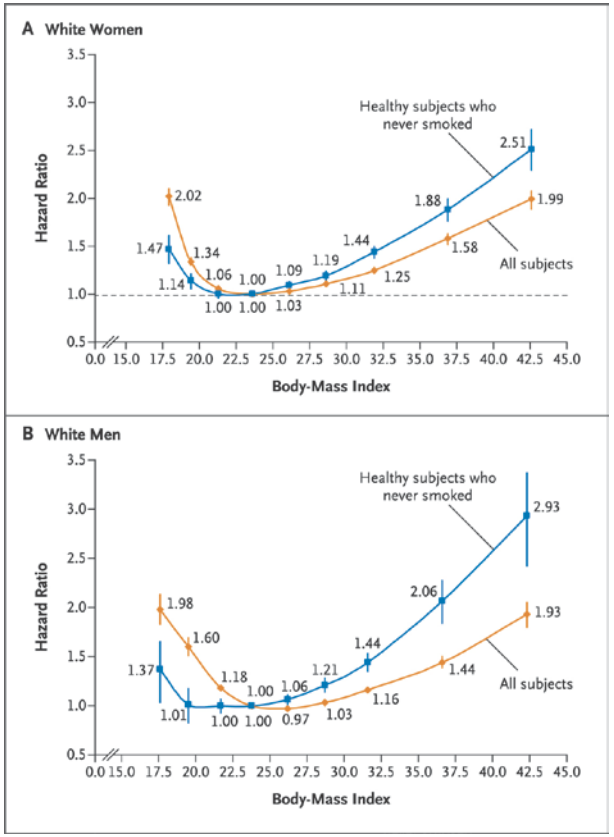
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
6	Hartemink, AJE 2006	NA	1 kg/m^2	RR=1.19 (95% CI 1.17–1.21)	
11	Vazquez, Epidemiol Rev 2007	NA	1 SD (4.3 kg/m^2)	Overall: RR=1.92 (95% CI: 1.70–2.17) Women: RR=2.4 (2.1, 2.7) Men: RR= 2.0 (1.4, 2.8) Mean age of cohort ≥50 yr: RR=2.0 (1.7, 2.3) Mean age of cohort <50 yr: RR=1.7(1.4, 2.0) per SD for BMI Asia: RR=2.4(1.7, 3.3) US: RR=1.7 (1.4, 2.1) Europe: RR=2.0 (1.6, 2.6) BMI<27 kg/m^2: RR: 2.0(1.7, 2.3) BMI>=27 kg/m2: RR:1.6 (1.3, 2.0)	

Spreadsheet 2.2.5. Overall Mortality—Results for BMI

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
3	DeGonzalez NEJM 2010	<85% (only 1 study measured height & weight)	5 kg/m2	HR=1.31 (1.29–1.33) over the range of 25.0 to 49.9 Women: 15-<25 kg/m2: HR=0.85 (0.80–0.89) 25-<50 kg/m2: HR=1.28 (1.26–1.31) Men: 15-<25 kg/m2: HR=0.90 (0.82–1.00) 25-<50 kg/m2: HR=1.36 (1.32–1.40)	Categorical data is not presented here since <85% of studies had measured BMI)

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
					

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
					

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
					

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
8	Lenz, Dtsch Arztebl Int 2009	100% (EPIC study) also included McGee study in their review → see below	23.5–25 25.0 to <26.5 26.5 to <28.0 28.0 to <30.0 30 to <35.0 ≥ 35 23.5 –25 25.0 to <26.5 26.5 to <28.0 28.0 to <30.0 30 to <35.0 ≥35	Women: REF RR = 1.01 (0.92–1.11) RR = 1.07 (0.97–1.18) RR = 1.11 (1.00–1.22) RR = 1.17 (1.07–1.29) RR = 1.65 (1.46–1.85) Men: REF RR = 0.91 (0.84–0.99) RR = 0.96 (0.88–1.04) RR = 1.08 (1.00–1.17) RR = 1.24 (1.14–1.35) RR = 1.94 (1.71–2.20) With increasing age, obesity plays an increasingly smaller role in the all-cause mortality (eSupplement,Table 2) (8, e4). After age 50, there is an increased mortality risk for women with a BMI >36 kg/m2 and for men with a BMI >40 kg/m2 (8). After age 65, obesity is hardly (e4) or not at all associated with a shortened life expectancy (8).	
9	McGee, Ann Epidemiol 2004	All	18.5–24.9 25.0–29.9 ≥30 18.5–24.9 25.0–29.9 ≥30	Women: REF RR = 0.968 (0.925–0.987) RR = 1.275 (1.183–1.373) Men: REF RR = 0.965 (0.922–1.009) RR = 1.201 (1.119–1.289)	
14	Whitlock (Prospective Studies Collaboration), Lancet. 2009	≥85% (54 out of 57 studies)	5 kg/m2	Overall: 15–25 kg/m2: RR=0.79 (0.77–0.82) 25–50 kg/m2: RR=1.29 (1.27–1.32) Men: 15–25 kg/m2: RR=0.79 (0.76–0.82) 25–50 kg/m2: RR=1.32 (1.29–1.36) Women: 15–25 kg/m2: RR=0.80 (0.75–0.85) 25–50 kg/m2: RR=1.26 (1.23–1.30)	

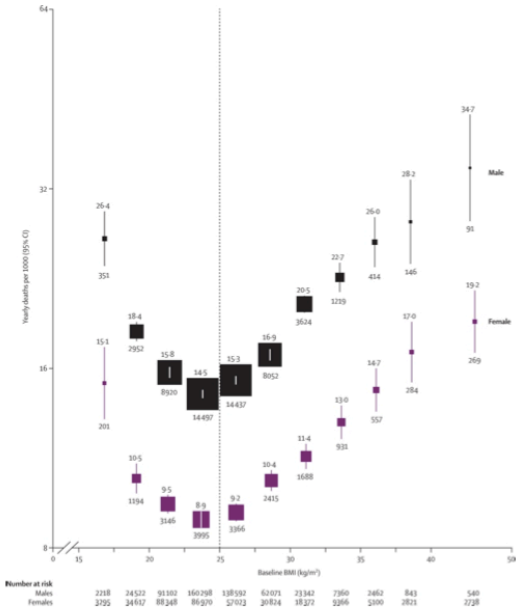
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
					

Figure 2.
All-cause mortality versus BMI for each sex in the range 15–50 kg/m^2 (excluding the first 5 years of follow-up)
Relative risks at ages 35–89 years, adjusted for age at risk, smoking, and study, were multiplied by a common factor (ie, floated) to make the weighted average match the PSC mortality rate at ages 35–79 years. Floated mortality rates shown above each square and numbers of deaths below. Area of square is inversely proportional to the variance of the log risk. Boundaries of BMI groups are indicated by tick marks. 95% CIs for floated rates reflect uncertainty in the log risk for each single rate. Dotted vertical line indicates 25 kg/m^2 (boundary between upper and lower BMI ranges in this report).

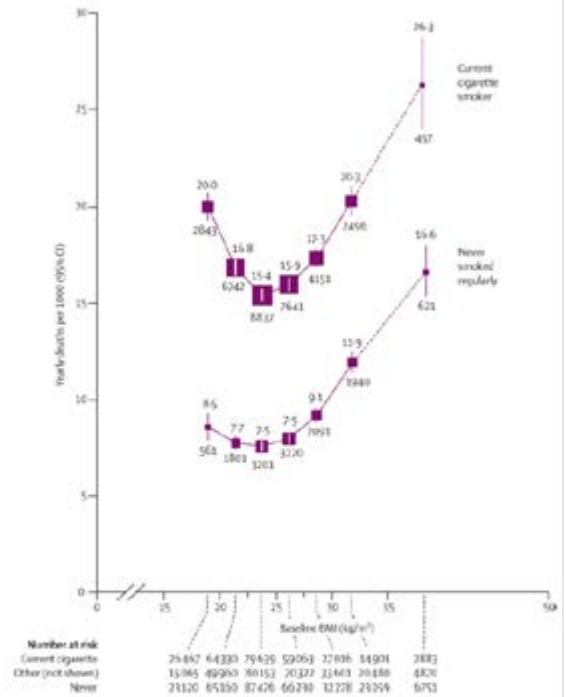
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
					

Figure 6.
All-cause mortality at ages 35–79 years versus BMI in the range 15–50 kg/m², by smoking status (excluding the first 5 years of follow-up)
Relative risks at ages 35–79 years, adjusted for age at risk, sex, and study, were multiplied by a common factor (ie, floated) so that the mean for all participants (including ex-smokers and anyone with missing smoking data) matches the European rate at ages 35–79 years in 2000. Results for ex-smokers and those with missing smoking data not shown (but are, taken together, only slightly above those for never smokers). Note that many smokers were at only limited risk, since they had not smoked many cigarettes during early adult life, or had stopped shortly after the baseline survey. Risk is indicated on an additive rather than multiplicative scale. The

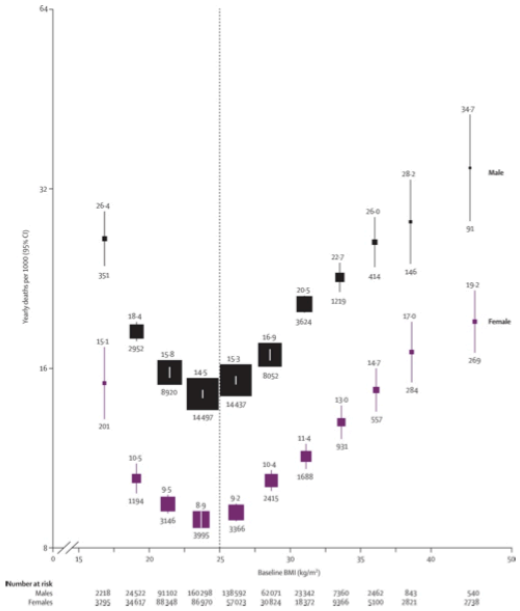
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
					

Figure 2.
All-cause mortality versus BMI for each sex in the range 15–50 kg/m^2 (excluding the first 5 years of follow-up)
Relative risks at ages 35–89 years, adjusted for age at risk, smoking, and study, were multiplied by a common factor (ie, floated) to make the weighted average match the PSC mortality rate at ages 35–79 years. Floated mortality rates shown above each square and numbers of deaths below. Area of square is inversely proportional to the variance of the log risk. Boundaries of BMI groups are indicated by tick marks. 95% CIs for floated rates reflect uncertainty in the log risk for each single rate. Dotted vertical line indicates 25 kg/m^2 (boundary between upper and lower BMI ranges in this report).

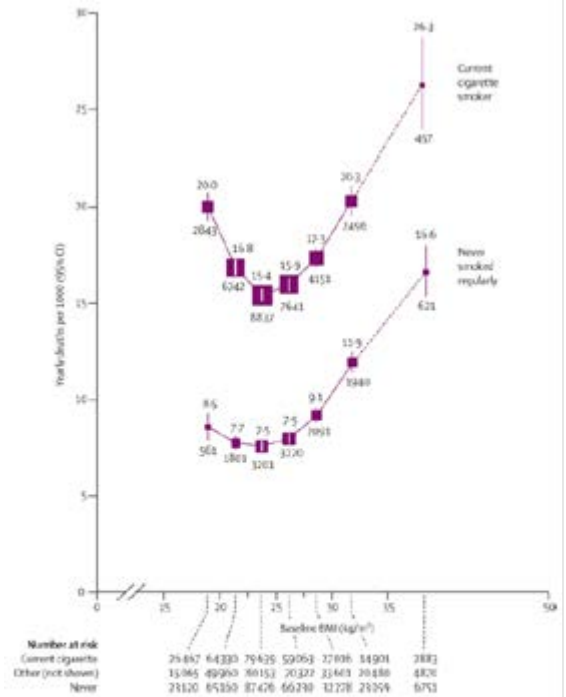
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
					

Figure 6.
All-cause mortality at ages 35–79 years versus BMI in the range 15–50 kg/m², by smoking status (excluding the first 5 years of follow-up)
Relative risks at ages 35–79 years, adjusted for age at risk, sex, and study, were multiplied by a common factor (ie, floated) so that the mean for all participants (including ex-smokers and anyone with missing smoking data) matches the European rate at ages 35–79 years in 2000. Results for ex-smokers and those with missing smoking data not shown (but are, taken together, only slightly above those for never smokers). Note that many smokers were at only limited risk, since they had not smoked many cigarettes during early adult life, or had stopped shortly after the baseline survey. Risk is indicated on an additive rather than multiplicative scale. The

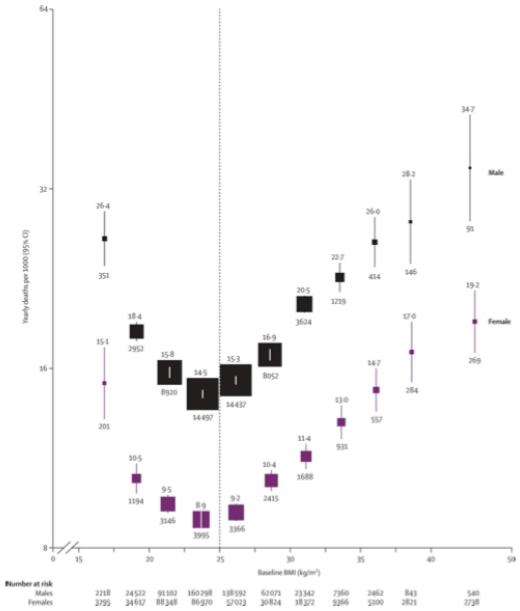
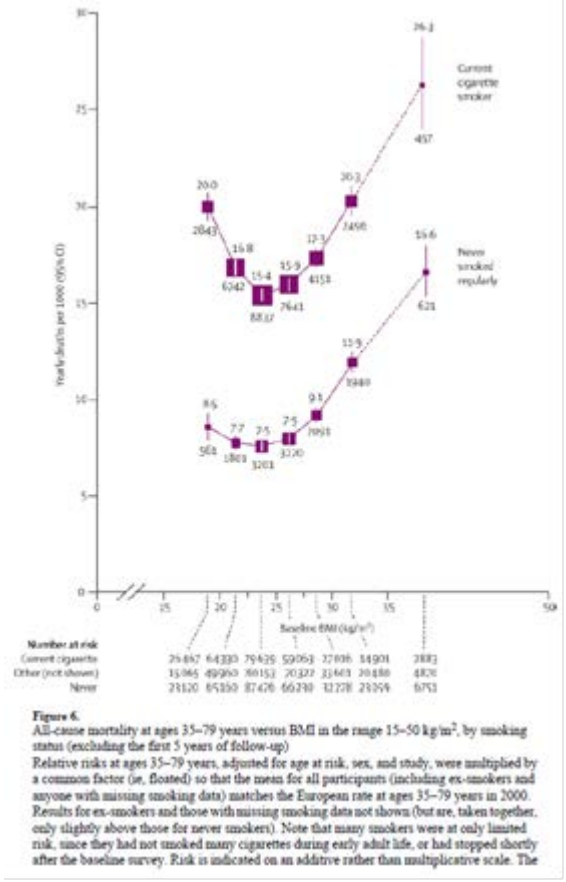
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
					

Figure 2.
All-cause mortality versus BMI for each sex in the range 15–50 kg/m^2 (excluding the first 5 years of follow-up)
Relative risks at ages 35–89 years, adjusted for age at risk, smoking, and study, were multiplied by a common factor (ie, floated) to make the weighted average match the PSC mortality rate at ages 35–79 years. Floated mortality rates shown above each square and numbers of deaths below. Area of square is inversely proportional to the variance of the log risk. Boundaries of BMI groups are indicated by tick marks. 95% CIs for floated rates reflect uncertainty in the log risk for each single rate. Dotted vertical line indicates 25 kg/m^2 (boundary between upper and lower BMI ranges in this report).

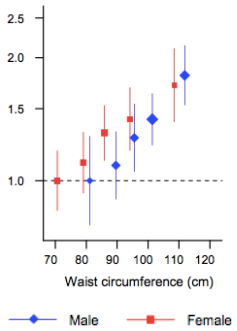
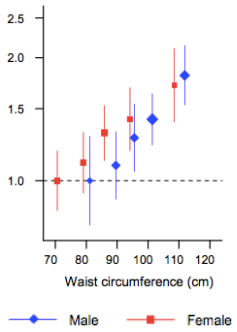
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
				 **Figure 6.** All-cause mortality at ages 35–79 years versus BMI in the range 15–50 kg/m², by smoking status (excluding the first 5 years of follow-up) Relative risks at ages 35–79 years, adjusted for age at risk, sex, and study, were multiplied by a common factor (ie, floated) so that the mean for all participants (including ex-smokers and anyone with missing smoking data) matches the European rate at ages 35–79 years in 2000. Results for ex-smokers and those with missing smoking data not shown (but are, taken together, only slightly above those for never smokers). Note that many smokers were at only limited risk, since they had not smoked many cigarettes during early adult life, or had stopped shortly after the baseline survey. Risk is indicated on an additive rather than multiplicative scale. The	
	Heiat, Arch Int Med, 2001	<85%	Various categories with number of levels ranging from 3 to 7 levels Some studies also tested continuous data	Most studies showed a negative or no association between BMI and all-cause mortality.	

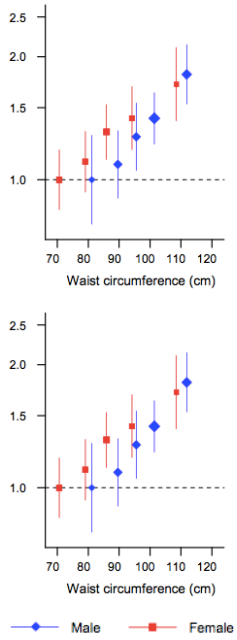
	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous BMI	Results	Notes
	Pischon, NEJM, 2008	≥ 85%	BMI Cutpoints <18.5 18.5 to <21.0 21.0 to <23.5 23.5 to <25.0 25.0 to <26.5 26.5 to <28.0 28.0 to <30.0 30.0 to <35.0 ≥35.0	Men <18.5 Adjusted RR=2.30 (1.84–2.86) 18.5 to <21.0 Adjusted RR=1.39 (1.24–1.57) 21.0 to <23.5 Adjusted RR=1.03 (0.94–1.12) 23.5 to <25.0 Adjusted RR=1.00 25.0 to <26.5 Adjusted RR=0.91 (0.84–0.99) 26.5 to <28.0 Adjusted RR=0.96 (0.88–1.04) 28.0 to <30.0 Adjusted RR=1.08 (1.00–1.17) 30.0 to <35.0 Adjusted RR=1.24 (1.14–1.35) ≥35.0 Adjusted RR = 1.94 (1.71–2.20) Women <18.5 Adjusted RR=1.71 (1.44–2.01) 18.5 to <21.0 Adjusted RR=1.22 (1.10–1.34) 21.0 to <23.5 Adjusted RR=1.00 (0.92–1.09) 23.5 to <25.0 Adjusted RR=1.00 25.0 to <26.5 Adjusted RR=1.01 (0.92–1.11) 26.5 to <28.0 Adjusted RR=1.07 (0.97–1.18) 28.0 to <30.0 Adjusted RR=1.11 (1.00–1.22) 30.0 to <35.0 Adjusted RR=1.17 (1.07–1.29) ≥35.0 Adjusted RR=1.65 (1.46–1.85)	

Spreadsheet 2.3.1. Combined Fatal and Non-Fatal CHD—Results for Waist Circumference

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous WC	Results	Notes
15	Wormser (Emerging risk factors collaboration), Lancet 2011	≥85% of participants (192,029 out of 221,934 participants)	1SD (12.6 cm)	Overall (random effects): HR=1.32 (1.24–1.40) 40–59 yr: HR=1.50 (1.37–1.63) 60–69 yr: HR=1.28 (1.20–1.37) ≥70 yr: HR=1.13 (1.06–1.21) p for interaction: <0.0001 Female: HR=1.31 (1.21–1.43) Male: HR=1.24 (1.17–1.32) p for interaction: 0.056 Non-white: HR=1.33 (1.17–1.51) White: HR=1.35 (1.27-–44) *p*=0.746	

Spreadsheet 2.3.2. Combined Fatal and Non-Fatal Stroke—Results for Waist Circumference

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous WC	Results	Notes
15	Wormser (Emerging Risk Factor Collaboration), Lancet 2011	≥85% of participants (192,029 out of 221,934 participants)	1SD (12.6 cm)	Overall: HR=1.25 (1.18–1.33) Women: HR=1.27 (1.12–1.43) Men: HR=1.32 (1.22–1.42) Interaction: *p*=0.429  	

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous WC	Results	Notes
				 40–59 yr: HR=1.45 (1.30–1.60) 60–69 y: HR=1.29 (1.20–1.40) ≥70 y: HR=1.10 (1.03–1.18) Interaction: p=0.001	

Spreadsheet 2.3.3. Combined Fatal and Non-Fatal CVD—Results for Waist Circumference

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous WC	Results	Notes
4	De Koning, Eur Heart J 2007	<85%	1 cm 1SD higher baseline WC (12.6 cm)	Overall: RR=1.03 (1.01–1.05) Men: RR=1.02 (0.99–1.04) Women: RR=1.05 (1.00–1.09) HR= 1.27 (1.20–1.33)	

Spreadsheet 2.3.4. Overall Mortality—Results for Waist Circumference

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous WC		Results	Notes
8	Lenz, Dtsch Arztebl Int 2009 [reference categories are lower than current cutpoints]	100% (one study; these results are from the EPIC study)	Cutpoints WC 70.1 to <75.6 WC 75.6 to <81.0 WC 81.0 to <89.0 WC≥89.0 WC 86.0 to <91.5 WC 91.5 to <96.5 WC 96.5 to <102.7 WC≥102.7	Reference WC <70.1 WC <70.1 WC <70.1 WC<70.1 WC<86.0 WC<86.0 WC<86.0 WC<86.0	Women: RR = 1.16 (1.05–1.28) RR = 1.21 (1.09–1.35) RR = 1.46 (1.30–1.64) RR = 1.78 (1.56–2.04) Men: RR=1.15 (1.05–1.26) RR=1.35 (1.22–1.50) RR=1.63 (1.46–1.83) RR=2.05 (1.80–2.33)	
	Pischon, NEJM, 2008	≥ 85%	WC Cutpoints Men <86 86 to <91.5 91.5 to <96.5 96.5 to <102.7 ≥102.7 Women <70.1 70.1 to <75.6 75.6 to <81.0 81.0 to <89.0 ≥89.0		Men <86 Adjusted RR with BMI=1.00 86 to <91.5 Adjusted RR With BMI=1.15 (1.05–1.26) 91.5 to <96.5 Adjusted RR with BMI=1.35 (1.22–1.50) 96.5 to <102.7 Adjusted RR with BMI=1.63 (1.46–1.83) ≥102.7 Adjusted RR with BMI=2.05 (1.80–2.33) Women <70.1 Adjusted RR with BMI=1.00 70.1 to <75.6 Adjusted RR With BMI=1.16 (1.05–1.28) 75.6 to <81.0 Adjusted RR With BMI=1.21 (1.09–1.35) 81.0 to <89.0 Adjusted RR With BMI=1.46 (1.30–1.64) ≥89.0 Adjusted RR With BMI=1.78 (1.56–2.04)	

Spreadsheet 2.3.5. Incident Diabetes—Results for Waist Circumference

	Author, Journal, Year	Measured (all, ≥85% or <85%)	Cutpoints / continuous WC	Results	Notes
11	Vazquez, Epidemiol Rev 2007	NA	1 SD (11.6 cm)	Overall: RR=1.87 (1.58, 2.20) Women: RR=2.3 (2.0, 2.6) Men: RR=2.9 (1.8, 4.9) <50 yr: RR=1.6 (1.4,1.9) >50 yr: RR=2.0 (1.6, 2.7) Asia: RR=2.4 (1.5, 4.0) US: RR=1.9 (1.4, 2.5) Europe: RR=2.1 (1.7, 2.6)	

Critical Question 3

Summary Table 3.1. Overall Dietary Intervention and Composition

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
CALERIE (Pittas et al.,2006; Das et al., 2007) RCT US, University Fair	G1: Baseline – 7 wks: usual diet; Treatment (wks 1–24): High-glycemic load diet (70% energy provided; 30% calorie restriction, 20% fat, 60% CHO, 20% protein) Wks 24–48: Individualized high- glycemic load diet (subjects prepared their own food; 30% calorie restriction, 20% fat, 60% CHO, 20% protein) G2: Baseline – 7 wks: Usual diet; Treatment (wks 1–24): Low glycemic load diet (70% energy provided; 30% calorie restriction, 30% fat, 40% CHO, 30% protein) Wks 24–48: Individualized low-glycemic load diet (subjects prepared their food; 30% calorie restriction, 30% fat, 40% CHO, 30% protein) G1 & G2: After wks 15–20, subjects were allowed 1,000 kcal/wk of discretionary foods not on the menu, and this amount was subtracted from the provided foods All food was provided No physical activity prescription	Adults 24–42 yrs of age, BMI 25–29.9, blood glucose <100 mg/dL (5.6 mmol/L) Weight, kg: G1: 79.3 G2: 78.8 Completers only BMI: G1: 27.6 G2: 27.6 Completers only *n*'s G1: 17 G2: 17	**6 mos** Weight loss (kg) G1: -7.2 G2: -7.7 *p*=0.69 Completers analysis **12 mos** Cannot use data: completers analysis only with attrition >10%	**Withdrawals, *n* (%):** **6 mos** G1: 1 (5.9) G2: 1 (5.9) **12 mos** G1: 2 (11.8) G2: 3 (17.6) Overall: 5 (14.7) **Dietary Compliance** Mean reported energy intake at 6 mos (kcal/day): G1: 2017 G2: 1972 *p*=0.70
Due et al., 2004 Due 2005; Skov 2002; Skov 1999; Skov 1999b) RCT Denmark, school / university Fair	G1: Medium protein—high-CHO, fat-reduced diet (12% protein, 58% CHO, 30% fat) G2: High protein—high-protein fat reduced diet (25% protein, 45% CHO, 30% fat) G3: Control—No change in dietary patterns (included for first 6 mos) G1 and G2: During first 6 mos:	Adults 18—56 yrs of age, BMI 25—34 Weight, kg: G1: 88.6 G2: 87.0 G3: 88.1 *n*'s G1: 25 G2: 25	**6 mos** **Weight change, kg (95% CI):** G1: -5.9 (-4.2 to -7.7) G2: -9.4 (-7.2 to -11.6) *p*=0.008 **BMI change, kg/m2 (95% CI):** G1: -2.1 (-1.5 to -2.7) G2: -3.3 (-2.5 to -4.0) *p* =0.007 **WC change, cm (95% CI):**	Withdrawals, *n* (%) **6 mos** G1: 2 (8.0) G2: 2 (8.0) G3: 1 (6.7) **12 mos** G1: 7 (28) G2: 2 (8) G3: NR

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
	Biweekly counseling sessions with a dietitian All food collected from a shop built at Department of Human Nutrition All food was provided Mos 6–12: Group-specific behavior therapy every 2nd week No physical activity prescription; subjects were instructed not to change physical activity pattern Duration: 12 mos Treatment: 6-–2 mos	G3: 15	G1: -4.2 (1.5 to -6.9) G2: -10.1 (-8.0 to -12.3) *p*=0.004 **12 mos** Cannot use data due to high differential attrition (20%)	**Dietary Compliance*** 0-6 mos Energy, MJ/day: G1: 10.8 (10.1–11.5) G2: 9.0 (8.2 –9.7) *p*=0.001 Protein, E%: G1: 12.0 (11.9–12.2) G2: 24.3 (24.0 –24.5) *p*<0.0001 CHO, E%: G1: 58.6 (58.3–58.9) G2: 46.3 (45.9–46.7) *p*<0.0001 Fat, E%: G1: 29.4 (29.1–29.7) G2: 29.5 (29.2–29.8) *Registered by shop computer system, calculated as mean daily values 24-Urea nitrogen excretion significantly greater in G2 throughout the study; *p*<0.001
Ebbeling et al., 2007 RCT US, Outpatient medical setting – hospital Fair	G1: Low-fat (55% CHO, 20% fat, 25% protein) G2: Low-glycemic load (40% CHO, 35% fat, 25% protein) G1 & G2: 6 workshops during the first 2 mos, then held monthly Private session during the initial month then five monthly individual telephone calls) Diets prescribed using ad libitum approach Duration: 18 mos Treatment: 6 mos Follow-up: 12 mos	Adults 18–35 yrs of age, BMI>30, 79.5% female, Weight, kg (SD): G1: 103.3 (15.1) G2: 103.5 (17.3) SBP, mmHg (SD): G1: 105.0 (12) G2: 108.0 (11) DBP, mmHg (SD): G1: 63.0 (8) G2: 62.0 (9) Fasting blood glucose, mg/dL (SD): G1: 86.0 (8)	Weight change **18 mos** No significant difference between groups in weight loss Data NR *p*=0.99 Weight change data (6, 12, and 18 mos) reported in graph only but differences not significant	Withdrawals, *n* (%): **6 mos** G1: 3 (8.1) G2: 4 (11.1) **18 mos** G1: 14 (37.8) G2: 8 (22.2) Dietary Compliance: Both diets resulted in reduction of approximately 400–500 kcal/day (data reported in graph only)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
	No *prescribed* calorie reduction	G2: 88.0 (10) HDL-C level, mg/dL (SD): G1: 57.0 (20) G2: 54.0 (13) LDL-C level, mg/dL (SD): G1: 102.0 (calculated) (35) G2: 126.0 (calculated) (34) TG level mg/dL (SD): G1: 112.0 (96) G2: 126.0 (34) *n*'s G1: 37 G2: 36		
Esposito et al., 2009 RCT Italy, university Good	G1: Mediterranean-style diet (1,500 women -1800 men kcal/d), <50% complex CHO, ≥30% fat (30–50g olive oil) G2: Low-fat diet based on AHA guidelines (1,500 women – 1,800 men kcal/d), ≤30% fat, ≤10% SF G1 & G2: -Physical Activity: participants advised to increase physical activity -Monthly visits with registered dietician during the 1st year and bimonthly thereafter Duration: 4 yrs Run-in: 2 wks Treatment: 4 yrs	Adults 30 to 75 yrs of age, BMI > 25, newly diagnosed type 2 diabetes, HbA1c <11%, sedentary (physical activity <1 hour/week), relatively gender-balanced BMI, kg/m^2 (SD): G1: 29.7 (3.4) G2: 29.5 (3.6) Weight, kg (SD): G1: 86.0 (10.4) G2: 85.7 (9.9) WC, cm (SD): G1: 98 (10.1) G2: 98 (10.0) SBP, mm Hg (SD): G1: 139 (12) G2: 140 (12) DBP, mm Hg (SD): G1: 87 (8) G2: 86 (8) n's G1: 108 G2: 107	**Changes at 1 yr** Weight, kg (SD): G1: -6.2 (3.2) G2: -4.2 (3.5) Difference (95% CI): -2.0 (-3.0 to -0.9) *p*=NR BMI, kg/m^2 (SD): G1: -2.4 (1.6) G2: -1.4 (0.9) Difference (95% CI): -1.0 (-2.2 to -0.3) *p*=NR WC, cm (SD): G1: -4.8 (3.0) G2: -3.5 (2.8) Difference (95% CI): -1.3 (-1.7 to -0.5) *p*=NR **4 yrs** Weight, kg (SD): G1: -3.8 (2.0) G2: -3.2 (1.9) Difference (95% CI): -0.6 (-1.6 to 1.2) *p*=NR BMI, kg/m^2 (SD): G1: -1.2 (0.7) G2: -0.9 (0.6) Difference (95% CI): -0.3 (-0.9 to 0.4)	Withdrawals *n*, (%) G1: 10 (9.3) G2: 10 (9.3) **Dietary Compliance** **Change in Nutrient Indexes** **Changes at 1 yr** Kcal/d (SD): G1: -570 (121) G2: - 525 (111) Difference (95% CI): -45 (-120 to 30) CHO, % (SD): G1: - 9.4 (3.1) G2: 1.5 (1.8) Difference (95: CI): -9.9 (-14 to -5.0) Protein, % (SD): G1: 1.6 (1.5) G2: 1.9 (1.7) Difference (95: CI): -0.3 (-0.9 to 0.6) Saturated fat, % (SD): G1: -0.5 (0.5) G2: -0.8 (0.7) Difference (95% CI):

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
			p=NR WC, cm (SD): G1: -3.0 (1.7) G2: -2.6 (2.0) Difference (95% CI): -0.4 (-0.9 to 0.5) *p* =NR [CI'S WERE USED TO DETERMINE SIGNIFICANCE]	0.3 (-0.5 to 1.1) Monounsaturated fat, % (SD): G1: 5.9 (3.7) G2: -1.4 (1.5) Difference (95% CI): 7.3 (5.0 to 12.0) Polyunsaturated fat, % (SD): G1: 2.4 (1.7) G2: -1.4 (1.2) Difference (95% CI): 3.8 (1.5–5.5) **4 yrs** Kcal/d G1: -450 (100) G2: -409 (92) Difference (95% CI) -41 (-109 to 35) CHO, % (SD): G1: -7.9 (4.1) G2: 0.1 (0.3) Difference (95: CI): -8.0 (-13.1 to -3.8) Protein, % (SD): G1: 1.3 (1.4) G2: 1.5 (1.6) Difference (95: CI): -0.2 (-0.8 to 0.4) Saturated fat, % (SD): G1: -0.2 (0.3) G2: -0.4 (0.5) Difference (95% CI): 0.2 (-0.5 to 0.6) Monounsaturated fat, % (SD): G1: 5.5 (3.3) G2: -1.0 (0.9) Difference (95% CI): 6.5 (3.5–10.7) Polyunsaturated fat, % (SD): G1: 2.6 (1.9)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
				G2: -1.1 (1.0) Difference (95% CI): 3.7 (1.4–6.0)
Foster et al., 2010 RCT US, 3 academic university medical centers Good	G1: Low-carbohydrate diet: limited carbohydrate intake (20 g/day for 3 mos) in the form of low–glycemic index vegetables with unrestricted consumption of fat and protein. After 3 mos, participants in the low-CHO diet group increased their CHO intake (5 g/day per wk) until a stable and desired weight was achieved G2: Low-fat diet: limited energy intake (1200–1500 for women and 1500–1800 kcal/d for men; 55% of calories from carbohydrates, ≤30% calories from fat; 15% from protein) G1 & G2: All participants received comprehensive, in-person group behavioral treatment weekly Topics included self-monitoring, stimulus control, and relapse management All participants were prescribed the same level of physical activity (principally walking), beginning at wk 4, with 4 sessions of 20 mins each and progressing by wk 19 to 4 sessions of 50 mins each Group sessions reviewed participants' completion of their eating and activity records, as well as other skill builders Participants in both groups were instructed to take a daily multivitamin supplement 75–90 min behavioral sessions weekly for 20 wks, every other week for 20 wks, and then every other month for the remainder of the 2-yr study period Duration: 2 yrs	Adults 18 to 65 yrs of age, 68% female, BMI 30 to 40 kg/m^2 Weight, kg (SD): G1: 103.3 (15.5) G2: 103.5 (14.4) BMI, kg/m^2 (SD): G1: 36.1 (3.59) G2: 36.1 (3.46) SBP, mmHg (SD): G1: 124.3 (14.1) G2: 124.6 (15.8) DBP, mmHg (SD): G1: 73.9 (9.4) G2: 76.0 (9.7) HDL-C, mg/dL (SD): G1: 46.2 (13.5) G2: 45.4 (11.7) LDL-C, mg/dL (SD): G1: 120.2 (25.7) G2: 124.0 (29.2) Triglyceride, mg/dL (SD): G1: 113.3 (54.6) G2: 124.0 (73.5) n's G1: 153 G2: 154	**6 mos** Weight change, kg (95% CI) G1: -12.18 (-13.1 to -11.2) G2: -11.34 (-12.4 to -10.3) *p*=0.25 **12 mos** Weight change, kg (95% CI) G1: -10.87 (-12.1 to -9.67) G2: -10.81 (-12.4 to -9.28) *p*=0.95	**Withdrawals, *n* (%):** 6 mos G1: 25 (16.3) G2: 19 (12.3) 12 mos G1: 40 (26.1) G2: 39 (25.3) 24 mos G1: 64 (41.8) G2: 49 (31.8) **Dietary Compliance** NR
McAuley et al., 2005 RCT New Zealand, school /	G1: High-fat (Atkins Diet)—no specific macronutrient targets except for CHOs; wks 1–2 participants were instructed to	Adult women 30–70 yrs of age, BMI >27 kg/m^2, insulin resistant Weight, kg (SD):	**Measurements at wk 16** **Weight, kg (SD)** G1: 89.1 (10.7) from 96.0	Withdrawals, *n* (%): **24 wks*** G1: 4 (12.9)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
university Fair	limit certain foods to consume less than 20 g CHO/day (wks 3–8 CHO was reintroduced by the addition of 5 g/day each week (a maximum of 50 g of CHO per day was consumed by wk 8); wks 8-–6 -increasing CHO intake from the specific food lists by 5 g/day each week was continued until each participant found the maximum level of CHO consumption without weight gain G2: High-protein (Zone Diet)—total energy provided by each meal and snack: 40% from low glycemic index CHO, 30% from protein and 30% from fat; participants advised to eat five times daily with no more than 5 hrs between meals; wks 8–16: subjects instructed to consume slightly larger portions in the evening to maintain body weight; wks 16-24: participants encouraged to continue consuming appropriate foods in quantities that facilitated weight maintenance G3: High CHO, high fiber (control group)—based on EASD guidelines focused on consumption of specific food groups in specified daily amounts (≥6 servings of breads and cereals, ≥3 servings of vegetables and two of fruit, ≥2 servings low-fat milk, ≥1 serving lean meat, dried beans or lentils. Advice to reduce dietary fat, salt, and sugar intakes; wks 8-16: slightly larger portions for their evening meal to maintain body weight; wks 16–24: similar advice All groups: Weekly reviews for wks 1–8 and wks 8–16; no contact wks 16–24) None of the diets was formally energy restricted during any phase Advised to participate in 30 min of any physical activity 5 days/wk Duration: 24 wks	G1: 96.0 (10.8) G2: 93.2 (14.5) G3: 98.0 (15.1) BMI, kg/m^2 (SD): G1: 36.0 (3.9) G2: 34.5 (5.3) G3: 36.6 (5.6) WC, cm (SD): G1: 108.9 (9.9) G2: 108.0 (11.5) G3: 109.1 (11.6) SBP, mmHG G1: 130 (14) G2: 124 (13) G3: 126 (11) DBP, mmHG G1: 83 (10) G2: 80 (9) G3: 81 (10) Total cholesterol, mmol/l G1: 5.8 (1.0) G2: 5.7 (1.0) G3: 5.9 (0.9) LDL-C, mmol/l G1: 3.8 (0.9) G2: 3.7 (0.8) G3: 3.9 (0.8) HDL-C, mmol/l G1: 1.17 (0.28) G2: 1.21 (0.23) G3: 1.16 (0.21) Triglyceride, mmol/l G1: 1.78 (0.76) G2: 1.86 (0.66) G3: 1.77 (0.57) n's G1: 31 G2: 30 G3: 32	G2: 86.2 (14.6) from 93.2 G3: 93.6 (14.6) from 98.0 BMI, kg/m^2 (SD) G1: 33.5 (3.8) from 36.0 G2: 32.0 (5.0) from 34.5 G3: 35.0 (5.5) from 36.6 **WC, cm (SD):** G1: 99.8 (10.0) from 108.9 G2: 100.3 (9.9) from 108.0 G3: 103.2 (10.9) from 109.1 **Measurements at week 24** **Weight, kg (SD)** G1: 88.9 (10.6) from 96.0 G2: 86.3 (14.2) from 93.2 G3: 93.3 (14.5) from 98.0 BMI, kg/m^2 (SD) G1: 33.1 (3.7) from 36.0 G2: 31.5 (5.1) from 34.5 G3: 34.9 (5.6) from 36.6 **WC, cm** G1: 99.1 (9.2) from 108.9 G2: 99.2 (10.9) from 108.0 G3: 102.2 (11.8) from 109.1	G2: 3 (10.0) G3: 2 (6.3) *3 post-randomization withdrawals, not specified by treatment group; group withdrawal rates here do not account for those exclusions **Dietary Compliance** **16 wks** Mean (SD) Energy, kJ/D (SD) G1: 6787 (2328) G2: 6397 (1474) G3: 6147 (1264) Total fat, % total energy (SD) G1: 46 (10) G2: 34 (7) G3: 28 (8) CHO, g (SD) G1: 482 (220) G2: 219 (94) G3: 221 (110) CHO, % TE (SD) G1: 26 (11) G2: 35 (8) G3: 45 (8) Total proteins, % (SD) G1: 24 (5) G2: 26 (6) G3: 22 (5) Fiber, g/4184 kJ (SD) G1: 9 (3) G2: 14 (4) G3: 13 (5) **24 wks:** Energy, kJ/D (SD) G1: 6797 (1818) G2: 6156 (1391) G3: 6114 (1232) Total fat, % (SD)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
	Wks 1–8: weight loss phase Wks 8–16: weight maintenance with supervision continued as in weight loss phase Wks 16–24: follow-up with no supervision			G1: 47 (8) G2: 35 (7) G3: 28 (7) CHO, g (SD) G1: 478 (251) G2: 243 (139) G3: 196 (75) CHO, % TE (SD) G1: 26 (11) G2: 35 (10) G3: 45 (7) Total proteins, % (SD) G1: 24 (6) G2: 26 (5) G3: 21 (3) Fiber, g/4184 kJ (SD) G1: 9 (3) G2: 13 (4) G3: 13 (3)
Poppitt et al., 2002 RCT UK Outpatient medical setting – clinic Fair	G1: Low-fat, high-complex CHO (reduced fat intake by 10% of total energy, ratio of simple to complex CHO to 1:2); participnts were provided with ≥60% of their total energy intake from the study grocery store G2: Low-fat, high simple CHO (reduced fat intake by 10% of total energy, ratio of simple to complex CHO 2:1); participants were provided with ≥60% of their total energy intake from the study grocery store G3: Control diet (maintaining fat intake at habitual amounts 35–40% of energy) All groups: Subjects came to the study grocery store on 1 or 2 occasions per week to collect foods and discuss their energy and macronutrient intakes with dietitian Ad libitum diet Run-in: 4 wks Treatment: 24 wks	Adults >38 yrs, BMI 27–40, at least 3 risk factors for metabolic syndrome Weight, kg (SD): G1: 91.2 (9.5) G2: 89.3 (15.7) BMI, kg/m2 (SD): G1: 32.3 (3.6) G2: 30.9 (3.0) *n*'s for baseline characteristics: G1: 14 G2: 14 n's: G1: 16 G2: 15	6 mos Weight change, kg: G1: -4.25 G2: -0.28 *p*<0.001 Completers analysis Results for control arm (G3) not considered here due to high differential attrition between it and G1 and G2.	Withdrawals, n (%): G1: 2 (12.5) G2: 1 (6.7) G3: 4 (26.7) **Mean reported dietary intake during treatment phase** Energy kJ/d (SD): G1: 8108 (2689) G2: 9578 (2600) Fat % of energy (SD): G1: 24.1 (5.36) G2: 21.1 (3.11) Complex CHO % of energy (SD): G1: 35.5 (3.89) G2: 28.5 (5.10) Simple CHO % of energy (SD): G1: 17.6 (8.05) G2: 28.9 (8.48)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
POUNDS LOST (Sacks 2009) RCT US, university Good	G1: Low-fat, average-protein (20% fat, 15% protein, and 65% CHO) G2: Low-fat, high-protein (20% fat, 25% protein, 55% CHO) G3: High-fat, average protein (40% fat, 15% protein, 45% CHO) G4: High-fat, high-protein (40% fat, 25% protein, 35% CHO) All groups: 750 kcal/day deficit calculated from resting energy expenditure and exercise level Group sessions led by registered dieticians were held once a week, 3 of every 4 wks during the first 6 mos and 2 of every 4 wks from 6 mos to 2 yrs; individual sessions were held every 8 wks for the entire 2 yrs Foods were similar across diets, but quantities differed to meet macronutrient goals Web-based self-monitoring tool reinforced adherence to target macronutrient levels Physical activity goals were established for sedentary participants, gradually increasing from 30 mins of moderate intensity exercise per week to 90 mins/wk during the first 6 mos, the same for each diet group. Duration Treatment: 2 yrs	Overweight or obese adults 30–70 yrs of age, BMI 25–40, 64% female, hypertension 35% Weight, kg (SD): G1: 94.0 (16) G2: 92.0 (13) G3: 92.0 (17) G4: 94.0 (16) *n*'s G1: 204 G2: 202 G3: 204 G4: 201	6 mos Participants in all groups had lost an average of kg (7% of their initial weight) 12 mos All groups began to regain weight after 12 mos 24 mos Mean weight loss, kg G1 + G3: -3.0 G2 + G4: -3.6 *p*=0.22 G1 + G2: -3.3 G3 + G4: -3.3 *p*=0.94 Mean difference in weight, kg G1 + G3 vs. G2 + G4: -0.6 (95% CI -1.6 to 0.4), *p*=0.22 G1 + G2 vs. G3 + G4: 0.04 (95% CI, -0.9 to 1.0), *p*=.94 G1 vs. G4: 0.6 (95% CI, -0.8 to 1.9), *p*=0.42 Mean difference in WC, cm: G1 + G3 vs. G2 + G4: -0.7 (95% CI -1.7 to 0.4), *p*=0.22 G1 + G2 vs. G3 + G4: 0.0 (95% CI -1.0 to 1.0), *p*=0.99 G1 vs. G4: 0.7 (95% CI -0.8 to 2.1), *p*=0.39	Withdrawals, *n* (%): **24 mos** G1: 35 (17.2) G2: 45 (22.3) G3: 53 (26.0) G4: 33 (16.4) Dietary Compliance **6 mos** Energy, kcal/d G1: 1636 G2: 1572 G3: 1607 G4: 1624 CHO, % G1: 57.5 G2: 53.4 G3: 49.1 G4: 43.0 Protein, %: G1: 17.6 G2: 21.8 G3: 18.4 G4: 22.6 Fat, %: G1: 6.2 G2: 25.9 G3: 33.9 G4: 34.3 Saturated fat, %: G1: 7.5 G2: 7.9 G3: 9.0 G4: 9.0 **24 mos** kcal/d G1: 1531 G2: 1560 G3: 1521 G4: 1413

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
				CHO, %: G1: 53.2 G2: 51.3 G3: 48.6 G4: 42.9 Protein, %: G1: 19.6 G2: 20.8 G3: 19.6 G4: 21.2 Fat, %: G1: 26.5 G2: 28.4 G3: 33.3 G4: 35.1 Saturated fat, %: G1: 8.0 G2: 8.9 G3: 9.8 G4: 10.5 **Biomarkers of adherence** **6 mos** Urinary nitrogen, g: G1: 11.1 G2: 11.9 G3: 10.3 G4: 12.6 **24 mos** Urinary nitrogen, g: G1: 11.8 G2: 11.8 G3: 11.2 G4: 12.5
PREFER Burke et al., 2006, Burke et al., 2007 US, Outpatient medical setting – hospital Fair	G1: Low-fat, lacto-ovo-vegetarian (LOV) diet (1200–1500 kcal/day women, 1500–1800 kcal/day men, 25% fat); group was instructed to eliminate meat, fish, and poultry over the first 6 wks of the study, beginning with breakfast, then lunch, then dinner	Adults 18–55 yrs of age, BMI 27–43, 87% female Weight, kg (SD): G1: 94.40 (14.23) G2: 95.25 (14.94)	6 mos Weight change, kg (SD): G1: -7.50 (6.00) G2: -6.97 (6.53) *p*=0.321 BMI change, kg/m^2 (SD): G1: -3.21 (2.06)	Withdrawals: 200 randomized; "to obtain a fair balance in size across the four groups, only 50% of those who chose the SBT were randomly selected for inclusion.

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
	G2: Standard calorie- and fat-restricted omnivorous diet (<90.5 kg 1200 kcal/day women, 1500 kcal/day men; >90.5 kg 1500 kcal/day women, 1800 kcal/day men, 25% fat); diet permitted meat, fish, and poultry G1 and G2: Were instructed to restrict consumption of calories (1200–1500 for women and 1500–1800 for men) and fat (25% of calories) Ad libitum Received 32 treatment sessions on standard cognitive-behavioral therapy (SBT) for weight management over a period of 12 mos; the main component of this approach included self-monitoring eating and exercise behaviors, goal setting, cognitive restructuring, stimulus control, demonstrations, and skill development Physical activity consisted of a recommendation to increase participants' activity to 150 min/day by 6th week and, thereafter, to increase or at least maintain that goal Duration: 18 mos Treatment: 12 mos Maintenance: 6 mos	*n*'s G1: 84 G2: 98	G2: -2.83 (2.07) *p*=0.125 WC change, kg/m^2 (SD): G1 women: -6.12 (7.34) G2 women: -5.50 (6.31) *p*=0.799 G1 men: -9.37 (5.90) G2 men: -11.78 (10.61) *p*=0.695 18 mos No differences between G1 and G2 in weight loss *p*=0.41 [weight outcome data were reported stratified by diet preference status of the subjects but the 'diet effect' was formally tested for the dietary pattern groups overall]	Fewer subjects preferred the SBT+LOV diet; therefore, 15 additional subjects who preferred the SBT diet were excluded to prevent the treatment preference–Yes SBT group from being significantly larger than the treatment preference–Yes SBT+LOV group." So of 185, withdrawals, *n* (%): G1: 12 (14.3) G2: 13 (13.3) And 3 post-randomization exclusions where treatment arm was not specified Overall: 28 (15.1) ITT analysis; BOCF Nutritional Measurements at 6 mos Kcal G1: 1487.78 G2: 1533.87 Total fat, %: G1: 25.76 G2: 27.08 Total CHO, %: G1: 61.37 G2: 55.74 Total proteins, %: G1: 15.07 G2: 17.86 PS ratio: G1: 0.95 G2: 0.80 Nutritional Measurements, mean change from baseline to 6 mos Kcal: G1: -535.98 G2: -519.80 *p*=0.836

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
				Total fat, %: G1: -9.59 G2: -8.51 *p*=0.436 Total CHO, %: G1: +11.06 G2: +7.12 *p*=0.013 Total proteins, %: G1: -0.08 G2: +2.14 p< 0.001 PS ratio: G1: 0.26 G2: 0.10 *p*=0.009
SMART study (Frisch et al., 2009) RCT Germany, Fair	G1: High-CHO group (DGE): >55% CHO, <30% fat, 15% protein, energy deficit 500 kcal/d G2. Low-CHO group (LOGI): 40% CHO, 35% fat, 25% protein, energy deficit 500 kcal/d Both groups: Weekly nutrition education and dietary counseling by phone with a nutritionist during the first six mos No PA prescription Duration: 12 mos Treatment: mos 1–6 Follow-up (no contact): mos 7–12	Overweight or obese adults 18–70 yrs of age, BMI>27, BMI, kg/m2 (SD): G1: 33.8 (4.8) G2: 33.5 (3.9) *n*'s: G1: 100 G2: 100 Sex (men), *n*: G1: 24 G2: 38 *p*=0.032	**6 mos** Weight loss, kg (SD): G1: -6.2 (4.8) G2: -7.2 (5.4) *p*=NR BMI change, kg/m (SD): G1: -2.1 (1.6) G2: -2.3 (1.8) *p*=0.250 WC circumference change, cm (SD): G1: -6.6 (5.3) G2: -8.0 (5.5) *p*=0.083 **12 mos** Weight loss, kg (SD): G1: -4.3 (5.1) G2: -5.8 (6.1) *p*=0.065 BMI change, kg/m (SD): G1: -1.5 (1.8) G2: -1.9 (2.1) *p*=0.110	Withdrawals, *n* (%): G1: 20 (20) G2: 15 (15) Overall: 35 (17.5) Dietary Compliance At mos 1, 3, 6, and 12, energy and nutrient intake (diet compliance) were assessed using a 3-day validated food record; amount of daily physical activity was assessed using a standardized, validated questionnaire. Calories, mean kcal/d (SD): 6 mos G1: 1783 (597) G2: 1742 (624) *p*=0.636 12 mos G1: 1854 (624) G2: 1866 (710) *p*=0.903 Carbohydrates, % energy (SD): 6 mos

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
			WC change, cm (SD): G1: -4.7 (8.9) G2: -6.9 (6.1) *p*=0.037	G1: 49.5 (7.6) G2: 40.9 (10.1) *p*< 0.001 12 mos G1: 50.1 (8.2) G2: 43.5 (9.9) *p*<0.001 Fat, % energy (SD): 6 mos G1: 29.7 (6.5) G2: 36.5 (9.5) *p*<0.001 12 mos G1: 30.2 (7.0) G2: 34.2 (8.7) *p* = 0.001 Protein, % energy (SD): 6 mos G1: 17.7 (4.0) G2: 19.3 (4.7) *p*=0.012 12 mos G1: 16.7 (3.1) G2: 18.9 (4.4) *p*<0.001
Thompson et al., 2005 RCT US, setting unclear Fair	G1. Lower fat, high dairy diet group (energy deficit 500 kcal, 30% fat, 20% protein, and 50% CHO, 4 servings of dairy/day) G2. Lower fat, high-dairy and high-fiber group (energy deficit of 500 kcal, 30% fat, 20% protein, and 50% CHO, 4 servings of dairy/day, increase of fiber, and reduction in glycemic index) G3: Standard lower fat diet group (energy deficit 500 kcal, 30% fat, 20% protein, and 50% CHO) All groups: Weekly visits during run-in and treatment	Adults 25–70 yrs of age, BMI 30–40, 86% female, stable weight during previous 6 mos Weight, kg (SD): G1: 98.7 (11.0) G2: 99.1 (17.0) G3: 98.1 (13.3) BMI, kg/m^2 (SD): G1: 35.0 (3.2) G2: 34.5 (3.0) G3: 35.0 (3.1) *n*'s G1: 30 G2: 31	Weight change, 48 wks Weight, kg (SD): G1: -8.8 (7.5) G2: -8.8 (7.9) G3: -9.1 (7.0) *p*=0.88 Other weight change outcomes: WC, hip circumference: cannot use the actual completer data, but can make a claim about the trend, and authors report there was no significant difference between ITT and completers	Withdrawals, *n* (%): G1: 8 (26.7) G2: 7 (22.6) G3: 3 (10.3) Overall: 18 (20) Participants who complied with diet and exercise over 75% of follow-up wks, *n* (%): G1: 18 (60.0) G2: 17 (54.9) G3: 18 (62.1) Dietary Compliance: N/A

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
	periods Individualized 1:1 instruction with a dietitian Exercise was standardized at 30 min or more, at least 4 times per week. Diet and activity were monitored Instructed to exercise Exercise was recorded daily but not addressed directly in protocol Minutes of exercise/day were recorded by participants Instructed Duration Run-in: 2 wks Treatment: 48 wks	G3: 29		(Completers only)
Turner-McGrievy et al., 2004; 2007 RCT US, School/ university Fair	G1. Low-fat, vegan diet (10% fat, 15% protein, 75% CHO); grains, vegetables, legumes, and fruits, with no limit on energy intake or portions. Participants were asked to exclude animal products, added oils, high-fat processed foods, avocados, olives, nuts, nut butters, and seeds because these foods are typically calorie dense G2. NCEP Step II (<60 g/day or 30% fat, SF <7%, polyunsaturated fatty acid (PUFA) <10%, and -<15%, cholesterol <200 mg/d); 15% of energy from protein and 55% from carbohydrate Ad libitum Physical activity as tolerated by participant Duration: 2 yrs Initial Treatment: wks 1-–4 Continued treatment with support: wks 14–52 Follow-up with no support: yrs 1–2	Post-menopausal women, BMI 26–44 BMI, kg/m^2 (SD): G1: 33.6 (5.2) G2: 32.6 (3.3) Weight, kg (SD): G1: 89.3 (13.4) G2: 86.1 (12.1) *n*'s: G1: 31 G2: 31 (3 post-randomization exclusions; modified ITT analysis conducted)	Weight, kg (SD) baseline/14 wks: G1: 89.3 (13.4)/ 83.5 (13.5) G2: 86.1 (12.1)/ 82.3 (12.0) *p*=NR Weight Change from baseline, kg **1 yr** G1: -4.9 G2: -1.8 P = 0.021 **2 yrs** G1: -3.1 G2: -0.8 *p* =0.022	**Withdrawals, n (%):** **14 wks:** G1: 3 (9.4) G2: 2 (6.3) 1 yr: G1:5 (16.1) G2:4 (12.9) **2 yrs** G1: 8 (25.8) G2: 6 (19.4) **Dietary Compliance** **14 wks:** MJ/d G1: 5.89 (1.78) G2: 5.96 (1.5) Total fat, %: G1: 11 G2: 20 Total CHO, %: G1: 78 G2: 62

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	Attrition Dietary Compliance
				Total proteins, %: G1: 12 G2: 18 Fiber, g: G1: 22 G2: 14 **1 yr:** NR **2 yrs:** NR

Summary Table 3.2. Low-Fat Approaches

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
Ebbeling et al., 2007 RCT US, Outpatient medical setting – hospital Fair	G1: Low-fat (55% CHO, 20% fat, 25% protein) G2: Low-glycemic load (40% CHO, 35% fat, 25% protein) G1 & G2: 6 workshops during the first 2 mos, then held monthly Private session during the initial month then five monthly individual telephone calls) Diets prescribed using ad libitum approach Duration: 18 mos Treatment: 6 mos Follow-up: 12 mos	Adults 18-35 yrs of age, BMI>30, 79.5% female, Weight, kg (SD): G1: 103.3 (15.1) G2: 103.5 (17.3) SBP, mmHg (SD): G1: 105.0 (12) G2: 108.0 (11) DBP, mmHg (SD): G1: 63.0 (8) G2: 62.0 (9) Fasting blood glucose, mg/dL (SD): G1: 86.0 (8) G2: 88.0 (10) HDL-C level, mg/dL (SD): G1: 57.0 (20) G2: 54.0 (13) LDL-C level, mg/dL (SD):	Weight change **18 mos** No significant difference between groups in weight loss Data NR *p*=0.99 Weight change data (6, 12, and 18 mos) Reported in graph only but differences not significant	**6 mos** **LDL-C (mg/dL) change (SE):** G1: -16.3 (3.3) G2: -5.8 (3.4) *p*=0.03 **HDL-C (mg/dL) change (SE):** G1: -4.4 (1.3) G2: +1.6 (1.4) *p*=0.02 **Triglyceride (mg/dL) change (SE):** G1: -4.0 (5.6) G2: -21.2 (4.7) *p*=0.02 **SBP (mm Hg) change (SE):** G1: -4.8 (2.3) G2: -5.1 (2.3) *p*=0.93 **DBP (mm Hg) change (SE):** G1: -2.0 (1.7) G2: -2.4 (1.7) *p*=0.88	Withdrawals, *n* (%): **6 mos** G1: 3 (8.1) G2: 4 (11.1) **18 mos** G1: 14 (37.8) G2: 8 (22.2) Dietary Compliance: Both diets resulted in reduction of approximately 400–500 kcal/day (data reported in graph only)

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
		G1: 102.0 (calculated) (35) G2: 126.0 (calculated) (34) Triglyceride level mg/dL (SD): G1: 112.0 (96) G2: 126.0 (34) *n*'s G1:37 G2: 36		**Blood glucose (mg/dL) change (SD):** G1: -0.3 (1.3) G2: +1.6 (1.3) *p*=0.31 **Blood insulin (mU/L) change (SE):** G1: -0.9 (0.8) G2: -2.1 (0.8) *p*=0.28 **18 mos** **LDL-C (mg/dL) change (SE):** G1: -10.6 (3.3) G2: -0.3 (3.4) *p*=0.03 **HDL-C (mg/dL) change (SE):** G1: -8.2 (1.5) G2: -3.7 (1.5) *p* =0.03 **Triglyceride (mg/dL) change (SE):** G1: +2.0 (6.0) G2: -9.0 (5.4) *p*=0.18 **SBP (mm Hg) change (SE):** 18 mos G1: +1.1 (2.3) G2: -3.2 (2.3) *p*=0.18 **DBP (mm Hg) change (SE):** G1: +2.9 (1.7) G2: -2.4 (1.7) *p*=0.22 **Blood glucose (mg/dL) change (SD):** G1: +1.4 (1.3) G2: +2.1 (1.3) *p* =0.73 **Blood insulin (mU/L) change (SE):** 18 mos G1: 0.0 (0.8) G2: -0.8 (0.8) *p*=0.49	

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
Foster et al., 2010 RCT US, 3 academic university medical centers Good	G1: Low-carbohydrate diet: limited carbohydrate intake (20 g/day for 3 mos) in the form of low–glycemic index vegetables with unrestricted consumption of fat and protein. After 3 mos, participants in low-carbohydrate diet group increased their carbohydrate intake (5 g/day per wk) until stable and desired weight was achieved G2: Low-fat diet: limited energy intake (1200–1500 for women and 1500–1800 kcal/d for men; 55% of calories from carbohydrates, ≤30% calories from fat; 15% from protein) G1 & G2: All participants received comprehensive, in-person group behavioral treatment weekly Topics included self-monitoring, stimulus control, and relapse management All participants were prescribed the same level of physical activity (principally walking), beginning at wk 4, with 4 sessions of 20 mins each and progressing by wk 19 to 4 sessions of 50 mins each Group sessions reviewed participants' completion of their eating and activity records, as well as other skill builders Participants in both groups were instructed to take a daily multivitamin supplement 75–90 minute behavioral sessions weekly for 20 wks, every other week for 20 wks, and then every other month for the remainder of the 2-yr study period Duration: 2 yrs	Adults 18–65 yrs of age, 68% female, BMI 30–40 kg/m^2 Weight, kg (SD): G1: 103.3 (15.5) G2: 103.5 (14.4) BMI, kg/m^2 (SD): G1: 36.1 (3.59) G2: 36.1 (3.46) SBP, mmHg (SD): G1: 124.3 (14.1) G2: 124.6 (15.8) DBP, mmHg (SD): G1: 73.9 (9.4) G2: 76.0 (9.7) HDL-C, mg/dL (SD): G1: 46.2 (13.5) G2: 45.4 (11.7) LDL-C, mg/dL (SD): G1: 120.2 (25.7) G2: 124.0 (29.2) Triglyceride, mg/dL (SD): **G1: 113**.3 (54.6) G2: 124.0 (73.5) *n*'s G1: 153 G2: 154	**6 mos** Weight change, kg (95% CI) G1: -12.18 (-13.1 to -11.2) G2: -11.34 (-12.4 to -10.3) p=0.25 **12 mos** Weight change, kg (95% CI) G1: -10.87 (-12.1 to -9.67) G2: -10.81 (-12.4 to -9.28) *p*=0.95	**6 mos** **Triglyceride change, mg/dL (95% CI)** G1: -40.06 (-45.7 to -34.4) G2: -24.30 (-31.2 to -17.4) *p*<0.001 **LDL-C change, mg/dL (95% CI)** G1: 0.54 (-3.25 to 4.33) G2: -9.52 (-12.9 to -6.15) *p*<0.001 **HDL-C change, mg/dL (95% CI)** G1: 6.21 (4.74 to 7.67) G2: 0.89 (-0.24 to 2.02) *p*<0.001 **Change in SBP, mmHg (95% CI)** G1: -7.36 (-9.26 to -5.47) G2: -6.97 (-8.89 to -5.05) *p*=0.78 **Change in DBP, mmHg (95% CI)** G1: -5.15 (-6.49 to -3.82) G2: -2.50 (-3.76 to -1.25) *p*=0.005 **12 mos** **Triglyceride change, mg/dL (95% CI)** G1: -31.52 (-39.5 to -23.6) G2: -17.92 (-28.3 to -7.58) *p*=0.039 **LDL-C change, mg/dL (95% CI)** G1: -8.57 (-12.9 to -4.26) G2: -8.66 (-12.7 to -4.56) *p*=0.98 **HDL-C change, mg/dL (95% CI)** G1: 7.96 (6.33 to 9.59) G2: 3.94 (2.52 to 5.36) P<0.001 **SBP change, mmHg (95% CI)** G1: -5.64 (-7.62 to -3.67) G2: -4.06 (-6.07 to -2.05) *p*=0.27	Withdrawals, *n* (%): 6 mos G1: 25 (16.3) G2: 19 (12.3) 12 mos G1: 40 (26.1) G2: 39 (25.3) 24 mos G1: 64 (41.8) G2: 49 (31.8) **Dietary Compliance** NR

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				DBP Change, mmHg (95% CI) G1: -3.25 (-4.74 to -1.76) G2: -2.19 (-3.58 to -0.79) *p*=0.31	
POUNDS LOST (Sacks 2009) RCT US, university Good	G1: Low-fat, average-protein (20% fat, 15% protein, and 65% CHO) G2: Low-fat, high-protein (20% fat, 25% protein, 55% CHO) G3: High-fat, average protein (40% fat, 15% protein, 45% CHO) G4: High-fat, high-protein (40% fat, 25% protein, 35% CHO) All groups: 750 kcal/day deficit calculated from REE and exercise level Group sessions led by registered dieticians were held once a week, 3 of every 4 wks during the first 6 mos and 2 of every 4 wks from 6 mos to 2 yrs; individual sessions were held every 8 wks for the entire 2 yrs Foods were similar across diets, but quantities differed to meet macronutrient goals Web-based self-monitoring tool reinforced adherence to target macronutrient levels Physical activity goals were established for sedentary participants, gradually increasing from 30 mins of moderate intensity exercise per week to 90 mins/ wk during the first six mos, the same for each diet group. Duration Treatment: 2 yrs	Overweight or obese adults 30–70 yrs of age, BMI 25–40, 64% female, hypertension 35% Weight, kg (SD): G1: 94.0 (16) G2: 92.0 (13) G3: 92.0 (17) G4: 94.0 (16) *n*'s G1: 204 G2: 202 G3: 204 G4: 201	**6 mos** Participants in all groups had lost an average of kg (7% of their initial weight) **12 mos** All groups began to regain weight after 12 mos **24 mos** **Mean weight loss, kg** G1 + G3: -3.0 G2 + G4: -3.6 *p*=0.22 G1 + G2: -3.3 G3 + G4: -3.3 *p*=0.94 **Mean difference in weight, kg** G1 + G3 vs. G2 + G4: -0.6 (95% CI -1.6 to 0.4), *p*=0.22 G1 + G2 vs. G3 + G4: 0.04 (95% CI, -0.9 to 1.0), *p*=0.94 G1 vs. G4: 0.6 (95% CI, -0.8 to 1.9), *p*=0.42 **Mean difference in WC, cm:** G1 + G3 vs. G2 + G4: -0.7 (95% CI -1.7 to 0.4), *p*=0.22 G1 + G2 vs. G3 + G4: 0.0 (95% CI -1.0 to 1.0), *p*=0.99 G1 vs. G4: 0.7 (95% CI -0.8 to 2.1), *p* =0.39	**6 mos** Changes from baseline **Total cholesterol, mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): 4.7 (1.8); *p*=0.01 High protein (G2+G4) – avg. protein (G1+G3): 2.3 (1.8); *p*=0.20 Highest CHO – lowest CHO: -7.0 (2.6); *p*=0.007 G1: -5.9 G2: -4.9 G3: -3.7 G4: -2.3 *p*=NR **LDL-C, mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): 4.4 (1.6); *p*=0.005 High protein (G2+G4) – avg. protein (G1+G3): 2.4 (1.6); *p*=0.13 Highest CHO – lowest CHO: -6.8 (2.3); *p*=0.003 G1: -6.6 G2: -4.8 G3: -3.2 G4: -1.1 *p*=NR **HDL-C, mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): 1.1 (0.05); *p*=0.01 High protein (G2+G4) – avg. protein (G1+G3): 1.1 (0.05); *p*=0.02 Highest CHO – lowest CHO: -2.2 (0.6); *p*=0.001 G1: -0.4 G2: +2.7 G3: +2.9	Withdrawals, n (%): **24 mos** G1: 35 (17.2) G2: 45 (22.3) G3: 53 (26.0) G4: 33 (16.4) Dietary Compliance **6 mos** Energy, kcal/day G1: 1636 G2: 1572 G3: 1607 G4: 1624 CHO, % G1: 57.5 G2: 53.4 G3: 49.1 G4: 43.0 Protein, %: G1: 17.6 G2: 21.8 G3: 18.4 G4: 22.6 Fat, %: G1: 6.2 G2: 25.9 G3: 33.9 G4: 34.3 Saturated fat, %: G1: 7.5 G2: 7.9 G3: 9.0 G4: 9.0 **24 mos** kcal/day G1: 1531 G2: 1560

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G4: +4.0 *p*=NR **Triglycerides, mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): -2.8 (4.3); *p*=0.52 High protein (G2+G4) – avg. protein (G1+G3): -5.4 (4.3); *p*=0.21 Highest CHO – lowest CHO: 8.1 (5.0); *p*=0.10 G1: -14.2 G2: -20.4 G3: -18.1 G4: -19.5 **Systolic , mm Hg (SE):** High fat (G3+G4) - low fat (G1+G2): 0.4 (0.7); *p*=0.59 High protein (G2+G4) – avg. protein (G1+G3): -1.0 (0.7); *p*=0.14 Highest CHO – lowest CHO: 0.6 (0.9); *p*=0.51 G1: -1.2 G2: -2.6 G3: -1.5 G4: -1.7 **DBP, mm Hg (SE):** High fat (G3+G4) - low fat (G1+G2): 0.1 (0.5); *p*=0.77 High protein (G2+G4) – avg. protein (G1+G3): -0.5 (0.5); *p*=0.32 Highest CHO – lowest CHO: 0.3 (0.7); *p*=0.62 G1: -1.4 G2: -3.1 G3: -2.3 G4: -1.8 **Blood glucose mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): 1.2 (0.6); *p*=0.04 High protein (G2+G4) – avg. protein (G1+G3): 0.5 (0.6); *p*=0.38	G3: 1521 G4: 1413 CHO, %: G1: 53.2 G2: 51.3 G3: 48.6 G4: 42.9 Protein, %: G1: 19.6 G2: 20.8 G3: 19.6 G4: 21.2 Fat, %: G1: 26.5 G2: 28.4 G3: 33.3 G4: 35.1 Saturated fat, %: G1: 8.0 G2: 8.9 G3: 9.8 G4: 10.5 **Biomarkers of adherence** **6 mos** Urinary nitrogen, g: G1: 11.1 G2: 11.9 G3: 10.3 G4: 12.6 **24 mos** Urinary nitrogen, g:

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				Highest CHO – lowest CHO: -1.7 (0.9); *p*=0.04 G1: -3.0 G2: -2.6 G3: -1.9 G4: -1.2 **Blood insulin, uu/ml (SE):** High fat (G3+G4) - low fat (G1+G2): 0.2 (0.4); *p*=0.68 High protein (G2+G4) – avg. protein (G1+G3): 0.0 (0.4); *p*=0.91 Highest CHO – lowest CHO: -0.2 (0.7); *p*=0.74 G1: -16.2 G2: -19.9 G3: -18.2 G4: -14.4 **24 mos** Changes from baseline **Total cholesterol, mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): 5.6 (1.9); *p*=0.003 High protein (G2+G4) – avg. protein (G1+G3): 0.2 (1.9); *p*=0.92 Highest CHO – lowest CHO: -5.8 (2.6); *p*=0.02 G1: -3.7 G2: -2.9 G3: -0.3 G4: -0.8 **LDL-C, mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): 5.1 (1.6); *p*=0.001 High protein (G2+G4) – avg. protein (G1+G3): 0.5 (1.6); *p*=0.74 Highest CHO – lowest CHO: -5.7 (2.2); *p*=0.01 G1: -5.9 G2: -3.9 G3: -0.2	G1: 11.8 G2: 11.8 G3: 11.2 G4: 12.5

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G4: -1.3 **HDL-C, mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): 0.7 (0.5); *p*=0.12 High protein (G2+G4) – avg. protein (G1+G3): 0.9 (0.5); *p*=0.05 Highest CHO – lowest CHO: -1.7 (0.7); *p*=0.01 G1: +5.6 G2: +6.5 G3: +6.3 G4: +8.8 **Triglycerides, mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): -1.2 (4.0); *p*=0.76 High protein (G2+G4) – avg. protein (G1+G3): -6.7 (4.0); *p*=0.10 Highest CHO – lowest CHO: 7.96 (6.0); *p*=0.19 G1: -11.5 G2: -16.6 G3: -12.4 G4: -16.7 **SBP, mm Hg (SE):** High fat (G3+G4) - low fat (G1+G2): 0.3 (0.7); *p*=0.64 High protein (G2+G4) – avg. protein (G1+G3): -0.2 (0.7); *p*=0.77 Highest CHO – lowest CHO: -0.1 (0.9); *p*=0.89 G1: -0.8 G2: -1.7 G3: -1.3 G4: -0.7 **DBP, mm HG (SE):** High fat (G3+G4) - low fat (G1+G2): 0.1 (0.5); *p*=0.85 High protein (G2+G4) – avg. protein (G1+G3): 0.2 (0.05); *p*=0.59 Highest CHO – lowest CHO: -0.3 (0.7); *p*=0.61	

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G1: -0.8 G2: -1.3 G3: -1.5 G4: -0.3 **Blood glucose mg/dL (SE):** High fat (G3+G4) - low fat (G1+G2): 1.1 (0.5); *p*=0.05 High protein (G2+G4) – avg. protein (G1+G3): 0.5 (0.6); *p*=0.34 Highest CHO – lowest CHO: -1.6 (0.8); *p*=0.06 G1: +1.1 G2: +1.0 G3: +1.6 G4: +2.8 **Blood insulin, uu/ml (SE):** High fat (G3+G4) - low fat (G1+G2): -0.1 (0.4); *p*=0.77 High protein (G2+G4) – avg. protein (G1+G3): -0.7 (0.4); *p*=0.07 Highest CHO – lowest CHO: 0.8 (0.6); *p*=0.19 G1: -2.4 G2: -11.5 G3: -6.4 G4: -9.2	

Summary Table 3.3. Higher (25–30% of Energy) Protein Approaches

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
CALERIE (Pittas et al., 2006; Das et al., 2007) RCT US, University Fair	G1: Baseline – 7 wks: usual diet; Treatment (wks 1–24): High glycemic load diet (70% energy provided; 30% calorie restriction, 20% fat, 60% CHO, 20% protein) Wks 24–48: Individualized high glycemic load diet (subjects prepared	Adults 24–42 yrs of age, BMI 25–29.9, blood glucose <100 mg/dL (5.6 mmol/L) Weight, kg: G1: 79.3	**6 mos** Weight loss (kg) G1: -7.2 G2: -7.7 p=0.69 Completers analysis	**6 mos** CRP (mg/L) change (SEM): G1: -0.41 (0.91) G2: -1.44 (0.44) *p*=0.13 Completers analysis	Withdrawals, *n* (%): 6 mos G1: 1 (5.9) G2: 1 (5.9) 12 mos G1: 2 (11.8)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	their own food; 30% calorie restriction, 20% fat, 60% CHO, 20% protein) G2: Baseline – 7 wks: Usual diet; Treatment (wks 1–24): Low glycemic load diet (70% energy provided; 30% calorie restriction, 30% fat, 40% CHO, 30% protein) Wks 24-48: Individualized low-glycemic load diet (subjects prepared their food; 30% calorie restriction, 30% fat, 40% CHO, 30% protein) G1 & G2: After wks 15–20, subjects were allowed 1000 kcal/wk of discretionary foods not on the menu, and this amount was subtracted from the provided foods All food was provided No PA prescription	G2: 78.8 Completers only BMI: G1: 27.6 G2: 27.6 Completers only *n*'s G1: 17 G2: 17	12 mos Cannot use data: completers analysis only with attrition >10%	Fasting insulin, HOMA, AUC for OGTTor FSIGTT: No differences between groups.	G2: 3 (17.6) Overall: 5 (14.7) Dietary compliance Mean reported energy intake at 6 mos (kcal/day): G1: 2017 G2: 1972 *p*=0.70
Due et al., 2004 Due 2005; Skov 2002; Skov 1999; Skov 1999b) RCT Denmark, school / university Fair	G1: Medium Protein -High-CHO fat reduced diet (12% protein, 58% CHO, 30% fat) G2: High Protein -High-protein fat reduced diet (25% protein, 45% CHO, 30% fat) G3: Control-No change in dietary patterns (included for first 6 mos) G1 and G2: During first 6 mos: Biweekly counseling sessions with a dietitian All food collected from a shop built at Department of Human Nutrition All food was provided Mos 6–12: Group-specific behavior therapy every 2nd week	Adults 18–56 yrs of age, BMI 25–34 Weight, kg: G1: 88.6 G2: 87.0 G3: 88.1 n's G1: 25 G2: 25 G3: 15	6 mos Weight change, kg (95% CI): G1: -5.9 (-4.2 to -7.7) G2: -9.4 (-7.2 to -11.6) *p*=0.008 BMI change, kg/m2 (95% CI): G1: -2.1 (-1.5 to -2.7) G2: -3.3 (-2.5 to -4.0) *p*=0.007 WC change, cm (95% CI): G1: -4.2 (1.5 to -6.9) G2: -10.1 (-8.0 to -12.3) *p*=0.004 12 mos Cannot use data due to high differential attrition (20%)	6 mos Blood glucose, mmol/L (95% CI): – Baseline; 6 mos G1: 4.9 (4.6–5.4); 4.9 (4.7–5.3) G2: 4.9 (4.6–5.2); 4.9 (4.6–5.1) Blood insulin, pmol/L (95% CI): Baseline; 6 mos G1: 50.0 (28.0–61.0); 43.0 (37.0–54.0) G2: 42.0 (32.0–78.0); 34.0 (25.0–62.0) Total cholesterol, mmol/L (95% CI) Baseline; 6 mos G1: 5.13 (4.6–5.5); 5.16 (4.3–5.6) G2: 4.86 (4.2–5.3); 4.55 (4.1–4.7) HDL-C, mmol/L (95% CI)	Withdrawals, *n* (%) 6 mos G1: 2 (8.0) G2: 2 (8.0) G3: 1 (6.7) 12 mos G1: 7 (28) G2: 2 (8) G3: NR Dietary compliance* 0–6 mos Energy, MJ/day: G1: 10.8 (10.1–11.5) G2: 9.0 (8.2–9.7) *p*=0.001 Protein, E%: G1: 12.0 (11.9–12.2)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	No PA prescription; subjects were instructed not to change PA pattern Duration: 12 mos Treatment: 6–12 mos			Baseline; 6 mos G1: 1.37 (1.1–1.5); 1.16 (1.0–1.4) G2: 1.35 (1.1–1.6); 1.32 (1.1–1.4) Triglycerides, mmol/L (95% CI): Baseline; 6 mos G1: 1.30 (1.0–1.7); 1.41 (1.0–2.1) G2: 1.34 (1.1–1.7); 1.19 (0.7–1.5) –CRP, mg/L (95% CI): Baseline; 6 mos G1: 2.9 (1.9–3.9); 2.1 (1.5–2.8) G2: 2.4 (1.5–3.3); 1.9 (1.2–2.7) 12 mos Cannot use data due to high differential attrition (20%)	G2: 24.3 (24.0–24.5) *p*<0.0001 CHO, E%: G1: 58.6 (58.3–58.9) G2: 46.3 (45.9 –46.7) *p*<0.0001 Fat, E%: G1: 29.4 (29.1–29.7) G2: 29.5 (29.2–29.8) *Registered by shop computer system, calculated as mean daily values 24-UN excretion significantly greater in G2 throughout the study; *p*< 0.001
McAuley et al., 2005 RCT New Zealand, school/university Fair	G1: High-fat (Atkins Diet)—no specific macronutrient targets except for CHOs; wks 1–2 -participants were instructed to limit certain foods to consume <20 g CHO/day (wks 3–8 - CHO was reintroduced by the addition of 5 g/day each week (a maximum of 50 g of CHO per day was consumed by wk 8); wks 8–16 -increasing CHO intake from the specific food lists by 5 g/day each week was continued until each participant found the maximum level of CHO consumption without weight gain G2: High-protein (Zone Diet)—total energy provided by each meal and snack: 40% from low-glycemic index CHO, 30% from protein, and 30% from fat; participants advised to eat five times daily with no more than 5 hrs between meals; wks 8–16 –	Adult women 30–70 yrs of age, BMI >27 kg/m^2, insulin resistant Weight, kg (SD): G1: 96.0 (10.8) G2: 93.2 (14.5) G3: 98.0 (15.1) BMI, kg/m^2 (SD): G1: 36.0 (3.9) G2: 34.5 (5.3) G3: 36.6 (5.6) WC, cm (SD): G1: 108.9 (9.9) G2: 108.0 (11.5) G3: 109.1 (11.6) SBP, mmHG G1: 130 (14) G2: 124 (13)	Measurements at wk 16 Weight, kg (SD) G1: 89.1 (10.7) from 96.0 G2: 86.2 (14.6) from 93.2 G3: 93.6 (14.6) from 98.0 BMI, kg/m^2 (SD) G1: 33.5 (3.8) from 36.0 G2: 32.0 (5.0) from 34.5 G3: 35.0 (5.5) from 36.6 WC, cm (SD): G1: 99.8 (10.0) from 108.9 G2: 100.3 (9.9) from 108.0 G3: 103.2 (10.9) from 109.1 Measurements at week 24 Weight, kg (SD) G1: 88.9 (10.6) from 96.0	Measurements at wk 16 SBP, mmHG (SD) G1: 123.0 (13) from 130 G2: 122 (10) from 124 G3:123 (11) from 126 DBP, mmHG (SD) G1: 79 (9) from 83 G2: 79 (7) from 80 G3: 81 (10) from 81 Total cholesterol, mmol/l G1: 5.4 (1.0) from 5.8 G2: 5.2 (0.8) from 5.7 G3: 5.4 (0.9) from 5.9 LDL-C, mmol/l G1: 3.6 (0.8) from 3.8 G2: 3.4 (0.8) from 3.7 G3: 3.7 (0.9) from 3.9 HDL-C, mmol/l G1: 1.25 (0.34) from 1.17	Withdrawals, *n* (%): 24 wks* G1: 4 (12.9) G2: 3 (10.0) G3: 2 (6.3) *3 post-randomization withdrawals, not specified by treatment group; group withdrawal rates here do not account for those exclusions Dietary Compliance 16 wks Mean (SD) Energy, kJ/day (SD) G1: 6787 (2328) G2: 6397 (1474) G3: 6147 (1264) Total fat, %TE (SD) G1: 46 (10) G2: 34 (7)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	subjects instructed to consume slightly larger portions in the evening to maintain body weight; wks 16–24 – participants encouraged to continue consuming appropriate foods in quantities that facilitated weight maintenance G3: HC-High CHO, high fiber (control group)—based on ESAD guidelines focused on consumption of specific food groups in specified daily amounts (≥6 servings of breads and cereals, ≥3 servings of vegetables and two of fruit, ≥2 servings low-fat milk, ≥1 serving lean meat, dried beans or lentils. Advice to reduce dietary fat, salt, and sugar intakes; wks 8–16 - slightly larger portions for their evening meal to maintain body weight; wks 16–24 - similar advice All groups: Weekly reviews for wks 1–8 and wks 8–16; no contact wks 16–24) None of the diets was formally energy restricted during any phase Advised to participate in 30 min of any physical activity 5 days/wk Duration: 24 wks Wks 1–8: weight loss phase Wks 8-–6: weight maintenance with supervision continued as in weight loss phase Wks 16–24: follow-up with no supervision	G3: 126 (11) -DBP, mmHG G1: 83 (10) G2: 80 (9) G3:81 (10) Total cholesterol, mmol/l G1: 5.8 (1.0) G2: 5.7 (1.0) G3: 5.9 (0.9) LDL-C, mmol/l G1: 3.8 (0.9) G2: 3.7 (0.8) G3: 3.9 (0.8) HDL-C, mmol/l G1: 1.17 (0.28) G2: 1.21 (0.23) G3: 1.16 (0.21) TG, mmol/l G1: 1.78 (0.76) G2: 1.86 (0.66) G3: 1.77 (0.57) *n*'s G1: 31 G2: 30 G3: 32	G2: 86.3 (14.2) from 93.2 G3: 93.3 (14.5) from 98.0 BMI, kg/m^2 (SD) G1: 33.1 (3.7) from 36.0 G2: 31.5 (5.1) from 34.5 G3: 34.9 (5.6) from 36.6 WC, cm G1: 99.1 (9.2) from 108.9 G2: 99.2 (10.9) from 108.0 G3: 102.2 (11.8) from 109.1	G2: 1.19 (0.32) from 1.21 G3: 1.13 (0.28) from 1.16 Triglyceride, mmol/l G1: 1.22 (0.67) from 1.78 G2: 1.23 (0.47) from 1.86 G3: 1.37 (0.54) from 1.77 Fasting glucose, mmol/l G1: 4.8 (0.40) from5.1 G2: 5.0 (0.5) from 5.1 G3: 4.8 (0.5) from 5.0 24 wks SBP, mmHG (SD) G1: 126 (14) from 130 G2: 121 (10) from 124 G3: 124 (11) from 126 DBP, mmHG (SD) G1: 81 (8) from 83 G2: 79 (7) from 80 G3: 82 (10) from 81 Total cholesterol, mmol/l G1: 5.5 (1.1) from 5.8 G2: 5.2 (0.9) from 5.7 G3: 5.3 (1.0) from 5.9 LDL-C, mmol/l G1: 3.7 (1.0) from 3.8 G2: 3.4 (0.8) from 3.7 G3: 3.5 (0.9) from 3.9 HDL-C, mmol/l G1: 1.26 (0.33) from 1.17 G2: 1.22 (0.26) from 1.21 G3: 1.12 (0.28) from 1.16 TG, mmol/l G1: 1.07 (0.41) from 1.78 G2: 1.28 (0.45) from 1.86 G3: 1.45 (0.70) from 1.77 Fasting glucose, mmol/l G1: 4.8 (0.6) from 5.1 G2: 4.9 (0.4) from 5.1 G3: 4.7 (0.4) from 5.0	G3: 28 (8) CHO, g (SD) G1: 482 (220) G2: 219 (94) G3: 221 (110) CHO, % TE (SD) G1: 26 (11) G2: 35 (8) G3: 45 (8) Total proteins, % (SD) G1: 24 (5) G2: 26 (6) G3: 22 (5) Fiber, g/4184 kJ (SD) G1: 9 (3) G2: 14 (4) G3: 13 (5) 24 wks: Energy, kJ/D (SD) G1: 6797 (1818) G2: 6156 (1391) G3: 6114 (1232) Total fat, % (SD) G1: 47 (8) G2: 35 (7) G3: 28 (7) CHO, g (SD) G1: 478 (251) G2: 243 (139) G3: 196 (75) CHO, % TE (SD) G1: 26 (11) G2: 35 (10) G3: 45 (7) Total proteins, % (SD) G1: 24 (6) G2: 26 (5) G3: 21 (3)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
					Fiber, g/4184 kJ (SD) G1: 9 (3) G2: 13 (4) G3: 13 (3)
POUNDS LOST (Sacks 2009) RCT US, university Good	G1: Low-fat, average-protein (20% fat, 15% protein, and 65% CHO) G2: Low-fat, high-protein (20% fat, 25% protein, 55% CHO) G3: High-fat, average protein (40% fat, 15% protein, 45% CHO) G4: High-fat, high-protein (40% fat, 25% protein, 35% CHO) All groups: 750 kcal/day deficit calculated from REE and exercise level Group sessions led by registered dieticianss were held once a week, 3 of every 4 wks during the first 6 mos and 2 of every 4 wks from 6 mos to 2 yrs; individual sessions were held every 8 wks for the entire 2 yrs Foods were similar across diets, but quantities differed to meet macronutrient goals Web-based, self-monitoring tool reinforced adherence to target macronutrient levels Physical activity goals were established for sedentary participants, gradually increasing from 30 mins of moderate intensity exercise per week to 90 mins/wk during the first six mos, the same for each diet group Duration Treatment: 2 yrs	Overweight or obese adults 30–70 yrs of age, BMI 25–40, 64% female, hypertension 35% Weight, kg (SD): G1: 94.0 (16) G2: 92.0 (13) G3: 92.0 (17) G4: 94.0 (16) *n*'s G1: 204 G2: 202 G3: 204 G4: 201	24 mos Mean weight loss, kg G1 + G3: -3.0 G2 + G4: -3.6 *p*=0.22 G1 + G2: -3.3 G3 + G4: -3.3 *p*=0.94 Mean difference in weight, kg G1 + G3 vs. G2 + G4: -0.6 (95% CI -1.6 to 0.4), *p*=0.22 G1 + G2 vs. G3 + G4: 0.04 (95% CI, -0.9 to 1.0), *p*=0.94 G1 vs. G4: 0.6 (95% CI, -0.8 to 1.9), *p*=0.42 Mean difference in WC, cm: G1 + G3 vs. G2 + G4: -0.7 (95% CI -1.7 to 0.4), *p*=0.22 G1 + G2 vs. G3 + G4: 0.0 (95% CI -1.0 to 1.0), *p*=0.99 G1 vs. G4: 0.7 (95% CI -0.8 to 2.1), *p*=0.39	6 mos Changes from baseline Total cholesterol, mg/dL (SE): High fat (G3+G4) - low fat (G1+G2): 4.7 (1.8); *p*=0.01 High protein (G2+G4) – avg. protein (G1+G3): 2.3 (1.8); *p*=0.20 Highest CHO – lowest CHO: -7.0 (2.6); *p*=0.007 G1: -5.9 G2: -4.9 G3: -3.7 G4: -2.3 *p*=NR LDL-C, mg/dL (SE): High fat (G3+G4) - low fat (G1+G2): 4.4 (1.6); *p*=0.005 High protein (G2+G4) – avg. protein (G1+G3): 2.4 (1.6); *p*=0.13 Highest CHO – lowest CHO: -6.8 (2.3); P=0.003 G1: -6.6 G2: -4.8 G3: -3.2 G4: -1.1 *p*=NR HDL-C, mg/dL (SE): High fat (G3+G4) - low fat (G1+G2): 1.1 (0.05); *p*=0.01 High protein (G2+G4) – avg. protein (G1+G3): 1.1 (0.05); *p*=0.02 Highest CHO – lowest CHO:	Withdrawals, *n* (%): 24 mos G1: 35 (17.2) G2: 45 (22.3) G3: 53 (26.0) G4: 33 (16.4) Dietary Compliance 6 mos Energy, kcal/day G1: 1636 G2: 1572 G3: 1607 G4: 1624 CHO, % G1: 57.5 G2: 53.4 G3: 49.1 G4: 43.0 Protein, %: G1: 17.6 G2: 21.8 G3: 18.4 G4: 22.6 Fat, %: G1: 6.2 G2: 25.9 G3: 33.9 G4: 34.3 Saturated fat, %: G1: 7.5 G2: 7.9 G3: 9.0 G4: 9.0 24 mos

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				-2.2 (0.6); *p*=0.001 G1: -0.4 G2: +2.7 G3: +2.9 G4: +4.0 *p*=NR Triglycerides, mg/dL (SE): High-fat (G3+G4) - low fat (G1+G2): -2.8 (4.3); *p*=0.52 High protein (G2+G4) – avg. protein (G1+G3): -5.4 (4.3); *p*=0.21 Highest CHO – lowest CHO: 8.1 (5.0); *p*=0.10 G1: -14.2 G2: -20.4 G3: -18.1 G4: -19.5 SBP, mm Hg (SE): High-fat (G3+G4) – low-fat (G1+G2): 0.4 (0.7); *p*=0.59 High protein (G2+G4) – avg. protein (G1+G3): -1.0 (0.7); *p*=0.14 Highest CHO – lowest CHO: 0.6 (0.9); *p*=0.51 G1: -1.2 G2: -2.6 G3: -1.5 G4: -1.7 DBP, mm Hg (SE): High-fat (G3+G4) - low fat (G1+G2): 0.1 (0.5); *p*=0.77 High-protein (G2+G4) – avg. protein (G1+G3): -0.5 (0.5); *p*=0.32 Highest CHO – lowest CHO: 0.3 (0.7); *p*=0.62 G1: -1.4 G2: -3.1	kcal/day G1: 1531 G2: 1560 G3: 1521 G4: 1413 CHO, %: G1: 53.2 G2: 51.3 G3: 48.6 G4: 42.9 Protein, %: G1: 19.6 G2: 20.8 G3: 19.6 G4: 21.2 Fat, %: G1: 26.5 G2: 28.4 G3: 33.3 G4: 35.1 Saturated fat, %: G1: 8.0 G2: 8.9 G3: 9.8 G4: 10.5 Biomarkers of adherence 6 mos Urinary nitrogen, g: G1: 11.1 G2: 11.9 G3: 10.3 G4: 12.6 24 mos Urinary nitrogen, g: G1: 11.8 G2: 11.8 G3: 11.2 G4: 12.5

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G3: -2.3 G4: -1.8 Blood glucose mg/dL (SE): High fat (G3+G4) - low fat (G1+G2): 1.2 (0.6); *p*=0.04 High protein (G2+G4) – avg. protein (G1+G3): 0.5 (0.6); *p*=0.38 Highest CHO – lowest CHO: -1.7 (0.9); *p*=0.04 G1: -3.0 G2: -2.6 G3: -1.9 G4: -1.2 Blood insulin, uu/ml (SE): High-fat (G3+G4) - low fat (G1+G2): 0.2 (0.4); *p*=0.68 High-protein (G2+G4) – avg. protein (G1+G3): 0.0 (0.4); *p*=0.91 Highest CHO – lowest CHO: -0.2 (0.7); *p*=0.74 G1: -16.2 G2: -19.9 G3: -18.2 G4: -14.4 24 mos Changes from baseline Total cholesterol, mg/dL (SE): High-fat (G3+G4) - low fat (G1+G2): 5.6 (1.9); *p*=0.003 High-protein (G2+G4) – avg. protein (G1+G3): 0.2 (1.9); *p*=0.92 Highest CHO – lowest CHO: -5.8 (2.6); *p*=0.02 G1: -3.7 G2: -2.9 G3: -0.3	

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G4: -0.8 LDL-C, mg/dL (SE): High-fat (G3+G4) - low fat (G1+G2): 5.1 (1.6); *p*=0.001 High-protein (G2+G4) – avg. protein (G1+G3): 0.5 (1.6); *p*=0.74 Highest CHO – lowest CHO: -5.7 (2.2); *p*=0.01 G1: -5.9 G2: -3.9 G3: -0.2 G4: -1.3 HDL-C, mg/dL (SE): High-fat (G3+G4) - low fat (G1+G2): 0.7 (0.5); *p*=0.12 High-protein (G2+G4) – avg. protein (G1+G3): 0.9 (0.5); *p*=0.05 Highest CHO – lowest CHO: -1.7 (0.7); *p*=0.01 G1: +5.6 G2: +6.5 G3: +6.3 G4: +8.8 Triglycerides, mg/dL (SE): High-fat (G3+G4) - low fat (G1+G2): -1.2 (4.0); *p*=0.76 High-protein (G2+G4) – avg. protein (G1+G3): -6.7 (4.0); *p*=0.10 Highest CHO – lowest CHO: 7.96 (6.0); *p*=0.19 G1: -11.5 G2: -16.6 G3: -12.4 G4: -16.7 SBP, mm Hg (SE): High-fat (G3+G4) - low fat	

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				(G1+G2): 0.3 (0.7); *p*=0.64 High-protein (G2+G4) – avg. protein (G1+G3): -0.2 (0.7); *p*=0.77 Highest CHO – lowest CHO: -0.1 (0.9); *p*=0.89 G1: -0.8 G2: -1.7 G3: -1.3 G4: -0.7 DBP, mm HG (SE): High-fat (G3+G4) - low fat (G1+G2): 0.1 (0.5); *p*=0.85 High-protein (G2+G4) – avg. protein (G1+G3): 0.2 (0.05); *p*=0.59 Highest CHO – lowest CHO: -0.3 (0.7); *p*=0.61 G1: -0.8 G2: -1.3 G3: -1.5 G4: -0.3 Blood glucose mg/dL (SE): High-fat (G3+G4) - low fat (G1+G2): 1.1 (0.5); *p*=0.05 High-protein (G2+G4) – avg. protein (G1+G3): 0.5 (0.6); *p*=0.34 Highest CHO – lowest CHO: -1.6 (0.8); *p*=0.06 G1: +1.1 G2: +1.0 G3: +1.6 G4: +2.8 Blood insulin, uu/ml (SE): High-fat (G3+G4) - low fat (G1+G2): -0.1 (0.4); *p*=0.77 High-protein (G2+G4) – avg. protein (G1+G3): -0.7 (0.4);	

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				p=0.07 Highest CHO – lowest CHO: 0.8 (0.6); *p*=0.19 G1: -2.4 G2: -11.5 G3: -6.4 G4: -9.2	
SMART study (Frisch et al., 2009) RCT Germany, Fair	G1: High-CHO group (DGE): >55% CHO, <30% fat, 15% protein, energy deficit 500 kcal/day G2. Low-CHO group (LOGI): 40% CHO, 35% fat, 25% protein, energy deficit 500 kcal/day Both groups: • Weekly nutrition education and dietary counseling by phone with a nutritionist during the first six mos • No physical activity prescription Duration: 12 mos Treatment: mos 1–6 Follow-up (no contact): mos 7–12	Overweight or obese adults 18–70 yrs of age, BMI>27, BMI, kg/m2 (SD): G1: 33.8 (4.8) G2: 33.5 (3.9) *n*'s: G1: 100 G2: 100 Sex (men), *n*: G1: 24 G2: 38 *p*=0.032	6 mos Weight loss, kg (SD): G1: -6.2 (4.8) G2: -7.2 (5.4) *p*=NR BMI change, kg/m (SD): G1: -2.1 (1.6) G2: -2.3 (1.8) *p*=0.250 WC change, cm (SD): G1: -6.6 (5.3) G2: -8.0 (5.5) *p*=0.083 12 mos Weight loss, kg (SD): G1: -4.3 (5.1) G2: -5.8 (6.1) *p*=0.065 BMI change, kg/m (SD): G1: -1.5 (1.8) G2: -1.9 (2.1) *p*=0.110 WC change, cm (SD): G1: -4.7 (8.9) G2: -6.9 (6.1) *p*=0.037	6 mos SBP change, mm Hg (SD): G1: -4.0 (15.0) G2: -6.0 (16.0) *p*=0.102 DBP change, mm Hg (SD): G1: -3.0 (9.0) G2: -3.0 (8.0) *p*=0.884 Triglycerides change, mmol/L (SD): G1: -0.03 (0.55) G2: -0.18 (0.40) *p*=0.005 Total cholesterol change, mmol/l (SD): G1: -0.07 (0.50) G2: -0.07 (0.56) *p*=0.926 LDL-C change, mmol/L (SD): G1: -0.03 (51) G2: -0.03 (0.50) *p*=0.921 HDL-C change, mmol/L (SD):* G1: -0.09 (0.19) G2: -0.02 (0.20) *p*=0.005 *Note: may be influenced by unbalanced sex 12 mos SBP change, mm Hg (SD): G1: -1.0 (15.0)	Withdrawals, *n* (%): G1: 20 (20) G2: 15 (15) Overall: 35 (17.5) Dietary Compliance At mos 1, 3, 6, and 12, energy and nutrient intake (diet compliance) were assessed using a 3 day validated food record; amount of daily physical activity was assessed using a standardized, validated questionnaire. Calories, mean kcal/d ay(SD): 6 mos G1: 1783 (597) G2: 1742 (624) *p*=0.636 12 mos G1: 1854 (624) G2: 1866 (710) *p*=0.903 Carbohydrates, % energy (SD): 6 mos G1: 49.5 (7.6) G2: 40.9 (10.1) *p*<0.001 12 mos G1: 50.1 (8.2) G2: 43.5 (9.9) *p*<0.001 Fat, % energy (SD): 6 mos G1: 29.7 (6.5) G2: 36.5 (9.5)

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G2: -5.0 (14.0) *p*=0.007 DBP change, mm Hg (SD): G1: -2.0 (8.0) G2: -3.0 (9.0) *p*=0.440 Triglycerides change, mmol/L (SD): G1: -0.04 (0.50) G2: -0.10 (0.47) *p*=0.164	*p*<0.001 12 mos G1: 30.2 (7.0) G2: 34.2 (8.7) *p*=0.001 Protein, % energy (SD): 6 mos G1: 17.7 (4.0) G2: 19.3 (4.7) *p*=0.012
				Total cholesterol change, mmol/l (SD): G1: + 0.13 (0.61) G2: +0.03 (0.75) *p*=0.259 LDL-C change, mmol/L (SD): G1: +0.06 (0.59) G2: +0.02 (0.65) p=0.564 HDL-C change, mmol/L (SD):* G1: -0.03 (0.17) G2: -0.02 (0.21) *p*=0.668 * Note: may be influenced by unbalanced sex	12 mos G1: 16.7 (3.1) G2: 18.9 (4.4) *p*<0.001

Summary Table 3.4. Low Carbohydrate Approaches (<30 g/day for at least a period)

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
Foster et al., 2010 RCT US, 3 academic	G1: Low-carbohydrate diet: limited carbohydrate intake (20 g/day for 3 mos) in the form of low–glycemic index vegetables with unrestricted consumption of fat and protein. After 3	Adults 18–65 yrs of age, 68% female, BMI 30–40 kg/m^2 Weight, kg (SD):	**6 mos** Weight change, kg (95% CI) G1: -12.18 (-13.1 to -11.2) G2: -11.34 (-12.4 to -10.3)	**6 mos** Triglyceride change, mg/dL (95% CI) G1: -40.06 (-45.7 to -34.4) G2: -24.30 (-31.2 to -17.4)	Withdrawals, *n* (%): 6 mos G1: 25 (16.3) G2: 19 (12.3)

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
university medical centers Good	mos, participants in low-carbohydrate diet group increased their carbohydrate intake (5 g/day per wk) until a stable and desired weight was achieved G2: Low-fat diet: limited energy intake (1200–1500 for women and 1500–1800 kcal/day for men; 55% of calories from carbohydrates, ≤30% calories from fat; 15% from protein) G1 & G2: All participants received comprehensive, in-person group behavioral treatment weekly; topics included self-monitoring, stimulus control, and relapse management; All participants were prescribed the same level of physical activity (principally walking), beginning at wk 4, with 4 sessions of 20 mins each and progressing by wk 19 to 4 sessions of 50 mins each; Group sessions reviewed participants' completion of their eating and activity records, as well as other skill builders; participants in both groups were instructed to take a daily multivitamin supplement 75–90 minute behavioral sessions weekly for 20 wks, every other week for 20 wks, and then every other month for the remainder of the 2-yr study period Duration: 2 yrs	G1: 103.3 (15.5) G2: 103.5 (14.4) BMI, kg/m^2 (SD): G1: 36.1 (3.59) G2: 36.1 (3.46) SBP, mmHg (SD): G1: 124.3 (14.1) G2: 124.6 (15.8) DBP, mmHg (SD): G1: 73.9 (9.4) G2: 76.0 (9.7) HDL-C, mg/dL (SD): G1: 46.2 (13.5) G2: 45.4 (11.7) LDL-C, mg/dL (SD): G1: 120.2 (25.7) G2: 124.0 (29.2) Triglyceride, mg/dL (SD): G1: 113.3 (54.6) G2: 124.0 (73.5) n's G1: 153 G2: 154	*p*=0.25 **12 mos** Weight change, kg (95% CI) G1: -10.87 (-12.1 to -9.67) 2: -10.81 (-12.4 to -9.28) *p*=0.95	*p*<0.001 LDL-C change, mg/dL (95% CI) G1: 0.54 (-3.25 to 4.33) G2: -9.52 (-12.9 to -6.15) *p*<0.001 HDL-C change, mg/dL (95% CI) G1: 6.21 (4.74–7.67) G2: 0.89 (-0.24 to 2.02) *p*<0.001 Change in SBP, mmHg (95% CI) G1: -7.36 (-9.26 to -5.47) G2: -6.97 (-8.89 to -5.05) *p*=0.78 Change in DBP, mmHg (95% CI) G1: -5.15 (-6.49 to -3.82) G2: -2.50 (-3.76 to -1.25) *p*=0.005 **12 mos** Triglyceride change, mg/dL (95% CI) G1: -31.52 (-39.5 to -23.6) G2: -17.92 (-28.3 to -7.58) *p*=0.039 LDL-C change, mg/dL (95% CI) G1: -8.57 (-12.9 to -4.26) G2: -8.66 (-12.7 to -4.56) *p*=0.98 HDL-C change, mg/dL (95% CI) G1: 7.96 (6.33–9.59) G2: 3.94 (2.52–5.36) *p*<0.001 Change in SBP, mmHg (95% CI) G1: -5.64 (-7.62 to -3.67) G2: -4.06 (-6.07 to -2.05) *p*=0.27 Change in DBP, mmHg (95% CI) G1: -3.25 (-4.74 to -1.76) G2: -2.19 (-3.58 to -0.79) *p*=0.31	12 mos G1: 40 (26.1) G2: 39 (25.3) 24 mos G1: 64 (41.8) G2: 49 (31.8) Dietary Compliance NR

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
McAuley et al., 2005 RCT New Zealand, school/university Fair	G1: High-fat (Atkins Diet)—no specific macronutrient targets except for CHOs; wks 1–2 -participants were instructed to limit certain foods to consume l<20 g CHO/day (wks 3–8 - CHO was reintroduced by the addition of 5 g/day each week (a maximum of 50 g of CHO per day was consumed by week 8); wks 8–16 -increasing CHO intake from the specific food lists by 5 g/day each week was continued until each participant found the maximum level of CHO consumption without weight gain G2: High-protein (Zone Diet)—total energy provided by each meal and snack: 40% from low-glycemic index CHO, 30% from protein, and 30% from fat; participants advised to eat five times daily with no more than 5 hrs between meals; wks 8–16 – subjects instructed to consume slightly larger portions in the evening to maintain body weight; wks 16–24 –participants encouraged to continue consuming appropriate foods in quantities that facilitated weight maintenance G3: HC-High CHO, high fiber (control group)—based on ESAD guidelines focused on consumption of specific food groups in specified daily amounts (≥6 servings of breads and cereals, ≥3 servings of vegetables and two of fruit, ≥2 servings low-fat milk, ≥1 serving lean meat, dried beans, or lentils. Advice to reduce dietary fat, salt, and sugar intakes; wks 8–16 - slightly larger portions for their evening meal to maintain body weight; wks 16–24 - similar advice All groups: • Weekly reviews for wks 1–8 and wks 8–16; no contact wks 16–24)	Adult women 30–70 yrs of age, BMI >27 kg/m^2,insulin resistant Weight, kg (SD): G1: 96.0 (10.8) G2: 93.2 (14.5) G3: 98.0 (15.1) BMI, kg/m^2 (SD): G1: 36.0 (3.9) G2: 34.5 (5.3) G3: 36.6 (5.6) WC, cm (SD): G1: 108.9 (9.9) G2: 108.0 (11.5) G3: 109.1 (11.6) SBP, mmHG G1: 130 (14) G2: 124 (13) G3: 126 (11) DBP, mmHG G1: 83 (10) G2: 80 (9) G3: 81 (10) Total cholesterol, mmol/l G1: 5.8 (1.0) G2: 5.7 (1.0) G3: 5.9 (0.9) LDL-C, mmol/l G1: 3.8 (0.9) G2: 3.7 (0.8) G3: 3.9 (0.8) HDL-C, mmol/l G1: 1.17 (0.28) G2: 1.21 (0.23) G3: 1.16 (0.21) Triglyceride, mmol/l G1: 1.78 (0.76)	**Measurements at wk 16** **Weight, kg (SD)** G1: 89.1 (10.7) from 96.0 G2: 86.2 (14.6) from 93.2 G3: 93.6 (14.6) from 98.0 BMI, kg/m^2 (SD) G1: 33.5 (3.8) from 36.0 G2: 32.0 (5.0) from 34.5 G3: 35.0 (5.5) from 36.6 **WC, cm (SD):** G1: 99.8 (10.0) from 108.9 G2: 100.3 (9.9) from 108.0 G3: 103.2 (10.9) from 109.1 **Measurements at wk 24** **Weight, kg (SD)** G1: 88.9 (10.6) from 96.0 G2: 86.3 (14.2) from 93.2 G3: 93.3 (14.5) from 98.0 BMI, kg/m^2 (SD) G1: 33.1 (3.7) from 36.0 G2: 31.5 (5.1) from 34.5 G3: 34.9 (5.6) from 36.6 **WC CM, cm** G1: 99.1 (9.2) from 108.9 G2: 99.2 (10.9) from 108.0 G3: 102.2 (11.8) from 109.1	**Measurements at wk 16** **SBP, mmHG (SD)** G1: 123.0 (13) from 130 G2: 122 (10) from 124 G3:123 (11) from 126 **DBP, mmHG (SD)** G1: 79 (9) from 83 G2: 79 (7) from 80 G3: 81 (10) from 81 **Total cholesterol, mmol/l** G1: 5.4 (1.0) from 5.8 G2: 5.2 (0.8) from 5.7 G3: 5.4 (0.9) from 5.9 **LDL-C, mmol/l** G1: 3.6 (0.8) from 3.8 G2: 3.4 (0.8) from 3.7 G3: 3.7 (0.9) from 3.9 **HDL-C, mmol/l** G1: 1.25 (0.34) from 1.17 G2: 1.19 (0.32) from 1.21 G3: 1.13 (0.28) from 1.16 **Trigylceride, mmol/l** G1: 1.22 (0.67) from 1.78 G2: 1.23 (0.47) from 1.86 G3: 1.37 (0.54) from 1.77 **Fasting glucose, mmol/l** G1: 4.8 (0.40) from5.1 G2: 5.0 (0.5) from 5.1 G3: 4.8 (0.5) from 5.0 **24 wks** **SBP, mmHG (SD)** G1: 126 (14) from 130 G2: 121 (10) from 124 G3: 124 (11) from 126 **DBP, mmHG (SD)** G1: 81 (8) from 83 G2: 79 (7) from 80 G3: 82 (10) from 81	Withdrawals, *n* (%): **24 wks*** G1: 4 (12.9) G2: 3 (10.0) G3: 2 (6.3) *3 post-randomization withdrawals, not specified by treatment group; group withdrawal rates here do not account for those exclusions **Dietary Compliance** **16 wks** Mean (SD) Energy, kJ/D G1: 6787 (2328) G2: 6397 (1474) G3: 6147 (1264) Total fat, %TE G1: 46 (10) G2: 34 (7) G3: 28 (8) Cholesterol, mg G1: 482 (220) G2: 219 (94) G3: 221 (110) CHO, % TE G1: 26 (11) G2: 35 (8) G3: 45 (8) Total proteins, % G1: 24 (5) G2: 26 (6) G3: 22 (5) Fiber, g/4184 kJ G1: 9 (3) G2: 14 (4) G3: 13 (5) **24 wks:**

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	• None of the diets was formally energy restricted during any phase • Advised to participate in 30 min of any physical activity 5 days/wk Duration: 24 wks Wks 1–8: weight loss phase Wks 8–16: weight maintenance with supervision continued as in weight loss phase Wks 16–24: follow-up with no supervision	G2: 1.86 (0.66) G3: 1.77 (0.57) *n*'s G1: 31 G2: 30 G3: 32		**Total cholesterol, mmol/l** G1: 5.5 (1.1) from 5.8 G2: 5.2 (0.9) from 5.7 G3: 5.3 (1.0) from 5.9 **LDL-C, mmol/l** G1: 3.7 (1.0) from 3.8 G2: 3.4 (0.8) from 3.7 G3: 3.5 (0.9) from 3.9 **HDL-C, mmol/l** G1: 1.26 (0.33) from 1.17 G2: 1.22 (0.26) from 1.21 G3: 1.12 (0.28) from 1.16 **Triglyceride, mmol/l** G1: 1.07 (0.41) from 1.78 G2: 1.28 (0.45) from 1.86 G3: 1.45 (0.70) from 1.77 **Fasting glucose, mmol/l** G1: 4.8 (0.6) from 5.1 G2: 4.9 (0.4) from 5.1 G3: 4.7 (0.4) from 5.0	Energy, kJ/D G1: 6797 (1818) G2: 6156 (1391) G3: 6114 (1232) Total fat, % G1: 47 (8) G2: 35 (7) G3: 28 (7) Cholesterol, mg G1: 478 (251) G2: 243 (139) G3: 196 (75) CHO, % TE G1: 26 (11) G2: 35 (10) G3: 45 (7) Total proteins, % G1: 24 (6) G2: 26 (5) G3: 21 (3) Fiber, g/4184 kJ G1: 9 (3) G2: 13 (4) G3: 13 (3)

Summary Table 3.5. Complex Versus Simple Carbohydrates

Study Cited, Design, Setting Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
Poppitt et al., 2002 RCT UK Outpatient medical setting – clinic Fair	G1: Low-fat, high-complex CHO (reduced fat intake by 10% of total energy, ratio of simple to complex CHO to 1:2); participants were provided with ≥60% of their total energy intake from the study grocery store G2: Low-fat, high simple CHO (reduced fat intake by 10% of total energy, ratio of simple to complex CHO 2:1); participants were provided with ≥60% of their total energy intake from the study grocery store G3: Control diet (maintaining fat intake at habitual amounts 35–40% of energy) All groups: Subjects came to the study grocery store on 1 or 2 occasions per week to collect foods and discuss their energy and macronutrient intakes with dietitian Ad libitum diet Run-in: 4 wks Treatment: 24 wks	Adults >38 yrs, BMI 27–40, at least 3 risk factors for metabolic syndrome Weight, kg (SD): G1: 91.2 (9.5) G2: 89.3 (15.7) BMI, kg/m^2 (SD): G1: 32.3 (3.6) G2: 30.9 (3.0) *n*'s for baseline characteristics: G1: 14 G2: 14 *n*'s: G1: 16 G2: 15	**6 mos** Weight change, kg: G1: -4.25 G2: -0.28 *p*<0.001 Completers analysis Results for control arm (G3) not considered here due to high differential attrition between it and G1 and G2.	**6 mos** Total cholesterol change, mmol/L: G1: -0.63 G2: -0.06 G1 vs. G2: *p*<0.05	Withdrawals, n (%): G1: 2 (12.5) G2: 1 (6.7) G3: 4 (26.7) Overall: 7 (15.2) **Mean reported dietary intake during treatment phase** Energy kJ/d (SD): G1: 8108 (2689) G2: 9578 (2600) Fat % of energy (SD): G1: 24.1 (5.36) G2: 21.1 (3.11) Complex CHO % of energy (SD): G1: 35.5 (3.89) G2: 28.5 (5.10) Simple CHO % of energy (SD): G1: 17.6 (8.05) G2: 28.9 (8.48)

Summary Table 3.6. Glycemic Load Dietary Approaches

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Selected Baseline Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
CALERIE Pittas et al., 2006; Das et al., 2007 RCT US, University Fair	G1: Baseline – 7 wks: usual diet; Treatment (wks 8–24): High-glycemic load diet (70% food provided; 30% calorie restriction, 20% fat, 60% CHO, 20% protein) Wks 24–48: Individualized high-glycemic load diet (subjects prepared	Adults 24–42 yrs of age, BMI 25–29.9, blood glucose <100 mg/dL (5.6 mmol/L) Weight, kg: G1: 79.3 G2: 78.8	6 mos Weight loss (kg) G1: -7.2 G2: -7.7 *p*=0.69 Completers analysis	6 mos CRP (mg/L) change (SEM): 6 mos G1: -0.41 (0.91) G2: -1.44 (0.44) *p*=0.13 Completers analysis	Withdrawals, *n* (%): 6 mos G1: 1 (5.9) G2: 1 (5.9) 12 mos G1: 2 (11.8) G2: 3 (17.6)

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Selected Baseline Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	their own food; 30% calorie restriction, 20% fat, 60% CHO, 20% protein) G2: Baseline – 7 wks: Usual diet; Treatment (wks 8–24): Low-glycemic load diet (100% food provided; 30% calorie restriction, 30% fat, 40% CHO, 30% protein) Wks 24–48: Individualized low-glycemic load diet (subjects prepared their food; 30% calorie restriction, 30% fat, 40% CHO, 30% protein) ALL food provided from Tufts kitchen G1 & G2: After wks 15–20, subjects were allowed 1000 kcal/wk of discretionary foods not on the menu, and this amount was subtracted from the provided foods	Completers only BMI: G1: 27.6 G2: 27.6 Completers only *n*'s G1: 17 G2: 17	12 mos* *Results determined to be of poor quality due to completers analysis	12 mos* *Results determined to be of poor quality due to completers analysis and attrition >10%	Overall: 5 (14.7) Dietary Compliance Mean reported energy intake at 6 mos (kcal/day): G1: 2017 G2: 1972 *p*=0.70
Ebbeling et al., 2007 RCT US, Outpatient medical setting – hospital Fair	G1: Low-glycemic load (40% CHO, 35% fat, 25% protein) G2: Low-fat (55% CHO, 20% fat, 25% protein) G1 & G2: 6 workshops during the first 2 mos, then held monthly; private session during the initial month then five monthly individual telephone calls) Diets prescribed using ad libitum approach Duration: 18 mos Treatment: 6 mos Follow-up: 12 mos	Adults 18–35 yrs of age, BMI>30, 79.5% female, Weight, kg (SD): G1: 103.5 (17.3) G2: 103.3 (15.1) *n*'s G1:36 G2: 37	Weight change 18 mos No significant difference between groups in weight loss Data NR *p*=0.99 Weight change data (6, 12, and 18 mos) reported in graph only but difference is not significant	**LDL-C (mg/dL) change (SE):** 6 mos G1: -5.8 (3.4) G2: -16.3 (3.3) *p*=0.03 18 mos G1: -0.3 (3.4) G2: -10.6 (3.3) *p*=0.03 **HDL-C (mg/dL) change (SE):** 6 mos G1: +1.6 (1.4) G2: -4.4 (1.3) *p*=0.02 18 mos G1: -3.7 (1.5) G2: -8.2 (1.5) *p*=0.03 **Triglyceride (mg/dL) change (SE):** 6 mos G1: -21.2 (4.7)	Withdrawals, *n* (%): **6 mos** G1: 4 (11.1) G2: 3 (8.1) **18 mos** G1: 8 (22.2) G2: 14 (37.8) Dietary Compliance: NR

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Selected Baseline Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G2: -4.0 (5.6) *p*=0.02 18 mos G1: -9.0 (5.4) G2: +2.0 (6.0) *p*=0.18 **SBP (mm Hg) change (SE):** 6 mos G1: -5.1 (2.3) G2: -4.8 (2.3) *p*=0.93 18 mos G1: -3.2 (2.3) G2: +1.1 (2.3) *p*=0.18 **DBP (mm Hg) change (SE):** 6 mos G1: -2.4 (1.7) G2: -2.0 (1.7) *p*=0.88 18 mos G1: 0.0 (1.7) G2: +2.9 (1.7) *p*=0.22 **Blood glucose (mg/dL) change (SD):** 6 mos G1: +1.6 (1.3) G2: -0.3 (1.3) *p*=0.31 18 mos G1: +2.1 (1.3) G2: +1.4 (1.3) *p*=0.73 **Blood insulin (mU/L) change (SE):** 6 mos G1: -2.1 (0.8) G2: -0.9 (0.8)	

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Selected Baseline Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				p=0.28 18 mos G1: -0.8 (0.8) G2: 0.0 (0.8) *p*=0.49	

Summary Table 3.7. CQ3—Dietary Patterns (Mediterranean Style and Vegetarian and Other Dietary Pattern Approaches)

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
Esposito et al., 2009 RCT Italy, university Good	G1: Mediterranean-style diet (1500 women, 1800 men kcal/day), <50% complex CHO, ≥30% fat (30–50g olive oil) G2: Low-fat diet based on AHA guidelines (1500 women, 1800 men kcal/d), ≤30% fat, ≤10% SF G1 & G2: • Physical activity: participants advised to increase physical activity • Monthly visits with registered dietician during the 1st year and bimonthly thereafter Duration: 4 yrs Run-in: 2 wks Treatment: 4 yrs	Adults 30–75 yrs of age, BMI >25, newly diagnosed type 2 diabetes, HbA_{1c} <11%, sedentary (physical activity <1 hr/wk), relatively gender-balanced BMI, kg/m^2 (SD): G1: 29.7 (3.4) G2: 29.5 (3.6) Weight, kg (SD): G1: 86.0 (10.4) G2: 85.7 (9.9) WC, cm (SD): G1: 98 (10.1) G2: 98 (10.0) SBP, mm Hg (SD): G1: 139 (12) G2: 140 (12) DBP, mm Hg (SD): G1: 87 (8) G2: 86 (8) *n*'s G1: 108	**Changes at 1 yr** Weight, kg (SD): G1: -6.2 (3.2) G2: -4.2 (3.5) Difference (95% CI): -2.0 (-3.0 to -0.9) *p*=NR BMI, kg/m^2 (SD): G1: -2.4 (1.6) G2: -1.4 (0.9) Difference (95% CI): -1.0 (-2.2 to -0.3) *p*=NR WC, cm (SD): G1: -4.8 (3.0) G2: -3.5 (2.8) Difference (95% CI): -1.3 (-1.7 to -0.5) *p*=NR **4 yrs** Weight, kg (SD): G1: -3.8 (2.0) G2: -3.2 (1.9) Difference (95% CI): -0.6 (-1.6	**Changes at 1 yr** **Need for antihyperglycemic drug therapy, %:** G1: 5.5 G2: 9.4 Difference (95% CI): -3.9 (-7.8 to 1.2) *p*=NR HbA1c, level ,% (SD): G1: -1.2 (1.0) G2: -0.6 (0.6) Difference (95% CI): -0.6 (-0.9 to -0.3) *p*=NR **Plasma glucose level, mmol/L (SD):** G1: -2.3 (1.9) G2: -1.1 (1.1) Difference (95% CI): -1.2 (-1.7 to -0.72) *p*=NR **Serum insulin level, pmol/L (SD):** G1: -14.0 (13.6)	Withdrawals *n*, (%) G1: 10 (9.3) G2: 10 (9.3) **Dietary Compliance** **Change in Nutrient Indexes** **Changes at 1 yr** Kcal/d (SD): G1: -570 (121) G2: - 525 (111) Difference (95% CI): -45 (-120 to 30) CHO, % (SD): G1: - 9.4 (3.1) G2: 1.5 (1.8) Difference (95: CI): -9.9 (-14 to -5.0) Protein, % (SD): G1: 1.6 (1.5) G2: 1.9 (1.7) Difference (95: CI): -0.3 (-0.9 to 0.6) Saturated fat, % (SD): G1: -0.5 (0.5) G2: -0.8 (0.7) Difference (95% CI):

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
		G2: 107	to 1.2) *p*=NR BMI, kg/m^2 (SD): G1: -1.2 (0.7) G2: -0.9 (0.6) Difference (95% CI): -0.3 (-0.9 to 0.4) *p*=NR WC, cm (SD): G1: -3.0 (1.7) G2: -2.6 (2.0) Difference (95% CI): -0.4 (-0.9 to 0.5) *p*=NR [CI'S WERE USED TO DETERMINE SIGNIFICANCE]	G2: -12.9 (12.9) Difference (95% CI): -1.1 (-6.9 to 7.4) *p*=NR **HDL-C, mmol/L (SD):** G1: +0.10 (0.12) G2: +0.025 (0.02) Difference (95% CI): +0.08 (0.04 to 0.12) *p*=NR **TG, mmol/L (SD):** G1: -0.44 (0.57) G2: -0.22 (0.45) Difference (95% CI): -0.22 (-0.32 to -0.10) *p*=NR **SBP, mm Hg (SD):** G1: -5.1 (4.2) G2: -2.0 (1.9) Difference (95% CI): -3.1 (-4.9 to -1.2) *p*=NR **DBP, mm Hg (SD):** G1: -4.0 (3.0) G2: -3.0 (4.0) Difference (95% CI): -1.0 (-4.0 to -1.0) *p*=NR **Changes at 4 yrs** **Need for antihyperglycemic drug therapy, %:** G1: 44.0 G2: 70.0 Difference (95% CI): -26.0 (-31.1 to -20.1) HbA1c, level ,% (SD): G1: -0.9 (0.6)	0.3 (-0.5 to 1.1) Monounsaturated fat, % (SD): G1: 5.9 (3.7) G2: -1.4 (1.5) Difference (95% CI): 7.3 (5.0 to 12.0) Polyunsaturated fat, % (SD): G1: 2.4 (1.7) G2: -1.4 (1.2) Difference (95% CI): 3.8 (1.5 to 5.5) **4 yrs** Kcal/d G1: -450 (100) G2: -409 (92) Difference (95% CI) -41 (-109 to 35) CHO, % (SD): G1: -7.9 (4.1) G2: 0.1 (0.3) Difference (95: CI): -8.0 (-13.1 to -3.8) Protein, % (SD): G1: 1.3 (1.4) G2: 1.5 (1.6) Difference (95: CI): -0.2 (-0.8 to 0.4) Saturated fat, % (SD): G1: -0.2 (0.3) G2: -0.4 (0.5) Difference (95% CI): 0.2 (-0.5 to 0.6) Monounsaturated fat, % (SD): G1: 5.5 (3.3) G2: -1.0 (0.9) Difference (95% CI): 6.5 (3.5 to 10.7)

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G2: -0.5 (0.4) Difference (95% CI): -0.4 (-0.9 to -0.1) **Plasma glucose level, mmol/L (SD):** G1: -1.7 (1.1) G2: -0.8 (0.8) Difference (95% CI): -0.9 (-1.6 to -0.2) *p*=NR **Serum insulin level, mmol/L (SD):** G1: -9.8 (8.9) G2: -5.6 (4.3) Difference (95% CI): -4.2 (-10.7 to 3.4) *p*=NR **HDL-C, mmol/L (SD):** G1: +0.09 (0.08) G2: +0.02 (0.02) Difference (95% CI): +0.07 (0.02 to 0.14) *p*=NR Triglyceride, mmol/L (SD): G1: -0.28 (0.28) G2: -0.07 (0.10) Difference (95% CI): -0.21 (-0.36 to -0.22) *p*=NR **SBP, mm Hg (SD):** G1: -2.5 (2.6) G2: -1.0 (1.0) Difference (95% CI): -1.5 (-4.5 to 1.2) *p*=NR **DBP, mm Hg (SD):** G1: -2.9 (1.9)	Polyunsaturated fat, % (SD): G1: 2.6 (1.9) G2: -1.1 (1.0) Difference (95% CI): 3.7 (1.4 to 6.0)

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
				G2: -1.5 (1.4) Difference (95% CI): -1.4 (-4.0 to 1.8) *p*=NR [CI'S WERE USED TO DETERMINE SIGNIFICANCE]	
PREFER Burke et al., 2006, Burke et al., 2007 US, Outpatient medical setting – hospital Fair	G1: Low-fat, lacto-ovo-vegetarian diet (1,200–1,500 kcal/day women, 1,500–1,800 kcal/day men, 25% fat); group was instructed to eliminate meat, fish, and poultry over the first 6 wks of the study, beginning with breakfast, then lunch, then dinner G2: Standard calorie- and fat-restricted omnivorous diet (<90.5 kg 1,200 kcal/day women, 1,500 kcal/day men; >90.5 kg 1,500 kcal/d women, 1800 kcal/d men, 25% fat); diet permitted meat, fish, and poultry G1 and G2: Were instructed to restrict consumption of calories (1,200–1,500 for women and 1,500–1800 for men) and fat (25% of calories). Ad libitum Received 32 treatment sessions on standard cognitive-behavioral therapy for weight management over a period of 12 mos; the main component of this approach included self-monitoring eating and exercise behaviors, goal setting, cognitive restructuring, stimulus control, demonstrations, and skill development Physical activity consisted of a recommendation to increase participants' activity to 150 min/d by 6th week and thereafter to increase or at least maintain that goal.	Adults 18–55 yrs of age, BMI 27–43, 87% female Weight, kg (SD): G1: 94.40 (14.23) G2: 95.25 (14.94) *n*'s G1: 84 G2: 98	**6 mos** Weight change, kg (SD): G1: -7.50 (6.00) G2: -6.97 (6.53) *p*=0.321 BMI change, kg/m^2 (SD): G1: -3.21 (2.06) G2: -2.83 (2.07) *p*=0.125 WC change, kg/m^2 (SD): G1 women: -6.12 (7.34) G2 women: -5.50 (6.31) *p*=0.799 G1 men: -9.37 (5.90) G2 men: -11.78 (10.61) *p*=0.695 **18 mos** No differences between G1 and G2 in weight loss *p*=0.41 [weight outcome data were reported stratified by diet preference status of the subjects but the 'diet effect' was formally tested for the dietary pattern groups overall]	**6 mos** Total cholesterol, Mm (SD) change from baseline: G1: -0.22 (0.66) G2: -0.09 (0.63) *p*=0.202 HDL-C change, mmol/L (SD) G1: -0.04 (0.19) G2: -0.06 (0.18) *p*=0.393 LDL-C change, mmol/L (SD) G1: -0.16 (0.54) G2: +0.05 (0.55) *p*=0.013 Triglycerides, mmol/L (SD): G1: -0.05 (0.66) G2: -0.17 (0.61) *p*=0.419 Blood Glucose change, mmol/L (SD): G1: -0.06 (0.54) G2: -0.03 (0.40) *p*=0.332 Blood Insulin change, pM (SD): G1: -29.67 (40.35) G2: -22.00 (39.75) *p*=0.140 **18 mos** No differences between G1 and G2 in:	Withdrawals: 200 randomized; "to obtain a fair balance in size across the four groups, only 50% of those who chose the SBT were randomly selected for inclusion. Fewer subjects preferred the SBT+LOV diet; therefore, 15 additional subjects who preferred the SBT diet were excluded to prevent the treatment preference–Yes SBT group from being significantly larger than the treatment preference–Yes SBT+LOV group." So of 185, withdrawals, *n* (%): G1: 12 (14.3) G2: 13 (13.3) And 3 post-randomization exclusions where treatment arm was not specified Overall: 28 (15.1) ITT analysis; BOCF **Nutritional Measurements at 6 mos** Kcal G1: 1487.78 G2: 1533.87 Total fat, %: G1: 25.76 G2: 27.08 Total CHO, %:

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	Duration: 18 mos Treatment: 12 mos Maintenance : 6 mos			Total cholesterol (*p*=0.91) LDL:HDL (*p*=0.06) Triacylglycerol (*p*=0.34) HOMA-IR (P = 0.53) [data were reported stratified by diet preference status of the subjects but the 'diet effect' was formally tested for the dietary pattern groups overall]	G1: 61.37 G2: 55.74 Total proteins, %: G1: 15.07 G2: 17.86 PS ratio: G1: 0.95 G2: 0.80
					Nutritional Measurements, mean change from baseline to 6 mos Kcal: G1: -535.98 G2: -519.80 p=0.836 Total fat, %: G1: -9.59 G2: -8.51 p=0.436 Total CHO, %: G1: +11.06 G2: +7.12 p=0.013 Total proteins, %: G1: -0.08 G2: +2.14 p<0.001 P/S (polyunsaturated/saturated) ratio: G1: 0.26 G2: 0.10 *p*=0.009
Turner-McGrievy et al., 2004; 2007 RCT US, School/ university	G1. Low-fat,,vegan diet (10% fat, 15% protein, 75% CHO); grains, vegetables, legumes, and fruits, with no limit on energy intake or portions. Participants were asked to exclude animal products, added oils, high-fat	Post-menopausal women, BMI 26–44 BMI, kg/m^2 (SD): G1: 33.6 (5.2) G2: 32.6 (3.3)	Weight, kg (SD) baseline/14 wks: G1: 89.3 (13.4)/ 83.5 (13.5) G2: 86.1 (12.1)/ 82.3 (12.0) *p*=NR	NR	**Withdrawals, n (%):** **14 wks:** G1: 3 (9.4) G2: 2 (6.3) 1 year:

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
Fair	processed foods, avocados, olives, nuts, nut butters, and seeds because these foods are typically calorie dense G2. NCEP Step II (<60 g/d or 30% fat, SF <7%, PUFA <10%, and MUFA <15%, cholesterol <200 mg/d); 15% of energy from protein and 55% from carbohydrate Ad libitum Physical activity as tolerated by participant Duration: 2 yrs Initial Treatment: Wks 1–14 Continued treatment with support: wks 14–52 Follow-up with no support: yrs1–2	Weight, kg (SD): G1: 89.3 (13.4) G2: 86.1 (12.1) *n*'s: G1: 31 G2: 31 (3 post-randomization exclusions; modified ITT analysis conducted)	Weight Change from baseline, kg **1 year** G1: -4.9 G2: -1.8 *p*=0.021 **2 yrs** G1: -3.1 G2: -0.8 *p*=0.022		G1: 5 (16.1) G2: 4 (12.9) **2 yrs** G1: 8 (25.8) G2: 6 (19.4) **Dietary Compliance** **14 wks:** MJ/d G1: 5.89 (1.78) G2: 5.96 (1.5) Total fat, %: G1: 11 G2: 20 Total CHO, %: G1: 78 G2: 62 Total proteins, %: G1: 12 G2: 18 Fiber, g: G1: 22 G2: 14 **1 yr:** NR **2 yrs:** NR
Thompson et al., 2005 RCT US, setting unclear Fair	G1. Lower fat, high-dairy diet group (energy deficit 500 kcal, 30% fat, 20% protein, and 50% CHO, 4 servings of dairy/day) G3. Lower fat, high-dairy and high-fiber group (energy deficit of 500 kcal, 30% fat, 20% protein, and 50% CHO, 4 servings of dairy/day, increase of fiber, and reduction in glycemic index) G3: Standard lower fat diet group (energy deficit 500 kcal, 30% fat,	Adults 25–70 yrs of age, BMI 30–40, 86% female, stable weight during previous 6 mos Weight, kg (SD): G1: 98.7 (11.0) G2: 99.1 (17.0) G3: 98.1 (13.3) BMI, kg/m^2 (SD): G1: 35.0 (3.2) G2: 34.5 (3.0)	Weight change, 48 wks Weight, kg (SD): G1: -8.8 (7.5) G2: -8.8 (7.9) G3: -9.1 (7.0) *p*=0.88 Other weight change outcomes: WC, hip circumference: cannot use the actual completer data, but can make a claim about the trend and authors report there was	N/A (Completers analysis with overall attrition >20%)	Withdrawals, *n* (%): G1: 8 (26.7) G2: 7 (22.6) G3: 3 (10.3) Overall: 18 (20) Participants who complied with diet and exercise over 75% of follow-up wks, *n* (%): G1: 18 (60.0) G2: 17 (54.9) G3: 18 (62.1) Dietary Compliance:

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, *n*	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	20% protein, and 50% CHO) All groups: Weekly visits during run-in and treatment periods Individualized 1:1 instruction with a dietitian Exercise was standardized at 30 min or more, at least 4 times per week. Diet and activity were monitored —instructed to exercise Exercise was recorded daily but not addressed directly in protocol Minutes of exercise/day were recorded by participants Duration Run-in: 2 wks Treatment: 48 wks	G3: 35.0 (3.1) n's G1: 30 G2: 31 G3: 29	no significant difference between ITT and completers		N/A (Completers only)

Summary Table 3.8. Meal Replacements and Adding Foods to Liquid Diets

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
Ashley et al., 2001 RCT US, university outpatient medical setting Fair	G1: Dietitian-led meal replacements shakes or bars) for 2 of 3 main meals; else USDA pyramid low-calorie diet (1,200 kcal/d, <30% fat) G2: Dietitian-led USDA pyramid low-calorie diet (1,200 kcal/day, <30% fat) G3*: Primary care office intervention incorporating meal replacements with individual physician and nurse visits All groups LEARN-based counseling; 26 sessions throughout the year.	Premenopausal women, 25–50 yrs of age, BMI 25–35 *n*'s G1: 38 G2: 37 Baseline characteristics provided for completers only G1: 26 G2: 23	**Weight loss at 1 yr** G1 lost, on average, 3.7 kg more than G2 *p*=0.008 [weight loss by group reported in figure only] Based on ITT using LOCF	NR by treatment group	Withdrawals, n (%): G1: 12 (31.6) G2: 14 (37.8) Dietary Compliance NR

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	Physical activity: unsupervised walking up to 10,000 steps/day Duration: Treatment: 1 yr *G3 does not meet I/E criteria for CQ3; results not reported here	Weight, kg (SD): G1: 83.5 (9.5) G2: 82.9 BMI, kg/m2 (SD): G1: 30.1 (2.9) G2: 29.9 (2.6)			
Wadden et al., 2004 RCT US, School / University Fair	G1: Meal Replacement: wks 2–13: 1,000 kcal/day diet with 4 servings/day of a liquid meal replacement (each serving: provided 160 kcal, with 14 g of protein, 20g of carbohydrate, and 3g of fat), combined with an evening meal of a frozen food entree, a serving of fruit, and a green salad; wks 14–17: decrease consumption of liquid diet, transition to 1,200-1,500 kcal/day diet of conventional foods G2: Balanced deficit diet: wks 2–40: self-selected balanced deficit diet (1200–1500 kcal/day, 15% protein, ≤30% fat, 55% CHO) *G3: Non-dieting approach: wks 1–6: give up dieting, do not restrict calorie intake; at wk 6: adopt a new eating plan (eating at least every 4 hrs, consuming any food that participants desired, stop eating when participants felt full); body image and self-esteem therapy for 40 wks All groups: Weekly group treatment sessions during wks 1–20; every-other week sessions during wks 22–40; follow-up group sessions at week 52 and week 65 Physical Activity: wks 2–20: aerobic activity 150 min/wk; wks 21–40: 180 min/wk Duration	Adult women, BMI 30–43 Weight, kg: G1: 96.2 G2: 99.2 G3: 96.1 Mean BMI, kg/m2: G1: 36.0 G2: 36.3 G3: 35.5 *n*'s: G1: 41 G2: 43 G3: 39	**At 20 wks** Weight change, % (SD) G1: -12.1 (6.7) G2: -7.8 (6.0) G1 vs. G2: P < 0.001 **At 40 wks** Weight change, % (SD) G1: -11.5 (8.9) G2: -8.4 (8.7) G1 vs. G2: *p*=NS **At 65 wks** Weight change,% (SD) G1: -8.6 (10.0) G2: -6.3 (8.4) G1 vs. G2: *p*=NS	NR	Withdrawals, *n* (%) **20 wks** G1: 4 (9.8) G2: 6 (14) G3: 1 (2.6) **40 wks** G1: 10 (24.4) G2: 13 (30.2) G3: 5 (12.8) **65 wks** G1: 13 (31.7) G2: 17 (39.5) G3: 11 (28.2) Dietary Compliance NR

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	Run-in: 1 wk Treatment: 40 wks Maintenance: 25 wks *G3 does not meet I/E criteria for CQ3; results not reported here				
Wien et al., 2003 RCT US, Outpatient medical setting – hospital Fair	G1: Low-calorie diet supplemented with 84 g/d of almonds; prescribed nutrient composition: 1,012 kcal, 32% CHO, 39% fat, 29% protein, 20 g fiber G2: Complex carbohydrate low-calorie diet: Subjects instructed on how to self-select a combination of complex carbohydrates daily from a food list that were equivalent in calories to 84 g almonds; list featured range of glycemic index complex carbohydrate-containing foods; also instructed to consume 2 tsp of safflower oil daily; nutrient composition: 1,015 kcal, 53% CHO, 18% fat, 29% protein, 32 g fiber G1 & G2: Prescribed Health Management Resources 70 Plus, a protein-sparing formulation, according to D&CVRRP guidelines Attended weekly clinic visits for assessments, followed by nutrition and behavior modification sessions Prescribed daily multivitamin and a salad Advised to refrain from exercise in wks 1–4 of the intervention; encouraged to walk 20–30 min/day 3-5 times/wk thereafter Run-in: 2 wks Duration: 24 wks Treatment: 24 wks	Adults 27–79 yrs of age, BMI 27–55 BMI, kg/m^2 (SD): G1: 39 (1) G2: 37 (1) Weight, kg (SD): G1: 113 (5) G2: 114 (5) WC, cm (SD): G1: 122 (5) G2: 117 (5) SBP, mmHg (SD): G1: 145 (4) G2: 138 (3) DBP, mmHg (SD): G1: 77 (2) G2: 78 (2) Fasting blood glucose, mg/Dl (SD): G1: 152 (12) G2: 152 (12) HDL-C, mg/Dl (SD): G1: 33 (2) G2: 33 (2) LDL-C, mg/Dl (SD): G1: 99 (5) G2: 108 (5) Triglycerides, mg/Dl (SD): G1: 180 (19) G2: 193 (16)	% change, 24 wks Weight: G1: -18 G2: -11 P < 0.0001 BMI: G1: -18 G2: -11 *p*<0.001 WC: G1: -14 G2: -9 *p*<0.05 Total body water: G1: -8 G2: -1 *p*<0.05 Fat mass: G1: -30 G2: -20 *p*<0.05	% change, 24 wks SBP: G1: -11 G2: 0 *p*<0.02 DBP: G1: -8 G2: -8 *p*=NS Total cholesterol: G1: -13 G2: -9 *p*=NS LDL-C: G1: -15 G2: -10 *p*=NS HDL-C: G1: -6 G2: +15 *p*<0.05 Triglycerides G1: -29 G2: -27 *p*=NS Blood Insulin: G1: -54 G2: -32 *p*=NS Blood Glucose: G1: -16 G2: -16	Withdrawals, *n* (%): G1: 8 (25) G2: 5 (15.2) Overall: 13 (20.0) Dietary Compliance: Compliance was monitored but no data reported No difference between groups in self-reported evaluation of satiety, palatability, or texture

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
		n's G1: 32 G2: 33		*p*=NS Ketone: G1: +260 G2: 0 *p*<0.02	

Summary Table 3.9. Very Low-Calorie-Diet (VLCD) Approaches

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
Lejeune et al., 2005 RCT The Netherlands, University outpatient medical clinic Fair	Weight loss phase: All participants received a 4--wk Very low-energy diet (VLED) (Modifast 2.1 MJ/day in addition to fruit and vegetables, 14% fat, 42% CHO, 44% protein) Protein was in a sachet of pure protein to be dissolved in water Weight maintenance phase: G1: Protein: Usual diet and additional 30 g protein/day (18–20% protein/day) G2: Control: Usual diet During weight maintenance phase, both groups visited university monthly for measurements and to meet with dietitian; dietary counseling provided upon request for all subjects Duration: Weight loss phase: 4 wks Weight maintenance phase: 6 mos Follow-up: 6 mos after weight maintenance phase, for measurement of body weight	Adults 18-60 yrs of age, BMI 25–35, good health (based on medical screening), non-smokers Weight, mean kg (SD): G1: 83.1 (11.1) G2: 83.4 (10.4) *n*'s: G1: 53 G2: 60 [120 randomized; 7 assigned to G1 withdrew during wk 1; ITT analysis included all 120]	**Weight, mean kg (SD):** **4 wks** G1: 76.7 (9.9) G2: 77.3 (9.9) *p*=NR (ns) **3 mos** G1: 76.7 (11.0) G2: 79.4 (10.9) *p*=NR (ns) **6 mos** G1: 77.5 (11.8) G2: 80.3 (11.6) *p*<0.05 **BMI, kg/m2 (SD):** **4 wks** G1: 27.0 (2.3) G2: 27.3 (2.6) *p*=NR (ns) **3 mos** G1: 27.0 (2.6) G2: 28.0 (3.0) *p*=NR (ns) **6 mos** G1: 27.3 (2.9) G2: 28.3 (3.2)	[blood glucose reported but for <60% of randomized participants]	Withdrawals G1: 7 (11.7) G2: 0 Compliance with the additional protein was shown by a higher amount of nitrogen in 24 hr urine in the protein group compared with the control group, g/d (SD): G1: 14·3 (3·5) G2: 11·2 (3·5) *p*<0·05

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
			p=NR (ns) % body fat **4 wks** G1: 35.6 (6.7) G2: 35.4 (6.9) *p*=NR (ns) **3 mos** G1: 33.7 (6.7) G2: 35.6 (6.9) *p*=NR (ns) **6 mos** G1: 33.8 (7.4) 36.2 (7.2) *p*=NR **Rate of regain, mean g/d (SD):** **3 mos** G1: 0.8 (42.5) G2: 22.9 (30.9) *p*< 0.05 **6 mos** G1: 4.7 (31.0) G2: 17.1 (20.0) p< 0.05		
Torgerson et al., 1999 RCT Sweden, inpatient medical setting Fair	G1: wks 1–16: Strict VLCD (456 kcal/day); G2: wks 1–16: VLCD-metabolic ward (456 kcal/day); G3: wks 1–16: VLCD-plus (456 kcal/day, 2 small meals/week) 30% fat, 50–55% CHO, 15–20% protein All groups: Wks 17–52: Hypocaloric diet for wks (500 kcal/day deficit, 25–30% fat, 50–55% CHO, 15–20% protein (2,100 kJ/day, 25–30% fat, 50–55% CHO, 15–20% protein) All patients provided with Modifast	Adults 20–60 yrs of age, BMI≥30, 77.7% female Weight, mean kg (SD): G1: 111.4 (15.5) G2: 107.2 (16.0) G3: 109.3 (16.0) –'s G1: 41 G2: 39 G3: 41	Weight loss, kg (SD): **16 wks** G1: -16.4 (10.8) G2: -16.0 (7.6) G3: -13.8 (8.6) G1 vs. G3: *p*=NR (ns) **24 wks** G1: -19.1 (10.5) G2: NR G3: -13.2 (9.8) G1 vs. G3: *p*<0.05 **52 wks** G1: -12.3 (10.0) G2: -10.2 (7.5)	NR by group	Withdrawals, *n* (%): 24 wks Overall: 21 (17.4) 52 wks G1: 19 (46.3) G2: 15 (38.5) G3: 14 (34.1) Attrition at 52 wks is too high to use 52 wk results Dietary Compliance: NR

Study Cited, Design, Setting, Quality Rating	Intervention Groups, Treatment Duration	Sample Characteristics, Group Size, n	Weight change	CVD Risk Factor Outcomes	Attrition Dietary Compliance
	during VLCD phase Duration Treatment: 52 wks		G3: -8.6 (11.8) G1 vs. G3: *p*=0.03		

Critical Question 4

Summary Table 4.1. Diet, Physical Activity, and Behavior Therapy Components in High-Intensity*, Onsite Lifestyle Interventions

*A high-intensity intervention is defined as providing 14 or more intervention sessions in the first 6 months.

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Weight Loss Trials Compared with Usual Care, Minimal Care, or No Care Control Interventions							
Outcome Data at 6 Months or Less as First Time Period Reporting							
PRIDE (The Program to Reduce Incontinence by Diet and Exercise) Subak et al., 2009 RCT, block randomization, 2:1 ratio, ITT is BOCF Weight is a secondary outcome US, outpatient	G1: Weight Loss Program *Diet:* Standard reduced-calorie diet (1,200–1,500 kcal./d, ≤30% fat), sample meal plans, vouchers for 2 meal replacements per day in months 1– 4, and 1 meal replacement per day thereafter *Physical Activity*: increased physical activity (brisk walking or activities of similar intensity) >200 min/wk *Behavior:* Behavioral skills (self-monitoring, stimulus control, and problem-solving) Comparator G2: Education	Duration: 6 mos Treatment: 0–6 mos Follow-up: NR Contacts G1: 24 (weekly sessions for 6 mo) G2: 4 (education sessions at mo 1, 2, 3 and 4) Provider G1: Experts in nutrition, exercise, and behavior change G2: Unclear	Women, >30 yr, with BMIs 25–50, with baseline incontinence *n*'s: G1: 226 G2: 112 Weight, kg (SD): G1: 98 (17) G2: 95 (16) BMI, kg/m^2 (SD) G1: 36.0 (6) G2: 36.0 (6)	At 6 mo Weight change, % (95% CI) G1: -8.0 (9, -7) G2: -1.6 (-2.7, -0.4) *p*<0.001 Weight change, kg (95% CI) G1: -7.8 (NR) G2: -1.5 (NR) *p*<0.001 Weight, kg (SD) G1: 90.0 (17.0) G2: 94.0 (17.0) *p*=NR	NA	NA	Withdrawals, *n* (%) G1: 5 (2.2) G2: 15 (13.4) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
medical setting Good	*Diet:* No intervention *Physical Activity*: no intervention *Behavior:* Educational sessions on weight loss, physical activity, and healthy eating habits						
Blumenthal et al., 2000 RCT, ITT, unclear if weight is BOCF Weight is a primary outcome US, outpatient medical setting Fair	G1: Weight Management *Diet*: 5021 J/d (women), 6276 J/d (men), 15–20% fat *Physical Activity*: aerobic exercise 55 min 3–4 times/wk *Behavior:* LEARN weight management program (lifestyle, exercise, attitudes, relationships, nutrition), self-monitoring of food intake and weight Comparators: G2: Exercise Only *Diet*: Usual diet Physical Activity: same as G1 *Behavior:* No intervention G3: Usual care *Diet*: Usual Physical Activity: Usual *Behavior:* No intervention	Duration: 26 wks Treatment: 26 wks Follow-up: NR Contacts: G1: plus 26 (weekly group sessions – LEARN program) G2: 72–96 min (weekly aerobic exercise sessions) G3: None Provider G1: Exercise physiologist and unclear for diet and behavioral interventions G2: Exercise physiologist G3: None	Adults, >29 ys, with BMIs of 25–37, and un-medicated high normal blood pressure or stage 1 to 2 hypertension *n*'s G1: 55 G2: 54 G3: 24 Weight, kg G1: 93.3 G2: 95.4 G3: 94.0 BMI, kg/m^2 G1: 32.1 G2: 32.8 G3: 32.6	At 6 mos Weight change, kg (SD) G1: -7.9 (6.0) G2: -1.8 (2.8) G3: +0.7 (3.3) G1 vs. G2: *p*=0.001 G1 + G2 vs. G3: *p*=0.001 Weight, kg (SD) G1: 85.4 (17.1) G2: 93.6 (14.2) G3: 94.7 (17.9) G1 vs. G2: *p*=NR G1 vs. G3: *p*=0.001	NA	NA	Withdrawals, *n* (%) G1: 9 (16.3) G2: 10 (18.5) G3: 2 (8.3) Attendance NR
DPP (Diabetes Prevention Program) Knowler et al., 2002 West et al., 2008 Knowler et al., 2009 RCT, West data presented here is secondary	G1: Intensive Lifestyle Modification *Diet*: Low-calorie and low-fat (<25%) *Physical activity*: Moderate intensity physical activity (walking) 150 min/wk *Behavior*: 16 lesson core curriculum on strategies for weight loss and physical activity changes, including self-monitoring of food intake,	Duration: average 2.8 yr Treatment: 30 mos Follow-up: NR Contacts: G1: 52 (16 individual sessions over 24 wk followed by bi-monthly individual or group sessions at minimum) G2: Annual 20–30 min	Adults, ≥25 yr, with BMIs of ≥24 (22 in Asians) and at high risk for diabetes *n*s for white, black, Hispanic participants G1: 962 G2: NR (1,082 for main study) G3: 985 Weight, kg (SD)	At 6 mo Weight change, kg (SD) G1: -7.1 (5.8) G2: NR G3: -2.2 (4.0) *p*=NR Weight change of at least 7% from baseline, % G1: 50 G2: NR	At 12 mo Weight change, kg (SD) G1: -7.1 (7.2) G2: NR G3: -2.8 (4.8) *p*=NR	At average of 2.8 yr Weight change, kg G1: -5.6 G2: -0.1 G3: -2.1 G1 vs. G3: *p*<0.001 G1 vs. G2: *p*<0.001 G2 vs. G3:	Withdrawals, *n* (%) G1: 107 (10) G2: 107 (10) G3: 106 (10) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
analysis using all available data without imputation for missing values or deleting incomplete observations, includes only White, African Americans and Hispanic participants (Asian Americans and Native Americans excluded) Weight is listed as a primary outcome for the secondary analysis US, 27 medical clinics Good	physical activity, and weight Comparator G2: Usual care + Placebo *Diet*: Food Guide Pyramid and NCEP Step 1 *Physical Activity*: Encouraged to increase physical activity (walking) 150 min/wk *Behavior*: Standard lifestyle recommendations G3: Usual care + Metformin *Diet*: Food Guide Pyramid and NCEP Step 1 *Physical Activity*: Encouraged to increase physical activity (walking) 150 min/wk *Behavior*: Standard lifestyle recommendations	meeting G3: Annual 20–30 min meeting Provider G1: Dietitians acted as Case Manager G2: same as G1 G3: same as G1	G1: 94.1 (20.8) G2: 94.3 (20.2) G3: 94.3 (19.9) BMI, kg/m^2 G1: 33.9 G2: 34.2 G3: 33.9	G3: NR		*p*<0.001 At 10 yr *absolute weight change data not reported; data presented in Figure only	
POWER (Practice-based Opportunities for Weight Reduction) – 1 of 3 independent trials Appel et al., 2011 RCT, ITT is LOCF Weight change from baseline to 24 mo is the	G1: Remote Support *Diet*: Recommended reduced calorie intake as part of DASH diet *Physical Activity*: Recommended increased exercise (no further detail provided) *Behavior*: Social cognitive theory framework incorporating behavior self-management approaches to set weight-related goals, self-monitor weight and weight-related behaviors (exercise and reduced calorie intake), increase self-efficacy and	Duration: 24 mo Treatment: 0–12 mo Follow-up: 12 mo Contacts: G1: 33 (12 weekly calls for the first 3 mo; one monthly call for next 3 mo; next 18 mo offered monthly calls; encouraged to log in to Web site on a weekly basis G2: 57 (nine 90 min group sessions and	Adults, ≥21 yr with one or more cardiovascular risk factor (hypertension,, hypercholesterol-emia or diabetes) n's G1: 139 G2: 138 G3: 138 Weight, kg (SD) G1: 102.1 (13.9) G2: 105.01 (13.9)	At 6 mo Weight change, % G1: -5.0 G2: -5.2 G3: -1.1 *p*=NS (value NR) Weight change, kg (SE) G1: -6.1 (0.5) G2: -5.8 (0.6) G3: -1.4 (0.4) *p*=NS (value NR) Proportion lost ≥5% baseline weight, *n*	NR	At 24 mo Weight change, % G1: -4.9 (0.8) G2: -5.2 (0.7) G3: -1.1 (0.6) G1 vs. G3: *p*<0.001 G2 vs. G3: p<0.001 G2 vs. G1: *p*=0.58 Weight change, kg (SE)	Withdrawal NR (Note: those without weight measurements at 24 mo: G1: 5%; G2: 4%; G3: 7% (% calculated by reviewer) Attendance at in-person visits, median Treatment

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
primary outcome US, primary care practices Good	social support, problem solving, included motivational interviewing, encouraged to lose 5% of weight; received Web-based support of learning modules, tools and reminders to record weight so can get feedback regarding weight loss progress Comparators G2: In-person support *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior*: Same as G1 but no motivational interviewing G3: Control *Diet*: None *Physical Activity*: None *Behavior*: Given brochures and a list of recommended Web sites promoting weight loss; met with a weight-loss coach at the time of randomization and, if desired, after the final data-collection visit	three 20 min individual sessions during first 3 mo; one 90 min group session and 2 20 min individual sessions during each of the following 3 mo; next 18 mo offered 2 monthly contacts – 1 group session and 1 individual session, with the latter conducted either in person or by telephone); also encouraged to log in to Web site on a weekly basis G3: 4 (baseline visit to collect data and meet with weight loss coach, and at 6, 12, and 24 mo follow-up visits for measurements only and 1 additional meeting with weight loss coach, if desired) Provider: G1: Weight loss coach and primary care provider (provided encouragement to work with coach) G2: same as G1 G3: Weight loss coach	G3: 104.4 (18.6) BMI, kg/m^2 (SD) G1: 36.0 (4.7) G2: 36.8 (5.2) G3: 36.8 (5.14)	(%) G1: 68 (52.7) G2: 57 (46.0) G3: 16 (14.2) G2 vs. G1*: p*<0.001 G3 vs. G2*: p*<0.001 G1 vs. G2*: p*=0.23 Proportion lost ≥10% baseline weight, *n (%)* G1: 30 (23.3) G2: -31 (25) G3: 4 (3.5) G2 vs. G1*: p*<0.001 G3 vs. G2*: p*<0.001 G1 vs. G2*: p*=0.92		G1: -4.6 (0.7) G2: -5.1 (0.8) G3: -0.8 (0.6) G1 vs. G3*: p*<0.001 G2 vs. G3*: p*<0.001 G2 vs. G1*: p*=0.77 Proportion lost ≥5% of baseline weight, *n* (%) G1: 50 (38.2) G2: 55 (41.4) G3: 24 (18.8) G1 vs. G3*: p*<0.001 G2 vs. G3*: p*<0.001 G2 vs. G1*: p*=0.73 Proportion lost ≥10% of baseline weight, *n* (%) G1: 24 (18.3) G2: 26 (19.5) G3: 11 (8.6) G1 vs. G3*: p*=0.02 G2 vs. G3*: p*=0.01 G2 vs. G1*: p*=0.69	G1: 14/15 G2: 14/21 G3: NA Follow-up G1: 16/18 G2: 16/36 G3: NA

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
TOHP-II (Trials of Hypertension Prevention, Phase II) Stevens et al., 2001 RCT Weight change is a primary outcome US, outpatient medical setting Good	G1: Weight Loss *Diet*: Reduced caloric intake; 1,500/1,200 kcal/day goals (men/women) *Physical Activity*: 30–45 min/day 4–5 days/wk; moderate exercise intensity (including brisk walking) *Behavior*: Self-directed behavior change, nutrition education, information on physical activity and social support for making and maintaining behavior changes (food diaries, graphs of activities, setting short-term goals, developing action plans to achieve objectives, alternative strategies for trigger problem eating) Comparator G2: Usual Care *Diet*: NR *Physical Activity*: NR *Behavior*: NR	Duration: 3 yr Treatment: 3 yr Follow-up: NR Contacts G1: ≤32 (1 individual counseling session followed by 14 weekly group meetings, 6 biweekly and then monthly group meetings up until mo 18) G2: NR Provider G1: Dietitians or Health Educators G2: None	Adults, ages 30–45, with BMIs of 26.1–37.4 (Men) 24.4/37.4 (Women) with non-medicated DBP of 83–89 mmHg and SBP <140 mmHg n's G1: 595 G2: 596 Weight, kg (SD) G1: Men: 98.9 (12.3) Women: 84.1 (11.9) G2: Men: 98.5 (11.7) Women: 82.9 (10.9) BMI, kg/m^2(SD) G1: Men: 31.0 (2.9) Women: 31.0 (3.6 G2: Men: 31.0 (2.9) Women: 30.8 (3.5)	*Note: completers data* At 6 mo Weight change, kg G1: -4.4 G2: +0.1 *p*<0.0001	NR	*Note: completers data* At 18 mo Weight change, kg G1: -2.0 G2: +0.7 *p*<0.0001 At 36 mo Weight change, kg G1: -0.2 G2: +1.8 *p*<0.0001	Withdrawals, *n* (%) G1: 48 (8) G2: 42 (7) % calculated by reviewer Attendance NR by group
ORBIT (Obesity Reduction Black Intervention Trial) Stolley et al., 2009 Fitzgibbon et al 2010 RCT, completers analysis Weight is a	G1: Weight Loss and Maintenance *Diet:* Weight loss phase: Low-fat, high-fiber diet (<30% fat, ≥25 g fiber) (≥5 servings/d fruits and vegs); maintenance phase: unclear/NR *Physical Activity:* Weight loss phase: Exercising at moderate to vigorous level 3–4 times/wk ≥30 min, including supervised exercise during group sessions; maintenance phase: continued exercise during group sessions *Behavior:* Weight loss phase:	Duration: 18 mo Treatment: 18 mo Weight loss: 0–6 mo Maintenance: 7–12 mos Follow-up: NR Contacts G1: 54 (2 sessions/wk for 24 wk, then monthly motivational interviewing sessions either face-to-face or by phone) G2: 6 (monthly phone	Adult, African American females, ages 30–65, with BMIs of 30–50 *n*'s: G1: 107 G2: 106 Weight, kg G1: 103.9 G2: 105.9 BMI, kg/m^2 G1: 38.7 G2: 39.8	*Note: completers data* At 6 mo Weight change, kg (SD) G1: -3.0 (4.9) G2: +0.2 (3.7) P< 0.001 Weight, kg (SD) G1: 101.3 (16.3) G2: 106.0 (17.5) P < 0.001 Subjects losing ≥ 5% from baseline, %	NR	*Note: completers data* At 18 mo Weight change, kg (SD) G1: -2.3 (7.4) G2: +0.5 (5.7) P = 0.003 Subjects losing ≥ 5% from baseline, % G1: 24 G2: 12 *p*=0.04	Withdrawals at 6 mo, *n* (%) G1: 7 (6.5) G2: 8 (7.5) Withdrawals for 7–18 mo G1: 7 G2: 0 Attendance at diet classes at 6 mo, % G1: 53.3 (31.5) G2: 52.5 (31.8)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
primary outcome US, academic setting Fair	discussion related to diet, physical activity and weight loss plus motivational interviewing sessions; Maintenance phase: unclear/NR Comparator G2: Control *Diet:* No intervention *Physical Activity:* No intervention *Behavior:* Weight loss phase: Newsletters and phone calls on general health and safety topics; Maintenance phase: unclear/NR continued newsletters/phone calls	calls to discuss/clarify newsletter content) Provider G1: Trained interventionist G2: Staff member not affiliated with weight loss intervention		G1: 26 G2: 5 *p*=NR			*p*=0.90 Attendance at diet classes from 7 to 18 mo, % G1: 27.1 (30.2) G2: NR
Outcome Data at Greater Than 6 Months as First Time Period Reporting							
Look AHEAD (Action for Health in Diabetes) Pi-Sunyer et al., 2007 Wadden et al., 2009 Wing et al., 2010 Wadden et al., 2011a RCT, completers analysis Weight is not listed in ET as a primary or secondary outcome US, outpatient medical setting	G1: Intensive Lifestyle *Diet*: Mo 0–6: ≤30% fat, ≤10% SF, 1,200–1,500 kcal/day <250 lb, 1,500–1,800 kcal/day >250 lb with use of MR; Mo 6–12: Personalized calorie target, optional 500 kcal/day deficit with use of meal replacements; *Physical Activity*: Goal of 175 min of moderate intensity physical activity per week; although walking encouraged, participants allowed to choose other types of moderate-intensity physical activity *Behavior*: Behavior change curriculum including self-monitoring of food intake and physical activity; "toolbox" approach of DPP to help participants achieve and maintain the study's weight loss and activity goals including problem	Duration: 1 yr Treatment: 1 yr Follow-up: NR Number of contacts: G1: 42 (Mo 0–6: 3 group weekly meetings (60–75 min) and 1 (20 min individual meeting per month; Mo 7–12: 2 group and 1 individual meeting per month G2: 4 (group educational/social support sessions) Provider: G1: Lifestyle counselor G2: Unclear	Adults, ages 45/55–74 yr (changed during 2nd yr of recruitment) with BMIs >25 or >27 if currently taking insulin; with HbA1cs <11%; SBPs <160 and DBPs <100 mm Hg ; triglycerides <600 mg/dL and CVD history *n*'s G1: 2,570 G2: 2,575 Weight, kg (SD) Women G1: 94.8 (17.9) G2: 95.4 (17.3) Men G1: 108.9 (19.0) G2: 109.0 (18.0)	NR	*Note: Completers data* At 12 mo Weight change, % (SD) G1: -8.6 (6.9) G2: -0.7 (4.8) *p*<0.001 Weight change, kg (SD) G1: -8.6 (8.2) G2: -0.7 (5.0) *p*<0.001 10% or greater weight reduction, % G1: 37.8 G2: 3.2 P < 0.001 7% or greater weight reduction from baseline, %	*Note: Completers data* At 4 yr Weight change, % (SD) G1: -4.7 (0.2) G2: -1.1 (0.2) *p*<0.001 Weight change, kg (SD) NR	Withdrawals, *n* (%) G1: 74 (3) G2: 112 (4) % calculated by reviewer Attendance, *n* (%) G1: 35.4 (7.3) G2: NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Fair	solving and motivational interviewing Comparator G2: Diabetes Support and Education *Diet:* None Physical Activity: None *Behavior*: General support and education (discussing topics related to diet, physical activity, and social support; received no counseling in behavioral strategies for changing diet and activity		BMI, kg/^{2} (SD) Women G1: 36.3 (6.2) G2: 36.6 (6.0) Men G1: 35.3 (5.7) G2: 35.1 (5.2)		G1: 55.2 % G2: 7.0 *p*<0.001		
Teixeira et al., 2010 RCT, ITT is BOCF Change in body weight is a primary outcome Portugal, school/ university Fair	G1: Weight loss *Diet:* Decrease daily caloric intake by 300–400 kcal *Physical activity:* No specific prescription but encouraged to find situations in their daily lives to increase caloric expenditure; pedometer offered *Behavior:* Cognitive behavior group sessions (based on self-determination theory; included aspects such as identifying personal resistances, overcoming lapses, establishing adequate goals, and implementing self-monitoring; topics covered emotional and external eating, improving body acceptance and body image Comparator G2: Control *Diet:* None *Physical Activity*: None *Behavior*: General health	Duration: 2 yr Treatment: 52 wk Follow-up: 1 yr Contacts G1: 30–120 min face-to-face meetings in groups of 25 to 30 participants) G2: Unclear (article states that curriculum based on several 3–6 week-long educational topics; format not described) Provider G1: 6 PhD or MS level exercise physiologists, nutritionists/dietitians and psychologists G2: Unclear/NR	Adult premenopausal females, ages 25–50, with BMIs between 25 and 40, free from major illnesses, not taking medications known to interfere with body weight regulation *n*'s G1: NR G2: NR Overall: 258 19 excluded from analyses due to medication to affect weight Weight, kg (SD) NR BMI, kg/m^2 Overall: 31.3 (4.1) Note: demographic data not reported by	NR	At 12 mo Weight change, % (SD) G1: -7.1 (7.0) G2: -1.7 (4.9) G1 vs. G2*: p*=NR Subjects with 5% weight loss from baseline, % G1: 61 G2: 16 G1 vs. G2: *p*<0.001 Subjects with 10% weight loss from baseline, % G1: 29 G2: 4 G1 vs. G2: *p*<0.001	At 24 mo Weight change, % (SD) G1: -4.9 (7.5) G2: -1.9 (6.9) G1 vs. G2*: p*=NR Subjects with 5% weight loss from baseline, % G1: 45 G2: 19 G1 vs. G2*:* *p*<0.001 Subjects with 10% weight loss from baseline, % G1: 18 G2: 8 G1 vs. G2*:* *p*<0.001	Withdrawals NR by group Attendance at sessions NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	education curriculum based on several educational courses on various topics (e.g., preventive nutrition, stress management, self-care, and effective communication skills)		treatment group; but article states intervention group did not differ from those in the control group in terms of BMI				
TONE (Trial of Non-pharmacologic Interventions in the Elderly) Whelton et al., 1998 Kumanyika et al., 2002 RCT, factorial analysis Weight loss is a secondary outcome US, school/ university Good	G1: Sodium Reduction and Weight Loss *Diet*: Weight loss diet with sodium restriction diet (goal of achieving and maintaining a 24-hr dietary sodium intake of 80 mmol (1800 mg) or less) and achieving and maintaining a weight loss of 4.5 kg (10 lb) or greater) by reducing calorie and fat intake *Physical activity*: Frequency and duration of activity individualized, with walking recommended most frequently. *Behavior* Combination of small group and individual meetings, (advised participants on ways to change eating patterns and increasing physical activity; food diaries used; primary goal was to provide participants with the core knowledge and behavior skills necessary to achieve behavior change) G2: Weight Loss Only *Diet*: Same as G1 without sodium restriction *Physical Activity*: Same as G1 *Behavior*: Same as G1 without focus on sodium restriction Comparators	Duration: 29 mo (median) Treatment (intensive): 4 mo Treatment (extended): 4 mo Maintenance: Unclear/NR Follow-up: 15–36 mo (range) 29 mo (median) Contacts: Treatment (intensive): G1: 16 (weekly sessions) G2: 16 (weekly sessions) G3: 16 (weekly sessions) G4: NR/ Unclear Treatment (extended): G1: 8 (biweekly sessions) G2: 8 (biweekly sessions) G3: 8 (biweekly sessions) G4: NR/ Unclear Maintenance: G1: NR (monthly sessions) G2: NR (monthly	Adults age 60–80 years, willing to participate, avg SBP <145mm Hg and DBP <85 mm Hg while taking a single antihypertensive medication or a single combination regimen consisting of a diuretic agent and a non-diuretic agent, stable health, independence in daily living, presumed capacity to alter diet and exercise as required by the study *n's* G1: 147 G2: 147 G3: 144* G4: 147 Weight, kg G1: 86.0 G2: 87.0 G3: 88.0 G4: 86.0 BMI, kg/m^2 G1: 31.2 G2: 31.0 G3: 31.2	NR	At 9 mo Mean Weight change, kg G1 & G2: -5.0 G3 & G4: -1.2 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.8 (3.1–4.5) G3 & G4: NR	At 18 mo Mean Weight change, kg G1 & G2: -4.4 G3 & G4: -0.8 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.6 (2.8–4.3) G3 & G4: NR At 30 mo Mean Weight change, kg G1 & G2: -4.7 G3 & G4: -0.9 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.9 (2.7-5.1) G3 & G4: -0.9 (0.4 -1.3) *-The mean weight loss in group 2 was 1.0 kg (95% CI -0.1-2.0) greater than in Group 1	Withdrawals, *n* (%) G1: 16 (10.9) G2: 10 (6.8) G3: 30 (8.8)* G4: 27 (7.9)* % calculated by reviewer Attendance at sessions, *n* (%) 9 mo: 884 (91) 18 mo: 829 (86) 30 mo: 441 (86) *-Both overweight and not overweight participants

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	G3: Sodium Reduction Diet: Sodium restricted diet (goal of achieving and maintaining a 24-hr dietary sodium intake of 80 mmol (1,800 mg) or less) *Physical Activity*: None *Behavior*: Combination of small group and individual meetings (advised participants on ways to change eating patterns; primary goal was to provide participants with the core knowledge and behavior skills necessary to achieve and maintain their desired reductions in sodium intake) G4: *Diet*: None *Physical Activity*: None *Behavior*: No study-related counseling in lifestyle change techniques but were invited to meetings on topics unrelated to the goals of the trial	sessions) G3: NR (monthly sessions) G4: Unclear/NR Provider: G1: Nutritionists and exercise counselors G2: Nutritionists and exercise G3: Nutritionists and exercise counselors G4: Nutritionists and exercise counselors	G4: 31.3 *Information reported here is for overweight subjects (*N*=585) only.				
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
ADAPT (The Arthritis, Diet and Activity, Promotion Trial) Messier et al., 2004 RCT, 2x2 factoral design, ITT was computed missing values Weight loss is a secondary	G1: Combined exercise and dietary weight loss *Diet*: 500 kcal/day deficit, nutrient intake NR, no food provided *Physical Activity*: 180 min/wk, aerobics and strength training *Behavior:* Behavior therapy of group dynamics and social cognitive theory Comparators G2: Dietary weight loss *Diet*: 500 kcal/day deficit, nutrient	Duration: 18 mo Treatment: 26 wk Follow-up: 6 to 18 months Contacts G1: 70 (diet: see G1 and exercise: see G2) G2: 44 (16 weekly sessions in months 1–4, then group/individual sessions biweekly sessions in months 5–6, then alternating every	Adults, ≥60 yr of age, with BMIs ≥28, sedentary life-style, knee osteoarthritis with pain, *n*'s G1: 76 G2: 82 G3: 80 G4: 78 Weight, kg (SEM) G1: 92 (0.2) G2: 95 (0.2) G3: 92 (0.2)	NR	NR	At 18 mo Weight change, % G1: -5.7 G2: -4.9 G3: -3.7 G4: -1.2 G1 vs. G4: $p<0.05$ G2 vs. G4: $p<0.05$ Weight change, kg (95% CI)	Withdrawals, *n* (%) G1: 18 (24) G2: 19 (23) G3: 16 (20) G4: 11 (14) % calculated by reviewer Attendance at sessions, % G1: 64 G2: 72 G3: 60

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
outcome US, school/ university Good	intake NR, no food provided *Physical Activity*: no exercise *Behavior:* Behavior therapy: group dynamics and social cognitive theory. Behavior change using self-regulatory skills including self-monitoring G3: Structured exercise *Diet*: usual diet *Physical Activity*: 180 min/wk, aerobics and strength training *Behavior:* No guided behavioral therapy G4: Healthy Lifestyle Control *Diet*: None *Physical Activity*: No exercise *Behavior:* No guided behavioral therapy	2 wk meetings/phone contacts plus newsletters in months 7–18 with the duration of each contact NR G3: 48 (exercise contacts: 3x/wk/60 min/session at facility in months 1–3, then option of doing home based, duration of contact NR G4: 12 (1 hr monthly meetings in months 1–3, monthly phone calls in months 4–6, then bimonthly phone calls from months 7–18) Provider G1: Both dietitian and exercise physiologist trained by health psychologist G2: Master's degree dietitian/ nutritionist Health Educator G3: Exercise Physiologist G4: Health Educator	G4: 96 (0.2) BMI, kg/m^2 (SD) G1: 34.0 (0.7) G2: 34.5 (0.6) G3: 34.2 (0.6) G4: 34.2 (0.6)			G1: -5.20 (0.85, 9.55) G2: -4.61 (0.38, 8.84) G3: -3.46 (-0.77, 7.69) G4: 1.10 (-3.00, 5.20) G1 vs. G4: $p<0.05$ G2 vs. G4: $p<0.05$	G4: 73

Summary Table 4.2. Evidence for the Comprehensive Interventions Compared with Usual Care, Minimal Care, or No-Treatment Control

*A high intensity intervention is defined as providing 14 or more intervention sessions in the first 6 months.

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Weight Loss Trials Compared with Usual Care, Minimal Care, or No Care Control Interventions							
Outcome Data at 6 Months or Less as First Time Period Reporting							
PRIDE (The Program to Reduce Incontinence by Diet and Exercise Subak et al., 2009 RCT, block randomization, 2:1 ratio, ITT is BOCF Weight is a secondary outcome US, outpatient medical setting Good	G1: Weight Loss Program *Diet:* Standard reduced-calorie diet (1200 – 1500 kcal/day, ≤30% fat), sample meal plans, vouchers for 2 meal replacements per day in months 1–4, and 1 meal replacement per day thereafter *Physical Activity*: increased physical activity (brisk walking or activities of similar intensity) >200 min/wk *Behavior:* Behavioral skills (self-monitoring, stimulus control, and problem-solving) Comparator G2: Education *Diet:* No intervention *Physical Activity*: No intervention *Behavior:* Educational sessions on weight loss, physical activity, and healthy eating habits	Duration: 6 mo Treatment: 0–6 mo Follow-up: NR Contacts G1: 24 (weekly sessions for 6 mo) G2: 4 (education sessions at months 1, 2, 3 and 4) Provider G1: Experts in nutrition, exercise, and behavior change G2: Unclear	Women, >30 yr, with BMIs 25–50, with baseline incontinence *n*'s: G1: 226 G2: 112 Weight, kg (SD): G1: 98 (17) G2: 95 (16) BMI, kg/m^2 (SD) G1: 36.0 (6) G2: 36.0 (6)	At 6 mo Weight change, % (95% CI) G1: -8.0 (9, -7) G2: -1.6 (-2.7, -0.4) *p*<0.001 Weight change, kg (95% CI) G1: -7.8 (NR) G2: -1.5 (NR) *p*<0.001 Weight, kg (SD) G1: 90.0 (17.0) G2: 94.0 (17.0) *p*=NR	NA	NA	Withdrawals, *n* (%) G1: 5 (2.2) G2: 15 (13.4) Attendance NR
Blumenthal et al., 2000 RCT, ITT, unclear if weight is BOCF Weight is a primary outcome	G1: Weight Management *Diet*: 5021 J/d (women), 6276 J/d (men), 15–20% fat *Physical Activity*: Aerobic exercise 55 min 3–4 times/wk *Behavior:* LEARN weight management program (lifestyle, exercise, attitudes, relationships,	Duration: 26 wk Treatment: 26 wk Follow-up: NR Contacts: G1: plus 26 (weekly group sessions – LEARN program) G2: 72-96 (weekly	Adults, > 29 years of age, with BMIs of 25–37, and un-medicated high normal BP or stage 1 to 2 hypertension n's G1: 55	At 6 mo Weight change, kg (SD) G1: -7.9 (6.0) G2: -1.8 (2.8) G3: +0.7 (3.3) G1 vs. G2*: p*=0.001 G1 + G2 vs. G3:	NA	NA	Withdrawals, *n* (%) G1: 9 (16.3) G2:10 (18.5) G3: 2 (8.3) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
US, outpatient medical setting Fair	nutrition), self-monitoring of food intake and weight Comparators: G2: Exercise Only *Diet*: Usual diet Physical Activity: same as G1 *Behavior:* no intervention G3: Usual care *Diet*: Usual Physical Activity: Usual *Behavior:* No intervention	aerobic exercise sessions) G3: None Provider G1: Exercise Physiologist and unclear for diet and behavioral interventions G2: Exercise Physiologist G3: None	G2: 54 G3: 24 Weight, kg G1: 93.3 G2: 95.4 G3: 94.0 BMI, kg/m^2 G1: 32.1 G2: 32.8 G3: 32.6	*p*=0.001 Weight, kg (SD) G1: 85.4 (17.1) G2: 93.6 (14.2) G3: 94.7 (17.9) G1 vs. G2*: p*=NR G1 vs. G3*: p*=0.001			
DPP (Diabetes Prevention Program) Knowler et al., 2002 West et al., 2008 Knowler et al., 2009 RCT, West data presented here is secondary analysis using all available data without imputation for	G1: Intensive Lifestyle Modification *Diet:* Low-calorie and low-fat (<25%) *Physical Activity*: Moderate intensity physical activity (walking) 150 min/wk *Behavior*: 16 lesson core curriculum on strategies for weight loss and physical activity changes, including self-monitoring of food intake, physical activity, and weight Comparator G2: Usual care + Placebo *Diet*: Food Guide Pyramid and NCEP Step 1 *Physical Activity*: Encouraged to increase physical activity (walking)	Duration: average 2.8 yr Treatment: 30 mo Follow-up: NR Contacts: G1: 52 (16 individual sessions over 24 wk, followed by bimonthly individual or group sessions at minimum) G2: Annual 20–30 min meeting G3: Annual 20–30 min meeting Provider G1: Dietitians acted as Case Manager	Adults, ≥25 yr of age, with BMIs of ≥24 (22 in Asians) and at high risk for diabetes *n*'s for White, African American, Hispanic participants G1: 962 G2: NR (1,082 for main study) G3: 985 Weight, kg (SD) G1: 94.1 (20.8) G2: 94.3 (20.2) G3: 94.3 (19.9) BMI, kg/m^2 G1: 33.9	At 6 mo Weight change, kg (SD) G1: -7.1 (5.8) G2: NR G3: -2.2 (4.0) *p*=NR Weight change of at least 7% from baseline, % G1: 50 G2: NR G3: NR	At 12 mo Weight change, kg (SD) G1: -7.1 (7.2) G2: NR G3: -2.8 (4.8) *p*=NR	At average of 2.8 yr Weight change, kg G1: -5.6 G2: -0.1 G3: -2.1 G1 vs. G3*: p*<0.001 G1 vs. G2*: p*<0.001 G2 vs. G3*: p*<0.001 At 10 yr *absolute weight change data not reported; data	Withdrawals, *n* (%) G1: 107 (10) G2: 107 (10) G3: 106 (10) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
missing values or deleting incomplete observations, includes only White, African American, and Hispanic participants (Asian Americans and Native Americans excluded) Weight is listed as a primary outcome for the secondary analysis US, 27 medical clinics Good	150 min/wk *Behavior*: Standard lifestyle recommendations G3: Usual care + Metformin *Diet*: Food Guide Pyramid and NCEP Step 1 *Physical Activity*: Encouraged to increase physical activity (walking) 150 min/wk *Behavior*: standard lifestyle recommendations	G2: same as G1 G3: same as G1	G2: 34.2 G3: 33.9			presented in Figure only	
POWER (Practice-based Opportunities for Weight Reduction) – 1 of 3 independent trials Appel et al, 2011 RCT, ITT is LOCF Weight change from baseline to 24 mo is the primary outcome	G1: Remote Support *Diet*: Recommended reduced calorie intake as part of DASH diet *Physical Activity*: Recommended increased exercise (no further detail provided) *Behavior*: Social cognitive theory framework incorporating behavior self-management approaches to set weight-related goals, self-monitor weight and weight-related behaviors (exercise and reduced calorie intake), increase self-efficacy and social support, problem solving, included motivational interviewing, encouraged to lose 5% of weight;	Duration: 24 mo Treatment: 0–12 mo Follow-up: 12 mo Contacts: G1: 33 (12 weekly calls for the first 3 mo; one monthly call for next 3 mo; next 18 mo offered monthly calls; encouraged to log in to Web site weekly G2: 57 (nine 90-min group sessions and three 20-min individual sessions during first 3 mo; one 90-min group session and 2 20-min	Adults, age ≥21 with one or more cardiovascular risk factor (hypertension, hypercholesterol-emia or diabetes) *n*'s G1: 139 G2: 138 G3: 138 Weight, kg (SD) G1: 102.1 (13.9) G2: 105.01 (13.9) G3: 104.4 (18.6) BMI, kg/m^2 (SD) G1: 36.0 (4.7) G2: 36.8 (5.2)	At 6 mo Weight change, % G1: -5.0 G2: -5.2 G3: -1.1 *p*=NS (value NR) Weight change, kg (SE) G1: -6.1 (0.5) G2: -5.8 (0.6) G3: -1.4 (0.4) *p*=NS (value NR) Proportion lost ≥5% baseline weight, *n* (%) G1: 68 (52.7) G2: 57 (46.0)	NR	At 24 mo Weight change, % G1: -4.9 (0.8) G2: -5.2 (0.7) G3: -1.1 (0.6) G1 vs. G3: *p*<0.001 G2 vs. G3: *p*<0.001 G2 vs. G1: *p*=0.58 Weight change, kg (SE) G1: -4.6 (0.7) G2: -5.1 (0.8)	Withdrawal NR (Note: those without weight measurements at 24 mo: G1: 5%; G2: 4%; G3: 7% (% calculated by reviewer) Attendance at in-person visits, median Treatment G1: 14/15 G2: 14/21

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
US, primary care practices Good	received Web-based support of learning modules, tools, and reminders to record weight so can get feedback regarding weight loss progress Comparators G2: In-person Support *Diet*: same as G1 *Physical Activity*: Same as G1 *Behavior*: Same as G1 but no motivational interviewing G3: Control *Diet*: None *Physical Activity*: None *Behavior*: Given brochures and a list of recommended Web sites promoting weight loss; met with a weight-loss coach at the time of randomization and, if desired, after the final data collection visit	individual sessions during each of the following 3 mo; next 18 mo offered 2 monthly contacts – 1 group session and 1 individual session, with the latter conducted either in person or by telephone); also encouraged to log in to Web site weekly G3: 4 (baseline visit to collect data and meet with weight loss coach, and at 6, 12, and 24 mo follow-up visits for measurements only and 1 additional meeting with weight loss coach, if desired) Provider: G1: Weight loss coach and primary care provider (provided encouragement to work with coach) G2: same as G1 G3: Weight loss coach	G3: 36.8 (5.14)	G3: 16 (14.2) G2 vs. G1: $p<0.001$ G3 vs. G2: $p<0.001$ G1 vs. G2: $p=0.23$ Proportion lost ≥10% baseline weight, *n* (%) G1: 30 (23.3) G2: -31 (25) G3: 4 (3.5) G2 vs. G1: $p<0.001$ G3 vs. G2: $p<0.001$ G1 vs. G2: $p=0.92$		G3: -0.8 (0.6) G1 vs. G3: $p<0.001$ G2 vs. G3: $p<0.001$ G2 vs. G1: $p=0.77$ Proportion lost ≥5% of baseline weight, *n* (%) G1: 50 (38.2) G2: 55 (41.4) G3: 24 (18.8) G1 vs. G3: $p<0.001$ G2 vs. G3: $p<0.001$ G2 vs. G1: $p=0.73$ Proportion lost ≥10% of baseline weight, *n* (%) G1: 24 (18.3) G2: 26 (19.5) G3: 11 (8.6) G1 vs. G3: $p=0.02$ G2 vs. G3: $p=0.01$ G2 vs. G1: $p=0.69$	G3: NA Follow-up G1: 16/18 G2: 16/36 G3: NA

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
TOHP-II (Trials of Hypertension Prevention, Phase II) Stevens et al., 2001 RCT Weight change is a primary outcome US, outpatient medical setting Good	G1: Weight Loss *Diet*: Reduced caloric intake; 1,500/1,200 kcal/day goals (men/women) *Physical Activity*: 30–45 min/day 4–5 days/wk; moderate exercise intensity (including brisk walking) *Behavior*: Self-directed behavior change, nutrition education, information on physical activity and social support for making and maintaining behavior changes (food diaries, graphs of activities, setting short term goals, developing action plans to achieve objectives, alternative strategies for trigger problem eating) Comparator G2: Usual Care *Diet*: NR *Physical Activity*: NR *Behavior*: NR	Duration: 3 yr Treatment: 3 yr Follow-up: NR Contacts G1: ≤32 (1 individual counseling session followed by 14 weekly group meetings, 6 biweekly and then monthly group meetings up until mo 18) G2: NR Provider G1: Dietitians or Health Educators G2: None	Adults, ages 30–45, with BMIs of 26.1–37.4 (men), 24.4–37.4 (women), with non-medicated DBPs of 83–89 mmHg and SBP <140 mmHg *n*'s G1: 595 G2: 596 Weight, kg (SD) G1: Men: 98.9 (12.3) Women: 84.1 (11.9) G2: Men: 98.5 (11.7) Women: 82.9 (10.9) BMI, kg/m^2 (SD) G1: Men: 31.0 (2.9) Women: 31.0 (3.6 G2: Men: 31.0 (2.9) Women: 30.8 (3.5)	*Note: completers data* At 6 mo Weight change, kg G1: -4.4 G2: +0.1 *p*<0.0001	NR	*Note: completers data* At 18 mo Weight change, kg G1: -2.0 G2: +0.7 *p*<0.0001 At 36 mo Weight change, kg G1: -0.2 G2: +1.8 *p*<0.0001	Withdrawals, *n* (%) G1: 48 (8) G2: 42 (7) % calculated by reviewer Attendance NR by group
ORBIT (Obesity Reduction Black Intervention Trial) Stolley et al., 2009 Fitzgibbon et al 2010 RCT, completers analysis Weight is a primary	G1: Weight Loss and Maintenance *Diet:* Weight loss phase: Low-fat, high-fiber diet (<30% fat, ≥25 g fiber) (≥5 servings/day fruits and vegs); Maintenance phase: Unclear/NR *Physical Activity:* Weight loss phase: Exercising at moderate to vigorous level 3–4 times/wk ≥30 min, including supervised exercise during group sessions; Maintenance phase: continued exercise during group sessions *Behavior:* Weight loss phase: discussion related to diet, physical	Duration: 18 mo Treatment: 18 mo Weight loss: 0–6 mo Maintenance: 7–12 mo Follow-up: NR Contacts G1: 54 (2 sessions/wk for 24 wk, then monthly motivational interviewing sessions either face-to-face or by phone) G2: 6 (monthly phone calls to discuss/clarify	Adult, African American females, ages 30–65, with BMIs of 30–50 *n*'s: G1: 107 G2: 106 Weight, kg G1: 103.9 G2: 105.9 BMI, kg/m^2 G1: 38.7 G2: 39.8	*Note: completers data* At 6 mo Weight change, kg (SD) G1: -3.0 (4.9) G2: +0.2 (3.7) *p*<0.001 Weight, kg (SD) G1: 101.3 (16.3) G2: 106.0 (17.5) *p*<0.001 Subjects losing ≥5% from baseline, % G1: 26 G2: 5	NR	*Note: completers data* At 18 mo Weight change, kg (SD) G1: -2.3 (7.4) G2: +0.5 (5.7) *p*=0.003 Subjects losing ≥5% from baseline, % G1: 24 G2: 12 *p*=0.04	Withdrawals at 6 months, *n* (%) G1: 7 (6.5) G2: 8 (7.5) Withdrawals for 7–18 mo G1: 7 G2: 0 Attendance at diet classes at 6 mo, % G1: 53.3 (31.5) G2: 52.5 (31.8) *p*=0.90

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
outcome US, academic setting Fair	activity, and weight loss plus motivational interviewing sessions; Maintenance phase: Unclear /NR Comparator G2: Control *Diet:* No intervention *Physical Activity:* No intervention *Behavior:* Weight loss phase: Newsletters and phone calls on general health and safety topics; Maintenance phase: Unclear/NR continued newsletters/phone calls	newsletter content) Provider G1: Trained interventionist G2: Staff member not affiliated with weight loss intervention		*p*=NR			Attendance at diet classes from 7–18 mo, % G1: 27.1 (30.2) G2: NR
Outcome Data at Greater Than 6 Months as First Time Period Reporting							
Look AHEAD (Action for Health in Diabetes) Pi-Sunyer et al., 2007 Wadden et al., 2009 Wadden et al., 2011a RCT, completers analysis Weight is not listed in ET as a primary or secondary outcome US, outpatient medical setting Fair	G1: Intensive Lifestyle *Diet*: Mo 0–6: ≤30% fat, ≤10% saturated fat, 1200–1500 kcal/day <250 pounds, 1500–1800 kcal/day >250 lbs with use of meal replacements; Mo 6–12: Personalized calorie target, optional 500 kcal/day deficit with use of meal replacements; *Physical Activity*: goal of 175 min of moderate intensity physical activity per week; although walking encouraged, participants allowed to choose other types of moderate-intensity physical activity *Behavior*: Behavior change curriculum including self-monitoring of food intake and physical activity; "toolbox" approach of DPP to help participants achieve and maintain the study's weight loss and activity goals including problem solving and motivational interviewing Comparator	Duration: 1 yr Treatment: 1 yr Follow-up: NR Number of contacts: G1: 42 (Mo 0–6: 3 group weekly meetings (60–75 min) and 1 (20 min individual meeting per month; Mo 7–12: 2 group and 1 individual meeting per month G2: 4 (group educational/social support sessions) Provider: G1: Lifestyle counselor G2: Unclear	Adults, ages 45–55 to 74 yr (changed during 2nd yr of recruitment) with BMIs >25 or >27 if currently taking insulin; with HbA1cs <11%; SBPs <160 and DBPs <100 mm Hg ; Triglycerides <600 mg/dL and CVD history *n*'s G1: 2,570 G2: 2,575 Weight, kg (SD) Women G1: 94.8 (17.9) G2: 95.4 (17.3) Men G1: 108.9 (19.0) G2: 109.0 (18.0) BMI, $kg/^2$ (SD) Women	NR	*Note: Completers data* At 12 mo Weight change, % (SD) G1: -8.6 (6.9) G2: -0.7 (4.8) *p*<0.001 Weight change, kg (SD) G1: -8.6 (8.2) G2: -0.7 (5.0) *p*<0.001 10% or greater weight reduction, % G1: 37.8 G2: 3.2 *p*<0.001 7% or greater weight reduction from baseline, % G1: 55.2 % G2: 7.0	*Note: Completers data* At 4 yr Weight change, % (SD) G1: -4.7 (0.2) G2: -1.1 (0.2) *p*<0.001 Weight change, kg (SD) NR	Withdrawals, *n* (%) G1: 74 (3) G2: 112 (4) % calculated by reviewer Attendance, *n* (%) G1: 35.4 (7.3) G2: NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	G2: Diabetes Support and Education *Diet:* None *Physical Activity*: None *Behavior*: General support and education (discussing topics related to diet, physical activity, and social support; received no counseling in behavioral strategies for changing diet and activity		G1: 36.3 (6.2) G2: 36.6 (6.0) Men G1: 35.3 (5.7) G2: 35.1 (5.2)		*p*<0.001		
Teixeira et al., 2010 RCT, ITT is BOCF Change in bodyweight is a primary outcome Portugal, school/ university Fair	G1: Weight Loss *Diet:* decrease daily caloric intake by 300–400 kcal *Physical activity:* No specific prescription but encouraged to find situations in their daily lives to increase caloric expenditure; pedometer offered *Behavior:* Cognitive behavior group sessions (based on self-determination theory; included aspects such as identifying personal resistances, overcoming lapses, establishing adequate goals, and implementing self-monitoring; topics covered emotional and external eating, improving body acceptance and body image Comparator G2: Control *Diet:* None *Physical Activity*: None *Behavior*: General health education curriculum based on several educational courses on various topics (e.g., preventive nutrition, stress management,	Duration: 2 yr Treatment: 52 wk Follow-up: 1 yr Contacts G1: 30–120 minute face-to-face meetings in groups of 25–30 participants G2: Unclear (article states that curriculum based on several 3–6 week-long educational topics; format not described) Provider G1: 6 PhD or MS level exercise physiologists, nutritionists/dietitians and psychologists G2: Unclear/NR	Adult premenopausal females, ages 25–50 yr, with BMI's between 25 and 40, free from major illnesses, not taking medications known to interfere with body weight regulation *n*'s G1: NR G2: NR Overall: 258 19 excluded from analyses due to medication to affect weight Weight, kg (SD) NR BMI, kg/m^2 Overall: 31.3 (4.1) Note: demographic data not reported by treatment group; but article states intervention group	NR	At 12 mo Weight change, % (SD) G1: -7.1 (7.0) G2: -1.7 (4.9) G1 vs. G2*: p*=NR Subjects with 5% weight loss from baseline, % G1: 61 G2: 16 G1 vs. G2: *p*<0.001 Subjects with 10% weight loss from baseline, % G1: 29 G2: 4 G1 vs. G2: *p*<0.001	At 24 mo Weight change, % (SD) G1: -4.9 (7.5) G2: -1.9 (6.9) G1 vs. G2*: p*=NR Subjects with 5% weight loss from baseline, % G1: 45 G2: 19 G1 vs. G2*: p*<0.001 Subjects with 10% weight loss from baseline, % G1: 18 G2: 8 G1 vs. G2*: p*<0.001	Withdrawals NR by group Attendance at sessions NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	self-care, and effective communication skills)		did not differ from those in control group in terms of BMI				
TONE (Trial of Non-pharmacologic Interventions in the Elderly) Whelton et al., 1998 Kumanyika et al., 2002 RCT, factorial analysis Weight loss is a secondary outcome US, school/ university Good	G1: Sodium Reduction and Weight Loss *Diet*: Weight loss diet with sodium restriction diet (goal of achieving and maintaining a 24-hour dietary sodium intake of 80mmol (≤1800 mg) and achieving and maintaining a weight loss of 4.5 kg (≥10 lb) *Physical Activity*: None *Behavior*: Combination of small group and individual meetings, (advised participants on ways to change eating patterns and increasing physical activity; primary goal was to provide participants with the core knowledge and behavior skills necessary to achieve and maintain their desired reductions in sodium intake) G2: Weight Loss Only *Diet*: Weight loss diet without sodium restriction (goal was achieving and maintaining a weight loss of 4.5 kg (≥10 lb) *Physical Activity*: None *Behavior*: Combination of small group and individual meetings; counseling on increasing physical activity and ways to change eating patterns; primary goal was to provide participants with the core knowledge and behavior skills necessary to achieve and maintain their desired reductions in body	Duration: 29 mo (median) Treatment (intensive): 4 mo Treatment (extended): 4 mo Maintenance: Unclear/NR Follow-up: 15–36 mo (range) 29 mo (median) Contacts: Treatment (intensive): G1: 16 (weekly sessions) G2: 16 (weekly sessions) G3: 16 (weekly sessions) G4: NR/unclear Treatment (extended): G1: 8 (biweekly sessions) G2: 8 (biweekly sessions) G3: 8 (biweekly sessions) G4: NR/ Unclear Maintenance: G1: NR (monthly sessions) G2: NR (monthly sessions) G3: NR (monthly	Adults age 60–80, willing to participate, avg SBP <145mm Hg and DBP <85 mm Hg while taking a single antihypertensive medication or a single combination regimen consisting of a diuretic agent and a non-diuretic agent, stable health, independence in daily living, presumed capacity to alter diet and exercise as required by the study *n*'s G1: 147 G2: 147 G3: 144* G4: 147 Weight, kg G1: 86.0 G2: 87.0 G3: 88.0 G4: 86.0 BMI, kg/m^2 G1: 31.2	NR	At 9 mo Mean Weight change, kg G1 & G2: -5.0 G3 & G4: -1.2 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.8 (3.1–4.5) G3 & G4: NR	At 18 mo Mean Weight change, kg G1 & G2: -4.4 G3 & G4: -0.8 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.6 (2.8-4.3) G3 & G4: NR At 30 mo Mean Weight change, kg G1 & G2: -4.7 G3 & G4: -0.9 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.9 (2.7-5.1) G3 & G4: -0.9 (0.4 -1.3) *-The mean weight loss in group 2 was 1.0 kg (95% CI -0.1-2.0) greater than in Group 1.	Withdrawals, *n* (%) G1: 16 (10.9) G2: 10 (6.8) G3: 30 (8.8)* G4: 27 (7.9)* % calculated by reviewer Attendance at sessions, *n* (%) 9 mo: 884 (91) 18 mo: 829 (86) 30 mo: 441 (86) *-Both overweight and not overweight participants.

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	weight) Comparators G3: Sodium Reduction *Diet*: Sodium restricted diet (goal of achieving and maintaining a 24-hour dietary sodium intake of 80mmol (≤1800 mg) *Physical Activity*: None *Behavior*: Combination of small group and individual meetings (advised participants on ways to change eating patterns; primary goal was to provide participants with the core knowledge and behavior skills necessary to achieve and maintain their desired reductions in sodium intake) G4: *Diet*: None *Physical Activity*: None *Behavior*: No study-related counseling in lifestyle change techniques but were invited to meetings on topics unrelated to the goals of the trial	sessions) G4: Unclear/NR Provider: G1: Nutritionists and exercise counselors G2: Nutritionists and exercise G3: Nutritionists and exercise counselors G4: Nutritionists and exercise counselors	G2: 31.0 G3: 31.2 G4: 31.3 *Information reported here is for overweight subjects (*N*=585) only.				
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
ADAPT (The Arthritis, Diet and Activity, Promotion Trial) Messier et al., 2004 RCT, 2x2 factoral design, ITT was computed	G1: Combined exercise and dietary weight loss *Diet*: 500 kcal/day deficit, nutrient intake NR, no food provided *Physical Activity*: 180 min/wk, aerobics and strength training *Behavior:* Behavior therapy of group dynamics and social cognitive theory Comparators G2: Dietary weight loss	Duration: 18 mo Treatment: 26 wk Follow-up: 6–18 mo Contacts G1: 70 (diet: see G1 and exercise: see G2) G2: 44 (16 weekly sessions in mo 1–4, then group/individual sessions biweekly sessions in mo 5–6,	Adults, ≥60 yr, with BMIs ≥28, sedentary lifestyle, knee OA with pain *n*'s G1: 76 G2: 82 G3: 80 G4: 78 Weight, kg (SEM) G1: 92 (0.2) G2: 95 (0.2)	NR	NR	At 18 mo Weight change, % G1: -5.7 G2: -4.9 G3: -3.7 G4: -1.2 G1 vs. G4: $p<0.05$ G2 vs. G4: $p<0.05$	Withdrawals, *n* (%) G1: 18 (24) G2: 19 (23) G3: 16 (20) G4: 11 (14) % calculated by reviewer Attendance at sessions, % G1: 64 G2: 72

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
missing values Weight loss is a secondary outcome US, school/ university Good	*Diet* : 500 kcal/day deficit, nutrient intake NR, no food provided *Physical Activity*: No exercise *Behavior:* Behavior therapy: group dynamics and social cognitive theory. Behavior change using self-regulatory skills including self-monitoring G3: Structured exercise *Diet* : Usual diet *Physical Activity*: 180 min/wk, aerobics and strength training *Behavior:* No guided behavioral therapy G4: Healthy Lifestyle Control *Diet* : None *Physical Activity*: No exercise *Behavior:* No guided behavioral therapy	then alternating every 2 wk meetings/phone contacts plus newsletters in mo 7–18 with the duration of each contact NR G3: 48 (exercise contacts: 3x/wk/60 min/session at facility in mo 1–3, then option of doing home-based, duration of contact NR G4: 12 (1 hr monthly meetings in mo 1–3, monthly phone calls in mo 4–6, then bimonthly phone calls from mo 7–18) Provider G1: Both dietitian and exercise physiologist trained by health psychologist G2: Master's degree dietitian/nutritionist Health Educator G3: Exercise Physiologist G4: Health Educator	G3: 92 (0.2) G4: 96 (0.2) BMI, kg/m^2 (SD) G1: 34.0 (0.7) G2: 34.5 (0.6) G3: 34.2 (0.6) G4: 34.2 (0.6)			Weight change, kg (95% CI) G1: -5.20 (0.85, 9.55) G2: -4.61 (0.38, 8.84) G3: -3.46 (-0.77, 7.69) G4: 1.10 (-3.00, 5.20) G1 vs. G4: p<0.05 G2 vs. G4: p<0.05	G3: 60 G4: 73
Comprehensive Interventions Compared to Other Comprehensive Intervention That Varied the Physical Activity or Behavior Therapy Component							
Outcome Data at 6 Months or Less as the First Time Period Reported							
Jeffery et al., 2003 Tate et al., 2007 RCT, ITT uses Rubin's	G1 High physical activity *Diet:* 1,000–1,500 kcal/day, <20% fat *Physical Activity:* High physical activity program with goal 2,500 kcal/wk (walking <75 min/day)	Duration: 30 mo Treatment: 0–18 mo Follow-up: 19–30 mo Contacts: G1: 42 (weekly meetings [months 1–6],	Adults, ages 25–50, who are overweight by 14–32 kg n's G1: 109 G2: 93	At 6 mo Weight change, kg (SD) G1: -9.0 (7.1) G2: -8.1 (7.4) p=0.45	At 12 mo Weight change, kg (SD) G1: -8.5 (7.9) G2: -6.1 (8.8) p=0.07	At 18 mo Weight change, kg (SD): G1: -6.7 (8.1) G2: -4.1 (8.3) p=0.04	Withdrawals, n (%) G1: 19 (21) G2: 25 (23) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
multiple imputation strategy Weight is a primary outcome US, school/ university Fair	*Behavior:* Group sessions of didactic presentations of material needed to develop obesity management skills, problem solving; included group discussions Comparator G2: Standard behavior therapy *Diet:* same as G1 *Physical Activity*: Regular physical activity program with goal 250 kcal/wk increased to 1000 kcal/wk (walking 30 min/day) *Behavior*: same as G1	then biweekly [months 6–12] then monthly [months 12–18]) G2: Same as G1 Provider: G1: Nutritionists, exercise physiologists, or psychologists (months 1 to 18) G2: Same as G1	Weight, kg NR BMI, kg/m^2 (SD) NR by groups Overall: 31.7 (2.6)			At 30 mo Weight change, kg (SD) G1: -2.86 (8.6) G2: -0.90 (8.9) *p*=NS (data NR) Weight regain at 18–30 mo, kg (SD) G1: +5.9 (5.9) G2: +5.3 (7.0) p=NS (data NR)	
Andersen et al., 1999 RCT, ITT is LOCF Body weight is a primary outcome US, school/ university Good	G1: Diet and structured aerobic exercise *Diet* : Low-fat, low-calorie diet (1,200 kcal/day) consistent with AHA guidelines *Physical Activity*: Step aerobic classes, 45 min 3 times/wk, 450–500 kcal/session *Behavior:* cognitive behavioral program (modified LEARN) Comparator G2: Diet and lifestyle activity *Diet*: Same as G1 *Physical Activity*: Increasing daily lifestyle physical activity by 30 min/day, incorporate physical activity in the daily schedules *Behavior:* Same as G1	Duration: 68 wk Treatment: 0–16 weeks Follow-up: 17–68 weeks Contacts: G1: 64 (aerobic classes 3x/wk; weekly LEARN sessions) G2: 16 (weekly LEARN sessions) Provider G1: Psychologist (master's or doctoral level), certified aerobics instructor G2: Psychologist (master's or doctoral level)	Adult women, all within 15 kg over ideal body weight, with no structured exercise program experience in prior 6 mo *n*'s (at enrollment): G1: 20 G2: 20 Weight, kg (SD): G1: 83.6 (8.6) G2: 90.5 (13.5) BMI, kg/m^2 (SD) G1: 31.4 (3.7) G2: 32.4 (4.5)	At 16 wk Weight, kg (SD): G1: -8.3 (3.8) G2: -7.9 (4.2) *p*=0.08	NR	At 68 wk Weight regain, kg (SD): G1: +1.6 (5.5) G2: +0.08 (4.6) *p*=0.06	Withdrawals, *n* (%) G1: 3(15) G2: 4 (20) % calculated by reviewer Attendance, at aerobic classes at week 16, % G1: 87.7 G2: NA (note: 234 (SD 330) kcal/day based on accelerometer units/day)
Jakicic et al., 1999 RCT, ITT is BOCF	G1: Long-bout exercise *Diet:* 6,276 kJ/day (>90 kg), 5,021 kJ/day (<90 kg), 2,092-4,184 kJ/day deficit, 20% fat	Duration: 18 mo Treatment: 0–18 mo Follow-up: NR	Adult women, ages 25–45, with body weights 20–75% higher than ideal	At 6 mo Weight, kg (SD) G1: -8.2 (5.5) G2: -7.5 (5.4)	NR–	At 18 mo Weight, kg (SD) G1: -5.8 (7.8) G2: -3.7 (6.6)	Withdrawals, *n* (%) G1: 12 (24) G2: 15 (29)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Weight is a primary outcome US, school/ university Fair	*Physical Activity*: 1 long-bout exercise 5 days/wk, 20 min/day (wk 1–4), 30 min/day (weeks 5–8), 40 min/day thereafter *Behavior*: Group meetings focused on behavioral strategies for modifying eating and exercise behaviors Comparators G2: Short-bout exercise *Diet:* Same as G1 *Physical Activity*: Short-bout exercise, 5 days/wk, 20 min/day, duration progressed from 20 min/day to 40/min/day by 9th week and thereafter; subjects instructed to divide exercise into multiple 10-minute bouts performed at convenient times throughout day and to increase bouts from 2–4 per day by wk 9 *Behavior*: Same as G1 G3: Short bout plus equipment exercise *Diet:* Same as G1 *Physical Activity*: Same as G2 but subject provided with motorized home treadmills *Behavior*: Same as G1	Contacts: G1: 42 (weekly group meetings [months 1–6] then biweekly meetings [6 months –12], then monthly meetings [months 13–18] G2: same as G1 G3: same as G1 Provider G1: Nutritionists, exercise physiologists, and behavioral therapists G2: same as G1 G3: same as G1	body weight and reported exercise of less than 20 min/day on <3 days/wk for previous 6 mo *n*'s G1: 49 G2: 51 G3: 48 Weight, kg: G1: 90.0 G2: 91.6 G3: 88.3 BMI, kg/m^2 (SD) G1: 32.9 (3.8) G2: 33.2 (4.0) G3: 32.2 (4.3)	G3: -9.3 (5.6) G3 vs. G2*: p*=0.05 G3 vs. G1*: p*=NS		G3: -7.4 (7.8) G3 vs. G2*: p*=0.05 G3 vs. G1*: p*=NS Weight regain during mo 6–18, kg (SD) G1: +2.6 (5.5) G2: +4.1 (5.6) G3: +1.8 (4.7) G3 vs. G2*: p*=0.05 G3 vs. G1*: p*=NS	G3: 6 (12.5) Attendance NR
Jakicic et al., 2003 Jakicic et al., 2008 RCT, mITT, BOCF Body weight is a primary	G1: Vigorous Intensity/High Duration *Diet:* 1200–1500 kcal/d, 20%–30% fat of energy intake *Physical Activity*: 5 days/wk for minimum of 10 min each time; 70–85% age-predicted maximal heart rate; high energy expenditure	Duration: 24 mo Treatment: 0–24 mo Follow-up: NR Contacts: G1: 72 (group sessions 1x/wk [mo 1–6], then 2x/mo [months 7–12], then 1x/mo [mo 13–18]	Adult women, ages 21–45, with BMIs of 27–40, reporting exercising <3 days/wk for <20 min/day during previous 6 m *n*'s G1: 50	At 6 mo Weight, kg (SD) G1: 77.9 (11.5) G2: 79.7 (15.7) G3: 80.1 (12.4) G4: 80.4 (14.4) *p*=NR Note: based on mITT	At 12 mo Weight change, kg (SD) G1: -8.9 (7.3) G2: -8.2 (7.6) G3: -6.3 (5.6) G4: -7.0 (6.4) *p*=NS (data NR)	At 18 mo Weight, kg (SD) G1: 80.1 (12.6) G2: 81.5 (17.0) G3: 82.7 (14.4) G4: 82.6 (14.3) *p*=NR Note: based on	Withdrawals, n (%) G1: 5 (10) G2: 9 (1.8) G3:11 (22) G4: 16 (12) Attendance NR by group

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
outcome US, outpatient medical setting - hospital Fair	(2,000 kcal/wk) *Behavior*: Group session focused on modifying eating and exercise behavior Comparators G2: Moderate Intensity/High Duration *Diet:* Same as *Physical Activity*: Same as G1 but at 50–65% age-predicted maximal heart rate *Behavior*: Same as G1 G3: Moderate Intensity/Moderate Duration *Diet:* Same as G1 *Physical Activity*: Same as G2 but energy expenditure 1,000 kcal/wk *Behavior*: Same as G1 G4: Vigorous Intensity/Moderate Duration *Diet:* same as G1 *Physical Activity*: Same as G1 but with energy expenditure of 1,000 kcal/wk *Behavior*: Same as G1	with no sessions during mo 19–25; phone calls 2/mo [mo 7–12], then 1x/mo [mo 13–18] and then 2x/mo [mo 19–24]) G2: same as G1 G3: same as G1 G4: same as G1 Provider G1: unclear for behavior group sessions, phone calls performed by member of the intervention team, exercise was unsupervised G2: same as G1 G3: same as G1 G4: same as G1	G2: 50 G3: 50 G4: 51 Note: Five excluded from analysis at 12 mo due to pregnancy or death Weight, kg (SD) G1: 87.3 (11.2) G2: 86.8 (14.6) G3: 87.2 (13.1) G4: 88.1 (14.6) BMI, kg/m^2 G1: 32.8 G2: 32.2 G3: 32.8 G4: 32.8	with *N*=191	Note: based on mITT with *N*=196 Weight, kg (SD) G1: 78.3 (12.9) G2: 79.6 (16.9) G3: 80.9 (13.6) G4: 81.0 (14.3) P = NR Note: based on mITT with *N*=191	mITT with *N*=191 At 24 mo Weight, kg (SD) G1: 81.6 (13.1) G2: 83.2 (18.3) G3: 83.9 (14.8) G4: 85.0 (15.2) *p*=0.85 Note: based on mITT with *N*=191	
West et al., 2007 RCT, unclear if ITT analysis used, *n*'s at different endpoints not reported; overall retention 93% at 18 mo	G1: Motivational Interviewing *Diet*: Caloric restriction prescribed (1,200-1,500 kcal/day) with a fat intake goal of 33 –42 g/day *Physical Activity*: Gradual increases in physical activity promoted with goal of at least 150 min/wk *Behavior:* Program focuses on attainable and sustainable changes in dietary and physical	Duration: 18 mo Treatment: 0–18 months Follow-up: NR Contacts G1: 47 (42 group sessions, weekly for 6 mo, biweekly for 6 mo then monthly for 6 mo; 5 individual motivational	Adult women, with type 2 diabetes treatment by oral medication, with BMIs of 27–50 and capable of walking for exercise *n*'s G1: 109 G2: 108 Weight, kg (SD):	*Note: completers data* At 6 mo Weight, kg (SD): G1: -4.7 (0.45) G2: -3.1 (0.47) *p*≥0.01	*Note: completers data* At 12 mo Weight, kg (SD): G1: -4.8 (0.59) G2: -2.7 (0.62) *p*≥0.02	*Note: completers data* At 18 mo Weight, kg (SD): G1: -3.5 (0.62) G2: -1.7 (0.63) *p*≥0.04	Withdrawals NR Attendance at group sessions, % G1: 52 G2: 43 *p*=NS

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Weight loss (kg) is the primary outcome US, academic setting Fair	activity habits, with strong emphasis on goal setting and problem solving to achieve successful behavioral change; motivational interviewing sessions explored personally relevant factors motivating a participant to lose weight and how weight loss fits into future goals Comparator G2: Attention Control *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 without the motivational interviewing sessions	interviewing sessions) G2: Same as G1 but 5 individual sessions were health education sessions not motivational interviewing Provider G1: Group-based behavioral weight control program was delivered by a multidisciplinary team (behaviorist, nutritionist, exercise physiologist, and diabetes educator); motivational interviewing sessions delivered by licensed clinical psychologists trained in motivational interviewing G2: Same as G1 but health education sessions delivered by Master's degree level health educators	G1: 97 (17) G2: 97 (15) BMI, kg/m^2 (SD) G1: 36.5 (5.4) G2: 36.5 (5.5)				

Summary Table 4.3. Efficacy/Effectiveness of Electronically Delivered, Comprehensive Interventions in Achieving Weight Loss

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
Compared with Usual Care, Minimal Control, or No Intervention (Includes Self-Directed)							
Electronic: Text Messaging							
Outcome Data at 6 Months or Less as First Time Period Reporting							
Haapala et al., 2009 RCT, ITT is BOCF or LOCF, whichever is greater Weight is a primary outcome Finland, unclear Fair	G1: Mobile Phone Weight Loss Program *Diet:* Reduction in caloric intake *Physical Activity*: Increase physical activity *Behavior:* Automated tailored text message responses to participants reporting, password protected Web site provides further information on attaining goals Comparator G2: Control group *Diet:* No intervention *Physical Activity*: No intervention *Behavior:* No intervention	Duration: 12 mo Treatment: 0–12 mo Follow-up: NR Contacts: G1: Varied by participant (after participants weight, diet, and activity daily reports via text messaging or Web site, supportive text messages were sent to mobile phone) G2: NR Provider: G1: Automated Weight Balance Mobile phone program G2: No provider	Adults, ages 25–44, with BMI's of 25–36, and access to a mobile phone and Internet connection –'s G1: 62 G2: 63 Weight, kg (SD) G1: 87.5 (12.6) G2: 86.4 (12.5) BMI, kg/m^2 (SD) G1: 30.6 (2.7) G2: 30.0 (2.8)	NR	At 12 mo Weight, kg (SD) G1: - 3.1 (4.9) G2: - 0.7 (4.7) *p*=0.245	NA	Withdrawals, *n* (%) G1: 17 (27) G2: 22 (35) % calculated by reviewer Attendance NR (Note: frequency of program usage faded from 8 wk to 3–4/wk by 12 mo)
Electronic: Internet							
Outcome Data at 6 Months or Less as First Time Period Reporting							
SHED-IT Morgan et al., 2009, 2010 RCT, parallel group, stratified by obesity level Body weight and % change from baseline	G1: Internet-based *Diet:* Modification of dietary habits *Physical Activity:* Modification of physical activity habits, pedometers provided *Behavior:* Lifestyle modification information session, encouraged to access CalorieKing™ Web site to self-monitor weight, food intake, and activity via submission of daily	Duration: 6 mo Treatment: 0–3 mo Follow-up: 4–6 mo Contacts: G1: 8 (1 face-to-face information session, 7 feedback sheets provided by e-mail) G2: 1 (1 face-to-face information session)	Adult men, ages 18–60, with BMI's of 25–37 *n*'s: G1: 34 G2: 32 Weight, kg (SD) G1: 99.1 (12.2) G2: 99.2 (13.7) BMI, kg/m^2 (SD)	**At 3 months** Weight change, kg (95% CI): G1: -4.8 (-6.4, -3.3) G2: -3.0 (-4.5, -1.4) *p*=NS (value NR) Weight reduction >5%, % G1: 55.6 G2: 28.0	NA	NA	Withdrawals, *n* (%) G1: 6 (17.6) G2: 5 (16.1) Attendance NR

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
are primary outcomes US, military research center Good	food diaries for first mo (then weekly in 2nd mo and 1 wk in 3rd mo); e-mail feedback from counselors Comparator G2: Waitlist Control: Self-help *Diet:* No intervention *Physical Activity:* No intervention *Behavior:* Lifestyle modification information session, provided with program booklet	Provider: G1: Member of research team G2: same as G1	G1: 30.1 (3.0) G2: 30.6 (2.7)	*p*=0.04 **At 6 months** Weight change, kg (95% CI): G1: -5.3 (-7.3, -3.3) G2: -3.5 (-5.5, -1.4) *p*=NS (value NR) Weight reduction >5%, % G1: 50.0 G2: 34.6 *p*=0.25			
Hunter et. al., 2008 RCT, two-group parallel design, ITT is BOCF Body change (kg and % change from baseline) a primary outcome US, military medical research center Good	G1: Behavioral Internet Treatment *Diet:* Calorie restriction of 1200–1500 kcal/day; fat intake <30% of total kcal; food diaries *Physical Activity:* Increase physical activity until expenditure is at least 1,000 kcals a wk *Behavior:* 24 weekly self-taught weight loss behavior intervention lessons about 20–30 min each available on Web site (stimulus control, behavior modification, and stress management) with feedback from counselor, LEARN manual provided Comparator G2: Usual care *Diet:* No prescribed intervention (nutrition consultants, healthy cooking classes and annual diet assessments available) *Physical Activity*: Usual group workouts at least 3 x/wk with fitness assessments available *Behavior:* No prescribed	Duration: 6 mo Treatment: 0–24 wk Follow-up: NR Contacts G1: 27 (1 in-person orientation, 24 weekly feedback, and brief motivational interviewing telephone calls scheduled at 4 and 8 wk post-baseline) G2: None Provider G1: Counselor (via Internet) G2: None	Adults, ages 18–65, whose weight is within 5 lbs or above their maximum allowable weight for US Air Force (BMI ≥25 in women and ≥ 27.5 n men) n's G1: 224 G2: 222 Weight, kg (SD): G1: 87.4 (15.6) G2: 86.6 (14.7) BMI, kg/m2 (SD) G1: 29.4 (3.0) G2: 29.4 (3.0)	**At 6 mo** Weight change, kg (SD) G1: -1.0 (3.7) G2: +0.5 (3.1) *p*=0.001 Weight reduction of 5%, % G1: 22.6 G2: 6.8 *p*<0.001	NA	NA	Withdrawals, *n* (%) G1: 34 (15) G2: 18 (8) % calculated by reviewer Attendance at 8 wk, as availability for motivational calls, *n* (%) G1: 176 (78.4) G2: NA Attendance through 6 mo, as Web site logins, mean (range) G1: 49.1 (1, 707) G2: NA

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
	intervention (weight loss classes available)						
Outcome Data at Greater Than 6 Months as First Time Period Reporting							
No trials							
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
No trials							
Compared with Other Comprehensive Electronic Interventions							
Outcome Data at 6 Months or Less as First Time Period Reporting							
Gold et al., 2007 RCT, pilot, ITT is BOCF Weight is a primary outcome US, Web-based Fair	G1. VTrim (online weight loss and maintenance program) *Diet:* Calorie goals ranges from 1200 to 2200/day *Physical Activity*: Gradual increase in exercise energy expenditure with ≥1000 calories/wk burn via aerobic activity (walking particularly encouraged) *Behavior*: Online therapist-led program with no structured curriculum although fundamental behavioral weight loss concepts presented online, but is interactive for consultation Comparator G2. eDiets.com (access to self-help commercial weight loss program) *Diet:* Reduced energy diet following US dietary Guidelines; 1,000 calories/day deficit (goal of 1–2 lb loss/wk, automated feedback based on self-reported weight *Physical Activity*: Encouraged exercise tailored to participants	Duration: 12 mo Treatment: G1: Weight loss: 0–6 mo Weight maintenance: 6–12 mo G2: 0–12 mo Follow-up: NR Contacts: G1: 39 (weekly hour long online chats with therapist for weight loss phase, biweekly for maintenance phase) G2: Same as G1 Provider: G1: Weight loss phase: Online therapist; Maintenance phase: Web site only G2: Web site, online expert and peer support	Adults, ages 18 yr, with BMI's >25 but ≤39.9 n's G1: 62 G2: 62 Weight, kg (SD) G1: 92.0 (15.7) G2: 90.2 (14.1) BMI, kg/m^2 (SD) G1: 32.3 (3.9) G2: 32.5 (4.2)	**At 6 mo** Weight change, % (SD) G1: -7.3 (7.8) G2: -3.6 (6.1) *p*=NR Weight change, kg (SD) G1: -6.8 (7.8) G2: -3.3 (5.8) *p*=0.005	**At 12 mo** Weight change, % (SD) G1: 5.5 (7.6) G2: 2.8 (5.5) *p*= NR Weight change, kg (SD) G1: 5.1 (7.1) G2: 2.6 (5.3) *p*=0.034	NA	Withdrawals, *n* (%) G1: 22 (31) G2: 14 (22) % calculated by reviewer Attendance at 6 mo, as logins to Web site, median (range) G1: 47 (25–65) G2: 193 (120–209) *p*<0.001 Attendance from 6–12 mo, as logins to Web site, median (range) G1: 14 (8–23) G2: 90 (21–154) *p*<0.001

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
	exercise abilities, likes and dislikes *Behavior*: Online therapist led program of fundamental behavioral weight loss concepts, no structured behavioral curriculum						
Tate et al., 2006 RCT, ITT is BOCF Change in bodyweight is a primary outcome US, worksite Good	G1: Slim-Fast Web site and Computer-automated Feedback *Diet:* Standard calorie-restricted diet of 1,200–1,500 kcal/day with advice on use of structural meals and meal replacements (2 meal replacements/day encouraged) *Physical Activity*: Exercise recommendations of minimum of 1,050 kcal/wk exercise *Behavior:* Instructed on how to use the Slim-Fast Web site: weekly weight reporting, weekly diet tips, weight loss e-buddy system, plus weekly behavioral lessons similar to those in the DPP, and automated feedback to diary entries Comparators G2: Slim-Fast Web site and Human E-mail Counseling *Diet:* See G1 *Physical Activity*: See G1 *Behavior:* See G1 but with human e-mail feedback to diary entries G3: Slim-Fast Web site and No Counseling *Diet:* See G1 *Physical Activity*: See G1 *Behavior:* See G1 but with no feedback	Duration: 6 mo Treatment: 0–6 mo Follow-up: NR Contacts: G1: 26 (weekly programmed feedback tailored to individual diary submission) G2: 26 (weekly e-mail feedback tailored to individual diary submission) G3: None Provider; G1: None (automated responses based on cognitive behavior therapy theory) G2: Weight loss counselor G3: None (Web site data only)	Adults, ages 20–65 yr with BMI's of 27–40 *n*'s: G1: 61 G2: 64 G3: 67 Weight, kg (SD) G1: 89.0 (13.2) G2: 89.0 (13.0) G3: 88.3 (13.9) BMI, kg/m^2 (SD) G1: 32.7 (3.5) G2: 32.8 (3.4) G3: 32.3 (3.7)	**At 3 mo** Weight change, kg (SD) G1: -4.1 (4.3) G2: -5.3 (4.2) G3: -2.3 (3.4) *p*=NR **At 6 mo** Weight change, kg (SD) G1: -3.5 (5.4) G2: -5.9 (6.2) G3: -2.3 (5.4) *p*=NR Weight loss of >5 %, % G1: 34 G2: 52 G3: 27 *p*=0.01	NA	NA	Withdrawals, *n* (%) G1: 17 (28) G2: 12 (19) G3: 8 (12) % calculated by reviewer Attendance, as median logins to Web site, *n* G1: 2 G2: 9 G3: 20 *p*=0.001
Outcome Data at Greater Than 6 Months as First Time Period Reporting							

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
No trials							
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
Tate et al., 2003 RCT, ITT is BOCF Change in body weight is a primary outcome US, outpatient medical setting - hospital Good	G1: Basic Internet Program and Behavioral Counseling *Diet:* 1,200–1,500 kcal/day, fat intake of ≤20% calories *Physical Activity*: Minimum of 1,000 kcal/wk exercise *Behavior:* Web site support with e-counseling, diet, and exercise recommendations Comparator G2: Basic Internet Program *Diet:* See G1 *Physical Activity*: See G1 *Behavior:* Web site support without e-counseling	Duration: 1 yr Treatment: 1 yr Follow-up: NR Contacts: G1: 53 (1 face-to-face counseling session, weekly tips, plus weekly communications via e-mail with assigned weight loss counselor) G2: 1 (1 face-to-face counseling session) Provider; G1: Behavioral Counselor (all held master's or doctoral degrees in health education, nutrition, or psychology) G2: None	Adults with BMI's of 27–40, and 1 or more risk factors for type 2 diabetes *n*'s: G1: 46 G2: 46 Weight, kg (SD) G1: 86.2 (14.3) G2: 89.4 (12.6) BMI, kg/m^2 (SD) G1: 32.5 (3.8) G2: 33.7 (3.7)	*Note: 3 mo and 6 mo data NR here due to completers analysis and >10% attrition*	**At 12 mo** Weight change, % G1: -4.8 G2: -2.2 *p*=0.03 Weight change, kg (SD) G1: -4.4 (6.2) G2: -2.0 (5.7) *p*=0.04 Difference as 95% CI: -0.1 to 4.9*; p*= -0.04	NA	Withdrawals, *n* (%) G1: 8 (17) G2: 7 (15) % calculated by reviewer Attendance at 12 mo assessment, % G1: NR G2: NR *p*=0.78 Overall: 84%
Compared with Other Comprehensive Interventions (Includes Onsite and/or Electronic)							
Outcome Data at 6 Months or Less as First Time Period Reporting							
Harvey-Berino et al., 2010 RCT, 3x3 repeated measures design, ITT is BOCF Weight loss is a primary	G1. Hybrid (Internet and in person) *Diet*: Calorie-restricted diet and given a dietary fat goal corresponding to ≤25% of calories from fat *Physical Activity*: Graded exercise goals progressing to 200 min/wk of moderate to vigorous exercise like walking; pedometers provided	Duration: 6 mo Treatment: 6 mo Follow-up: NR Contacts: G1: 24 (1 hr weekly sessions, access to Internet treatment but once a month an in-person group	Adults, with BMIs between 25 and 50 n's G1: 161 G2: 158 G3: 162 Weight, kg (SD) G1: 96.5 (16) G2: 97.2 (18.7)	**At 6 mo** Weight change, % (SD): G1: -6.0 (5.8) G2: -5.7 (5.4) G3: -7.9 (6.2) *p*<0.01 Note: G3 superior to G1 and G2 as	NA	NA	Withdrawals, *n* (%) G1: 8 (4.9) G2: 2 (1.2) G3: 8 (5.1) % calculated by reviewer Attendance at sessions, % (SD) G1: 72 G2: 76

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
outcome US, medical center and Internet Fair	*Behavior:* Unlimited access to an interactive Web site, includes self-monitoring, stimulus control, problem solving, goal setting, relapse prevention and assertiveness training; all educational materials delivered electronically Comparators G2. Internet *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 with a new lesson each week online, access to an online database to help monitor calorie intake as well as online educational resources, a bulletin board for group communication, weekly tips and recipes, a BMI calculator, and local physical activity events) G3. In person *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 but received paper journal for monitoring dietary intake and physical activity, as well as a commercially available calorie- and fat-counting book	meeting substituted for an online chat) G2: 24 (1 hr weekly group sessions in secure online chat room) G3: 24 (1 hr weekly group sessions) Provider: G1: Behaviorally trained graduate students, clinical psychologists, and registered dietitians with extensive weight management experience G2: Same as G1 G3: Same as G1	G3: 97.4 (18.5) BMI, kg/m^2 (SD) G1: 35.6 (5.7) G2: 36/0 (5.7) G3: 35.6 (5.5)	determined by "pair-wise comparisons," *p* values not given for comparisons noted as significant by authors; also noted no significant differences between G1 and G2 Weight change, kg (SD): G1: -5.7 (5.5) G2: -5.5 (5.6) G3: -7.6 (5.2) *p*<0.01 Weight change ≥7%, % G1: 42.0 G2: 37.3 G3: 53.2			G3: 71
Womble et al., 2004 RCT, ITT is LOCF Change in body weight is a primary outcome	G1: eDiets.com *Diet:* Diet of conventional foods matching participant's needs, likes, and lifestyle *Physical activity*: Personalized prescriptions of physical activity based on self-reported levels of CV endurance and muscular strength	Duration: 52 wk Treatment: G1: Weight loss: 0 to–52 wk G2: Weight loss: 0–16 wk; Weight maintenance: 16–36 wk	Adult women, ages 18–65 with BMIs of 27–40 *n*'s G1: 23 G2: 24 Weight, kg (SD) G1: 93.4 (12.6)	**At 16 wk** Weight change, % (SD) G1: -0.9 (3.2) G2: -3.6 (4.0) *p*=0.01 Weight change, kg (SD)	**At 52 wk** Weight change, % (SD) G1: -1.1 (4.0) G2: -4.0 (5.1) *p*=0.04 Weight change, kg (SD)	NA	Withdrawals, *n* (%) G1: 8 (35) G2: 8 (33) Adherence as mean attendance at scheduled meetings, *n* (SD) G1: 7.6 (3.2)

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
US, electronic, commercial Fair	*Behavior*: Twice monthly newsletters sent via e-mail, free one-year membership in eDiets™ internet weight loss program G2: Weight loss manual *Diet:* Self-selected diet of conventional table foods *Physical activity*: Increased physical activity (walking up to 30 min/day) *Behavior:* LEARN manual, Weight Maintenance Survival Guide weight control behaviors (e.g., stimulus control, slowing eating, cognitive restructuring)	Follow-up: NR Contacts: G1: 5 (individual meetings at baseline and at 8, 16, 26, and 52 wk; no personalized feedback) G2: 5 (individual meetings at baseline and at 8, 16, 26, and 52 wk; no personalized feedback) Provider G1: eDiets.com; psychologist G2: LEARN Manual; psychologist	G2: 87.9 (10.8) BMI, kg/m^2 (SD) G1: 33.9 (3.2) G2: 33.0 (3.0)	NR	NR		G2: 8.1 (3.4) (Note: mean logons to Web site, *n (SD)* *G1: 1*7.7 (21.1) G2: NR)
Outcome Data at Greater Than 6 Months as First Time Period Reporting							
No trials							
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
No trials							
Evidence of Weight Loss in Comprehensive Electronic (Interactive Equipment) Interventions							
Compared with Other Comprehensive Intervention (Internet or Onsite)							
Weight Loss Outcome Data at 4 Months or Greater							
Byrne et al., 2006 RCT, stratified by age, sex and BMI, ITT is LOCF Weight loss is the primary outcome Australia,	G1: Personalized weight management program –electronic *Diet*: Ad librium low-fat and energy-reduced diet advice *Physical Activity*: Increase of physical activity *Behavior*: Received a transmitter belt, receiver watch, program user's manual, diet diary, tape measure, calorie-counting book;	Duration: 32 wk Treatment: 32 wk Follow-up: NR Contacts: G1: 1 training session and encouraged to e-mail staff with questions if there were problems with the program, 16 weekly	Adults, ages 30–45, with BMIs of 27 to 32, sedentary and ready to change *n*'s G1: 33 G2: 41 Weight, kg: G1: 85.7	**At 16 wk** Weight change, kg (SE) G1: -4.46 (0.5) G2: -2.35 (0.6) *p*=NS (value NR) **At 32 wk** Weight change from 16 wk, kg (SE) G1: -0.39 (0.5)	NA	NA	Withdrawals, *n* (%) G1: 9 (22) G2: 6 (18) Attendance at sessions NR

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
outpatient medical setting – clinic Fair	program calculates weight loss or maintenance goals based on information provided by subjects Comparator G2: Standard care *Diet*: Same as G1 *Physical Activity*: Increase of physical activity following the Australian National Physical Activity Guidelines *Behavior*: Consultation of simple advice to reducing energy intake and increase physical activity with clear directions that the goal should be to lose no greater than 1 kg/wk	visits for weight and waist measurements G1: 1 single consultation, but weekly visits for assessment Provider G1: Health professional with dual qualification in dietetics and exercise physiology G2: same as G1	G2: 87.2 BMI, kg/m^2 G1: 29.3 G2: 29.3	G2: +0.12 (0.6) *p*=NS (value NR) Weight change from baseline, kg (SE) G1: -4.84 (0.5) G2: -2.19 (0.6) *p*<0.05			
Evidence of Weight Maintenance in Comprehensive Electronic (Interactive Technology with Phone Feedback) Interventions							
Comprehensive Electronic Intervention Compared with Personal Contact or Self-Directed Control							
Weight Loss Outcome Data at 6 Months or Greater							
Harvey-Berino et al., 2004 Weight maintenance trial RCT, two phase, ITT is BOCF US, 10 interactive television (ITV) sites around University of Vermont Fair	Prior to randomization to weight maintenance, all participants received 24 sessions over 6 mo of group behavioral weight loss program (prescribed 1,000–2500 kcal/day diet based on body weight, increase in programmed and lifestyle activity and behavior modification skills). Mean weight loss achieved of 7.8 kg (SD: 5.3) G1. Internet support *Diet*: Reduced calorie intake (4,186 10,465\kJ/day) *Physical Activity*: Programmed unsupervised activity (walking)1,000 kcal/wk *Behavior:* Group counseling via interactive television; Web-based	Duration: 18 mo Treatment: Weight loss: 0–6 mo Weight maintenance: 7–12 mo Follow-up: NR Contacts: G1: 52 (26 biweekly chat room discussion, 26 biweekly e-mails) G2: 6 monthly meetings G3: 52 (26 biweekly group sessions, 26 biweekly phone sessions)	Adults, age >18, with BMIs ≥25 *n*'s G1: 77 G2: 78 G3: 77 Weight, kg (SD) G1: 82.7 (16.3) G2: 80.5 (14.4) G3: 81.2 (14.2) BMI, kg/m^2 (SD) G1: 28.9 (3.8) G2: 29.3 (5.2) G3: 29.0 (4.3)	**At 6 mo** Weight change, kg (SD): G1: -8.4 (6.1) G2: -7.6 (4.9) G3: -7.6 (5.0) *p*=0.33 Note: Weight change is calculated from run-in weight, not randomization weight	NR	**At 18 mo** Weight change as in maintained weight loss, % G1: 8.2 G2: 6.0 G3: 5.6 *p*=0.22 Weight change, kg (SD): G1: -4.7 (6.9) G2: -4.2 (7.0) G3: -3.9 (5.9) *p*=0.23	Withdrawals, *n* (%) G1: 25 (32) G2: 15 (19) G3: 16 (21) % calculated by reviewer Attendance at meetings, *n* (SD) G1: 7.7 (5.3) G2 excluded because of minimal contact G3: 10 (5.1) *p*=0.02

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
	program with online self-monitoring and 26 bi-weekly therapist-led chat room discussions of eating, activity, and behavioral goals for weight loss maintenance Comparators G2. Minimal in-person support *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Group counseling via interactive television, Maintenance: 6 monthly group onsite counseling sessions that discussed eating, activity, and behavioral goals for weight loss maintenance G3. Frequent in-person support: *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Group counseling via interactive television, Maintenance: 26 biweekly group onsite counseling sessions that discussed eating, activity, and behavioral goals for weight loss maintenance	Provider: G1: Therapist for treatment sessions, health educators and dietitians (site facilitators) G2: Same as G1 G3: Same as G1					
WLM (Weight Loss Maintenance Trial) Svetkey et al. 2008 Weight maintenance trial RCT, two phase, multicenter	Prior to randomization to weight loss maintenance, all received group-based behavioral intervention (20 sessions over 6 mo) and had to lose ≥4kg to be eligible for randomization (8.5 kg mean weight loss achieved) G1: Interactive technology-based intervention *Diet:* Reduced caloric intake following DASH dietary pattern *Physical Activity*: Increasing moderate physical activity from 180	Duration: 30 mo Treatment: Weight loss: -6 to 0 mo Maintenance: 0–30 mo Follow-up: NR Contacts: G1: 50 (No personal counseling; automated e-mail and telephone prompts if Web site not visited at least weekly	Adults, with BMIs of 25–45, taking medication for hypertension, dyslipidemia, or both, no active CVD *n*'s: G1: 348 G2: 342 G3: 342 Mean weight at randomization/post weight loss, kg (SD)	**At 6 mo** Difference in weight change between groups, kg G1 vs. G3: -0.8 *p*=0.003 G1 vs. G2: -0.1 *p*=0.73 G2 vs. G3: -0.9 *p*=0.001	**At 12 mo** Difference in weight change between groups, kg G1 vs. G3: -1.0 *p*=0.005 G1 vs. G2: -0.6 *p*=0.11 G2 vs. G3: -1.6 *p*<0.001	**At 18 mo** Difference in weight change between groups, kg G1 vs. G3: -1.1 *p*=0.003 G1 vs. G2: -0.7 *p*=0.08 G2 vs. G3: -1.8 *p*<0.001 **At 30 mo** Weight change	Withdrawals, *n* G1: 21 (6) G2: 25 (7) G3: 22 (6) % calculated by reviewer Note: 1 death per group, not included in ITT analysis Attendance, as % of contacts G1: 77

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
Primary outcomes: Weight change from randomization to end of study, weight maintenance, weight reduction from entry, and no more than 3% weight gain from randomization US, outpatient medical setting–clinic Good	to 225 min/wk , unsupervised *Behavior:* Unlimited access to interactive Web site (instructed to log on ≥1 time/wk) with monitoring via Web site check-ins including reports of weight, food diaries and exercise; Web site included social support bulletin boards and automated counseling programs; reinforced key theoretical constructs such as motivation, support, problem solving, relapse prevention, etc. covered in weight loss phase Comparators G2: Personal contact intervention *Diet:* Same as G1 *Physical Activity*: Same as G1 *Behavior:* Traditional lifestyle change; reinforced key theoretical constructs such as motivation, support, problem solving, relapse prevention, etc. covered in weight loss phase G3: Self-directed minimal intervention *Diet:* Same as G1 *Physical Activity*: Same as G1 *Behavior:* Received printed lifestyle guidelines with diet and physical activity recommendations at start, two brief meetings with an interventionist	contacted via e-mail, automated calls and personal calls if failed to log on) G2: 37 (Monthly, 5–15 min calls to reinforce adherence to lifestyle changes; 45–60 min in-person meetings every 4th mo) G3: 2 (Brief face-to-face meeting at baseline and at mo 12) Provider: G1: Automated Web site and telephone system G2: Trained interventionist G3: same as G2	G1: 88.6 (15.4) G2: 88.7 (16.9) G3: 87.4 (15.3) Mean BMI, kg/m^2 (SD) at randomization to maintenance (post weight loss) G1: 34.2 (4.8) G2: 34.2 (4.9) G3: 34.0 (4.8)			from randomization, kg (SD) G1: +5.2 (0.3) G2: +4.0 (0.3) G3: +5.5 (0.3) *p*<0.001 Difference in weight change between groups, kg (95% CI) G1 vs. G3: -0.3 (-1.2 to 0.6), *p*=0.51 G1 vs. G2: -1.2 (2.1 to 0.3) *p*=0.008 G2 vs. G3: -1.5 (-2.4 to -0.6) *p*=0.001 Weight reduction ≥ 5% from entry weight, % G1: 35.3 G2: 42.2 G3: 33.9 G2 vs. G3: *p*=0.02	(mo with ≥1 contact) G2: 91 (completed monthly intervention contacts) G3: NR Overall: 94%
Evidence of Weight Maintenance in Comprehensive Electronic (Internet) Interventions							
Comprehensive Electronic Intervention Compared with Personal Contact or Self-Directed Control							
Weight Loss Outcome Data at 6 Months or Greater							

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
Wing et al., 2006 Weight maintenance trial RCT, two phase, implied ITT with imputed regain of 0.3 kg/mo for dropouts Weight gain is a primary outcome US, academic medical center Good	Prior to randomization to weight loss maintenance, all participants were required to have lost at least 10% of body weight during prior 2 yr; mean weight loss of 19.3 kg prior to randomization G1: Internet *Diet*: When participant had a gain ≥2.3 kg, low-calorie, low-fat diet prescribed and meal replacements provided *Physical Activity*: Prescribed 60 min/day *Behavior:* Given scale, required to report weight weekly via Internet; self-monitoring of food and exercise; different prescriptions based on weight change (i.e., green, yellow, or red zone); in-person support and group support via chat) Comparators G2: Face-to-Face *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 but required to report weight weekly via telephone system G3: Control *Diet*: None *Physical Activity*: None *Behavior:* Quarterly newsletter with information on diet, exercise, and weight control, no intervention contact	Duration: 18 mo Treatment: 0–18 mo Follow-up: None Contacts: Mix of individual and group G1: 21 (weekly via internet for first month, then monthly) G2: 21 (in-person, weekly group meetings for first month, then monthly) G3: No contacts Provider: G1: Nutritionists, exercise physiologists, and clinical psychologists with master's or PhD G2: Same as G1 G3: None	Adults who had lost ≥10% of their body weight over the prior 2 yr *n*'s G1: 104 G2: 105 G3: 105 Weight, kg (SD): G1: 76.0 (16.4) G2: 78.6 (17.1) G3: 78.8 (14.8) BMI, kg/m^2 (SD) at randomization to maintenance/post weight loss G1: 28.1 (4.6) G2: 29.1 (5.0) G3: 27.7 (4.7)	**At 6 mo** Weight change, kg (SD) G1: +1.2 (4.2) G2: - 0.02 (4.3) G3: +1.5 (3.6) G2 vs. G3*: p*=0.02	**At 12 mo** Weight change, kg (SD) G1: +3.1 (7.5) G2: +1.3 (6.0) G3: +3.0 (5.7) *p*=NR	**At 18 mo** Weight change, kg (SD) G1: +4.7 (8.6) G2: +2.5 (6.7) G3: +4.9 (6.5) G2 vs. G3*: p*=0.05 Weight gain of ≥2.3 kg, % G1: 54.8 G2: 45.7 G3: 72.4 G1 vs. G3*: p*=0.008 G2 vs. G3*: p*<0.001 G1 vs. G2*: p*=0.19	Withdrawals, *n* (%) G1: 3 (3) G2: 13 (12) G3: 7 (7) % calculated by reviewer Attendance at mo 1–6 sessions, % G1: 65.7 G2: 78.7 G3: NR Attendance at mo 7–12 sessions, % G1: 41.2 G2: 53.5 G3: NR Attendance at mo 13–18 sessions, % G1: 34.2 G2: 41.5 G3: NR G1 vs. G2*: p*=0.005 (over entire study period)
Weight Loss Outcome Data at 12 Months or Greater							

Study Cited, Design, Setting, Primary Outcome, Quality Rating	Intervention Groups, Component Details	Study Duration, Contacts, Provider	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	≥1 year mean weight loss (kg/% change)	Attrition Attendance
Healthy Weight for Life Cussler et al., 2008 Weight maintenance trial RCT, two phase, ITT is BOCF Weight regain a primary outcome US, school/ university setting Good	Randomized after a 4-mo behavioral weight loss program of an energy deficit of 300–500 kcal/day, general exercise advice with individualized goals for energy intake and expenditure, group counseling where sessions dealt with 4 components of behavior change: physical activity, nutrition and healthy eating, social support, and the mind/body connection; Achieved weight loss at 4 mo: G1: 5.3 kg, G2: 5.2 kg, no significant differences between groups G1: Internet *Diet*: Usual diet *Physical Activity*: Usual activity *Behavior:* Internet support (private mail, bulletin board, chat rooms, curriculum materials, links to other Web sites of interest), support groups encouraged to meet once a week Comparator G2: Self-directed weight maintenance intervention *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 but without Internet though subjects permitted to continue to meet and practice the principles learned during mo 1–4	Duration: 12 mo Treatment: Weight Maintenance: 0–12 mo Follow-up: NR Contacts: G1: Unknown (self-directed Internet use that allowed contact with study staff) G2: 0 (no further contact) Provider: G1: Intervention team G2: Same as G1	Adult perimenopausal women, ages 40 to 55 years, with BMI's of 25 to 38 *n*'s G1: 66 G2: 69 Weight, kg (SD) G1: 84.6 (12.9) G2: 82.8 (10.7) BMI (SD) G1: 31.0 (3.9) G2: 30.4 (3.3)	NR	**At 12 months** Weight, kg (SD) G1: +0.4 (5.0) G2: +0.6 (4.0) *P* = NS (value NR)	NA	Withdrawals, *n* (%) G1: 14 (21) G2: 10 (14) Attendance at sessions, % NR by group Overall: 90.8%

Summary Table 4.4. Efficacy/Effectiveness of Comprehensive, Telephone-Delivered Lifestyle Interventions for Achieving Weight Loss

*A high-intensity intervention is defined as providing 14 or more intervention sessions in the first 6 months.

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Trials That Compared Onsite vs. Telephone-Delivered Programs for Inducing Weight Loss							
Outcome Data at 6 Months Or Less as First Time Period Reporting							
Rock et al., 2010 RCT, ITT is BOCF US, academic Weight loss over time based on an interaction between treatment group and time is the primary outcome Fair	G1: Center-Based Jenny Craig *Diet:* low-fat,1,200-2,000 kcal/day diet including prepackaged prepared food items delivered to participants door *Physical Activity*: Prescribed goal of 30 mins. ≥5 days/wk *Behavior:* Brief, weekly individual contacts with an in-person counselor, as provided in the Jenny Craig program Comparators G2: Telephone-based Jenny Craig *Diet:* Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1, but provided via telephone contacts G3. Usual Care *Diet:* Deficit of 500 to 1,000 kcal/day, provided sample meal plans by dietetic professional *Physical Activity*: Increased physical activity recommended *Behavior:* Two 1-hr sessions, combined with monthly check-in via e-mail and telephone, provided with publicly available print material on diet and physical activity	Duration: 24 mo Treatment: 0–18 mo Follow-up: 18–24 mo Contacts: G1: 104 (brief individual contact, weekly for 2 yr) G2: same as G1 but via telephone G3: 2 (2 individual visits in 2 yr) Deliverer: G1: Jenny Craig consultant G2: same as G1 G3: Dietetic professional	Overweight and obese women, ages 18–69 *n*'s G1: 169 G2: 164 G3: 113 Post-randomization exclusions: G1: 2 G2: 0 G3: 2 Weight, kg (95% CI) G1: 92.2 (90.7, 93.7) G2: 92.9 (91.1, 94.7) G3: 91.0 (89.0, 92.9) BMI, kg/m^2 (95% CI) G1: 33.8 (33.3, 34.4) G2: 33.8 (33.3, 34.3) G3: 34.0 (33.4, 34.6)	**At 6 mo** Weight change, kg (95% CI) G1: -9.2 (-9.9, -8.4) G2: -8.3 (-9.1, -7.5) G3: -2.9 (-3.8, -2.0) *p*<0.001 for G1 vs. G3 and G2 vs. G3	**At 12 mo** Weight change, % (95% CI) G1: -10.9 (-9.7, -12.1) G2: -9.2 (-7.8, -10.6) G3: -2.6 (-1.4, -3.8) Weight change, kg (95% CI) G1: -10.1 (-11.2, -9.0) G2: -8.5 (-9.7, -7.2) G3: -2.4 (-3.6, -1.2) *p*<0.001 for G1 vs. G3 and G2 vs. G3	**At 24 mo** Weight change, % (95% CI) G1: -7.9 (-6.5, -9.3) G2: -6.8 (-5.2, -8.4) G3: -2.1 (-0.7, -3.5) Weight change, kg (95% CI) G1: -7.4 (-8.7, -6.1) G2: -6.2 (-7.6, -4.9) G3: -2.0 (-3.3, -0.6) G1 vs. G3: *p*<0.001 G2 vs. G3: *p*<0.001	Withdrawals *n* (%) G1: 18 (11) G2: 11 (7) G3: 8 (7) % calculated by reviewer Attendance as completion of every contact during 18–24 mo, %: G1: 24.6 G2: 39.2 G3: NR Attendance as those that did not speak to their counselors between 18–24 mo,%: G1: 35.9 G2: 23.8 G3: NR
POWER (Practice-based Opportunities for Weight Reduction) – 1	G1: Remote Support Diet: Recommended reduced calorie intake as part of DASH diet Physical Activity: Recommended increased exercise (no further detail	Duration: 24 mo Treatment: 0–12 mo Follow-up: 12 mo Contacts: G1: 33 (12 weekly calls	Adults, age ≥21 with one or more CV risk factor (hypertension, hypercholesterol-emia or diabetes) *n*'s	**At 6 mo** Weight change, % G1: -5.0 G2: -5.2 G3: -1.1	NR	**At 24 mo** Weight change, % G1: -5.0 G2: --5.2 G3: -1.1	Withdrawal NR (Note: those without weight measureme

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
of 3 independent trials Appel et al., 2011 RCT, ITT Weight change from baseline to 24 mo is the primary outcome US, primary care practices Good	provided) Behavior: Social cognitive theory framework incorporating behavior self-management approaches to set weight-related goals, self-monitor weight and weight-related behaviors (exercise and reduced calorie intake), increase self-efficacy and social support, problem solving, included motivational interviewing, encouraged to lose 5% of weight; received Web-based support of learning modules, tools, and reminders to record weight so can get feedback regarding weight loss progress G2: In-person Support Diet: same as G1 Physical Activity: Same as G1 Behavior: Same as G1 but no motivational interviewing Comparator G3: Control Diet: None Physical Activity: None Behavior: Given brochures and a list of recommended Web sites promoting weight loss; met with a weight-loss coach at the time of randomization and, if desired, after the final data collection visit	for the first 3 mo; one monthly call for next 3 mo; next 18 mo offered monthly calls; encouraged to log in to Web site on a weekly basis G2: 57 (nine 90-min group sessions and three 20-min individual sessions during first 3 mo [weekly]; one 90-min group session and 2 20-min individual sessions during each of the following 3 mo [< weekly]; next 18 mo offered 2 monthly contacts – 1 group session and 1 individual session [biweekly], with the latter conducted either in person or by telephone); also encouraged to log-in to Web site on a weekly basis G3: 4 (baseline visit to collect data and meet with weight loss coach, and at 6, 12, and 24 mo follow-up visits for measurements only and 1 additional meeting with weight loss coach, if desired) Provider: G1: Weight loss coach and primary care provider (provided encouragement to work	G1: 139 G2: 138 G3: 138 Weight, kg (SD) G1: 102.1 (13.9) G2: 105.01 (13.9) G3: 104.4 (18.6) BMI, kg/m2 (SD) G1: 36.0 (4.7) G2: 36.8 (5.2) G3: 36.8 (5.14)	*p*=NS (value NR) Proportion lost ≥5% baseline weight, *n* (%) G1: 68 (52.7) G2: 57 (46.0) G3: 16 (14.2) G2 vs. G1*:* *p*<0.001 G3 vs. G2*:* *p*<0.001 G1 vs. G2*:* *p*=0.23 Proportion lost ≥10% baseline weight, *n* (%) G1: 30 (23.3) G2: -31 (25) G3: 4 (3.5) G2 vs. G1*:* *p*<0.001 G3 vs. G2*:* *p*<0.001 G1 vs. G2*:* *p*=0.92		*p*=NS (value NR) Weight change, kg (SE) G1: -4.6 (0.7) G2: -5.1 (0.8) G3: -0.8 (0.6) *p* =NS (value NR) Proportion lost ≥ 5% baseline weight, *n* (%) G1: 50 (38.2) G2: 55 (41.4) G3: 24 (18.8) G2 vs. G1*:* *p*<0.001 G3 vs. G2*:* *p*<0.001 G1 vs. G2*:* *p*=0.73 Proportion lost ≥10% baseline weight, *n* (%) G1: 24 (18.3) G2: 26 (19.5) G3: 11 (8.6) G2 vs. G1*:* *p*=0.02 G3 vs. G2*:* *p*=0.01 G1 vs. G2*:* *p*=0.69	nts at 24 mo: G1: 5%; G2: 4%; G3: 7% (% calculated by reviewer) Attendance at in-person visits, median Treatment G1: 14/15 G2: 14/21 G3: NA Follow-up G1: 16/18 G2: 16/36 G3: NA

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
		with coach) G2: Same as G1 G3: Weight loss coach					
Outcome Data at 12 Months or Greater as First Time Period Reporting							
Perri et al., 2008 RCT, ITT used a 0.3 kg/mo for missing values Weight is the primary outcome US, school/ university Good	Run-in for all groups: DPP-based program (low-calorie, 1,200 kcal/day diet), 30 min/day of walking lifestyle modification, group counseling; weight change at end of 6 mo: G1: -9.4 (SE: 0.6), G2: -10.1 (0.6), G3: -10.5 (0.6); randomization took place following initial lifestyle treatment G1: Telephone counseling *Diet:* Unclear if initial diet plan continued *Physical Activity:* Unclear if initial physical activity plan continued *Behavior:* Lifestyle modification with telephone counseling sessions to address barriers to maintaining eating and exercise behaviors required for sustaining weight loss Comparators G2: Face-to-face counseling *Diet:* Unclear if initial diet plan continued *Physical Activity:* Unclear if initial physical activity plan continued *Behavior:* Lifestyle modification with face-to-face counseling sessions to address barriers to maintaining eating and exercise behaviors required for sustaining weight loss G3: Educational Control	Duration: 18 mo Treatment Run-in: -6 to 0 mo Maintenance: 0–12 months Follow-up: NR Contacts: G1: 26 (biweekly sessions via telephone) G2: 26 (biweekly sessions via face-to-face) G3: None Provider G1: Family and consumer sciences agents or individuals with Bachelors or Masters degrees in nutrition, exercise science, or psychology G2: Same as G1 G3: No provider	Adult women, ages 50–75 yr, with BMIs>30 and weight <159.1 kg n's G1: 72 G2: 83 G3: 79 Weight, kg: G1: 96.4 G2: 97.8 G3: 95.0 BMI, kg/m^2 G1: 36.9 G2: 37.1 G3: 36.2	NR	**At 12 mo** Weight change from 0–12 months, kg (SD) G1: +1.2 (0.7) G2: +1.2 (0.6) G3: +3.7 (0.7) G1 vs. G3*: p*=0.03 G2 vs. G3*: p*=0.02	NA	Withdrawals, *n* (%) G1: 2 (2.8) G2: 8 (9.6) G3: 4 (5.1) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Diet: Unclear *Physical Activity:* Unclear *Behavior:* Education via newsletters with tips for maintaining weight loss progress and recipes for low-calorie meals						

Summary Table 4.5. Efficacy/Effectiveness of Comprehensive Weight Loss Programs in Patients Within a Primary Care Practice Compared With Usual Care

Trials are organized by weight loss vs. weight maintenance, then by first outcome time period reported, then by greatest weight loss (with completers analysis data, or data not presented as kg or % being listed last)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Weight Loss Trials							
Outcome Data at 6 Months or Less as First Time Period Reporting							
POWER (Practice-based Opportunities for Weight Reduction) – 1 of 3 independent trials Wadden et al., 2011b RCT, ITT Change in body weight is the primary outcome US, primary care practices Good	G1: Brief Lifestyle Counseling *Diet*: Diets prescribed based on weight: <113.4 kg (balanced diet of 1,200–1,500 kcal/day), ≥113.4 kg (1,500–1,800 kcal/day diets of 15–20% kcal protein, 20–35% fat, rest from carbohydrate); give a calorie-counting book *Physical Activity*: Instructed to gradually increase physical activity to 180 min/wk; given a pedometer *Behavior:* Given Aim for A Healthy Weight handouts; during quarterly visits to own PCP for diabetes, also get monthly brief counseling sessions (following DPP approach) with an auxiliary health care provider (included weigh-in, review of food records, goals) Comparator G2: Usual Care *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Received same Aim for A Healthy Weight handout; as part of usual medical care with own PCP, weight recommendations provided by PCP during quarterly scheduled visits, no specific behavioral	Duration: 24 mo Treatment: 24 mo Follow-up: NR Contacts: G1: 33 (quarterly visits with PCP for 24 mo, plus monthly brief [10–15 min.] counseling sessions, plus 1 more counseling visit in mo 1. In year 2, phone contact allowed every other month in lieu of in-person contact) G2: 8 (quarterly visits with PCP) Provider: G1: Medical Assistant (Lifestyle Coach) G2: Primary Care Physician	Adults, ≥21 years, with BMIs 30–50, with at least 2 of 5 criteria for metabolic syndrome (elevated WC, elevated BP, impaired fasting glucose, elevated triglycerides, low HDL-C) *n's* G1: 131 G2: 130 Weight, kg (SD): G1: 106.3 (17.3) G2: 111.2 (20.0) BMI, kg/m^2 (SD) G1: 37.8 (4.7) G2: 39.0 (4.8)	At 6 mo Weight change, % (SD) G1: -3.5 (0.5) G2: -1.8 (0.5) G2 vs. G1: *p*=0.004 Weight change, kg (SD) G1: -3.5 (0.5) G2: -2.0 (0.5) G2 vs. G1: *p*=0.023	At 12 mo Weight change, % (SD) G1: -3.5 (0.6) G2: -2.1 (0.6) G2 vs. G1: *p*=0.078 Weight change, kg (SD) G1: -3.4 (0.6) G2: -2.3 (0.6) G2 vs. G1: *p*=0.208	At 18 mo Weight change, % (SD) G1: -3.1 (0.6) G2: -1.7 (0.6) G2 vs. G1: *p*=0.100 Weight change, kg (SD) G1: -3.0 (0.7) G2: -1.9 (0.7) G2 vs. G1: *p*=0.210 At 24 mo Weight change, % (SD) G1: -2.9 (0.7) G2: -1.6 (0.6) G2 vs. G1: *p*=0.130 Weight change, kg (SD) G1: -2.9 (0.7) G2: -1.7 (0.7) G2 vs. G1: *p*=0.230	Withdrawals, *n* (%) G1: 19 (15) G2: 20 (15) % calculated by reviewer Attendance at PCP sessions, % (SD) G1: 69.0 (29.1) G2: 71.8 (28.6) Attendance at weight loss coaching sessions, % (SD) G1: 56.1 (28.8) G2: NA

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	strategies for changing eating and activity habits provided *Note: Enhanced Brief Lifestyle Counseling Intervention arm not reported here because weight loss medications were offered*						
Outcome Data at Greater Than 6 Months as First Time Period Reporting							
Christian et al., 2008 RCT, ITT is LOCF Weight loss as fraction of subjects achieving a clinically meaningful weight loss (5% reduction in body weight) included as a primary outcome US, outpatient clinic Good	G1: Lifestyle Change Pre-intervention computer-based assessment generated tailored plan to set self-management goals with feedback on barriers to improving diet, physical activity, planning guide for participants, companion report for physician counseling *Diet*: Individualized diet recommendations *Physical Activity*: Individualized physical activity recommendations *Behavior:* Motivational interviewing counseling during quarterly visits with physician to help patients make changes in dietary and physical activity behaviors, including discussing patient's tailored lifestyle change goal and encouragement in attaining goals; also provided with planning guide with supplemental information on diabetes and achieving a healthy lifestyle Comparator G2: Control *Diet*: None *Physical Activity*: None *Behavior:* Health educational	Duration: 1 yr Treatment: 52 wk Follow-up: NR Contacts: G1: 4 (once every 3 mo to review goal sheet with physician) G2: 4 (once every 3 mo to receive usual care) Provider: G1: Physician G2: Physician	Latino/Hispanic adults in community health centers, ages 18–75, with BMIs of ≥25, a diagnosis of type 2 diabetes, uninsured, Medicaid eligible, or Medicare enrolled *n*'s G1: 155 G2: 155 Weight, kg G1: 93.15 G2: 90.09 Note: converted from lbs to kg by reviewer BMI, kg/m^2 G1: 35.4 G2: 34.8	NR	At 12 mo Weight change, kg G1: -0.08 G2: +0.63 *p*=0.23 *Note: converted from lb to kg by reviewer, lb data:* *G1: - 0.18 (10.92)* *G2: +1.39 (10.60)* p=*0.23* Weight reduction of ≥5% from baseline, *n* (%) G1: 30 (21) G2: 14 (11) *p*=0.02	NA	Withdrawals, *n* (%) G1: 14 (9) G2: 23(15) Attendance at sessions NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	materials on diabetes, diet, and exercise						
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
REACH (Reasonable Eating and Activity to Change Health) Logue et al., 2005 RCT, parallel group trial, ITT is BOCF Weight change is the primary outcome US, outpatient medical setting – group practice Fair	G1: Transtheoretical Model *Diet*: Written dietary prescriptions based on the information from the dietary recalls (standard prescription to reduce calories, increase fruit and vegetables, reduce fat) *Physical Activity*: Increased activity and physical activity (prescription based on reported energy expenditure) *Behavior:* Transtheoretical model and chronic disease care program (patients mailed stage and behavior-matched workbooks that correspond to most recent stage of change profile; brief monthly telephone calls from trained weight loss advisor applying processes of change that correspond to patients profile Comparator G2: Augmented Usual Care *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Counseling based on USDA Food Guide Pyramid or a Soul Food Guide Pyramid	Duration: 2 yr Treatment: 24 mo Follow-up: NR Contacts: G1: 36 (stage of change assessments every other month and monthly phone calls) G2: 0 (only assessments and submission of dietary and exercise recalls every 6 mo) Provider: G1: Physician, dietitian, weight loss advisor (trained to apply the processes of change) G2: Dietitian	Adults within the 15 affiliated practices, ages 40–69, with BMIs >27 or waist-to-hip ratios >0.950 in men or >0.800 in women *n*'s G1: 329 G2: 336 Weight, kg (SD): NR BMI, *n* by range (%) G1: 25 to 29.9: 59 (18) 30 to 34.5: 119 (37) 35 to 39.0: 69 (21) 40.0+: 79 (24) G2: 25 to 29.9: 73 (22) 30 to 34.5: 107 (32) 35 to 39.0: 82 (24) 40.0+: 74 (22)	NR	NR	*Note: completers analysis data (used chart abstracted data for missing weights)* At 24 mo Weight change, kg (95% CI) G1: -0.39 (-1.1, 0.4) G2: -0.16 (-1, -0.7) *p*=0.50	Withdrawals, *n* (%) G1: 58 (18) G2: 70 (21) Attendance at sessions NR
Weight Maintenance Trials							
Outcome Data at 6 Months or Less as First Time Period Reporting							
No trials							
Outcome Data at Greater Than 6 Months as First Time Period Reporting							

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
No trials							
Outcome Data at Greater Than 12 months as First Time Period Reporting							
GOAL (Groningen Overweight and Lifestyle study) ter Bogt et al., 2009 RCT, ITT is BOCF Weight included as a primary outcome The Netherlands, outpatient medical setting – private practices Fair	G1: Nurse Practitioner - Lifestyle *Diet*: No specific prescription but given diet advice *Physical Activity*: No specific prescription but given a pedometer *Behavior*: Lifestyle intervention including extensive conversation on history of slimming and motivation to change lifestyle/lose weight and development of a treatment plan, feedback on food diary, physical activity, attainability of goals and, if necessary, refer to dietitian Comparator G2: General Practitioner – usual care *Diet*: No intervention *Physical activity*: No intervention *Behavior:* Offered one visit to discuss from a screening and, thereafter, usual general practitioner care	Duration: 1 yr Treatment: 12 mo Follow-up: NR Contacts G1: 5 (4 individual visits, 1 feedback session by phone) G2: 1 (via phone to discuss screening results) Provider G1: Nurse Practitioner G2: General Practitioner	Adults, ages 40–70 yr, BMIs 25–40, with hypertension and/or dyslipidemia *n*'s G1: 225 G2: 232 Weight, kg: NR BMI, kg/m^2 (SD) G1: 29.5 (3.1) G2: 29.6 (3.6)	NR	At 1 yr Weight change (adjusted for gender, age, BMI, weight change between screening and baseline), % (95% CI) G1: -1.9 (-2.5, -1.2) G2: -0.9 (-1.5, -0.2) *p*<0.05 BOCF Weight losers and stabilizers, % G1: 77 G2: 65 *p*<0.05	NA	Withdrawals (*n*): G1: 24 (11) G2: 17 (7.3) Attendance at sessions NR

Summary Table 4.6. Efficacy/Effectiveness of Commercial-Based, Comprehensive Lifestyle Interventions in Achieving Weight Loss

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Compared with Usual Care, Minimal Control, or No Intervention							

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Rock et al., 2010 Note: Electronically delivered RCT, ITT is BOCF US, academic Weight loss over time based on an interaction between treatment group and time is the primary outcome Fair	G1: Center-Based Jenny Craig *Diet:* low-fat, 1,200–2,000 kcal/day diet including prepackaged, prepared food items [ADD: food delivered] *Physical Activity*: Prescribed goal of 30 min ≥5 days/wk *Behavior:* Brief, weekly individual contacts with an in-person counselor, as provided in the Jenny Craig program Comparators G2: Telephone-based Jenny Craig *Diet:* Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1, but provided via telephone contacts G3. Usual Care *Diet:* Deficit of 500–1000 kcal/day, provided sample meal plans by dietetic professional *Physical Activity*: Increased physical activity recommended *Behavior:* Two 1-hr sessions, combined with monthly check-in via e-mail and telephone, provided with publicly available print material on diet and physical activity	Duration: 24 mo Treatment: 0–18 mo Follow-up: 18–24 mo Contacts: G1: 104 (individual, weekly for 2 yr) G2: same as G1 G3: 2 (2 individual visits in 2 yr) Deliverer: G1: Jenny Craig consultant G2: Same as G1 G3: Dietetic professional	Overweight and obese women, ages 18–69 *n*'s G1: 169 G2: 164 G3: 113 Post-randomization exclusions: G1: 2 G2: 0 G3: 2 Weight, kg (95% CI) G1: 92.2 (90.7, 93.7) G2: 92.9 (91.1, 94.7) G3: 91.0 (89.0, 92.9) BMI, kg/m^2 (95% CI) G1: 33.8 (33.3, 34.4) G2: 33.8 (33.3, 34.3) G3: 34.0 (33.4, 34.6)	**At 6 mo** Weight change, kg (95% CI) G1: -9.2 (-9.9, -8.4) G2: -8.3 (-9.1, -7.5) G3: -2.9 (-3.8, -2.0) *p*<0.001 for G1 vs. G3 and G2 vs. G3	**At 12 mo** Weight change, % (95% CI) G1: -10.9 (-9.7, -12.1) G2: -9.2 (-7.8, -10.6) G3: -2.6 (-1.4, -3.8) Weight change, kg (95% CI) G1: -10.1 (-11.2, -9.0) G2: -8.5 (-9.7, -7.2) G3: -2.4 (-3.6, -1.2) *p*<0.001 for G1 vs. G3 and G2 vs. G3	**At 24 mo** Weight change, % (95% CI) G1: -7.9 (-6.5, -9.3) G2: -6.8 (-5.2, -8.4) G3: -2.1 (-0.7, -3.5) Weight change, kg (95% CI) G1: -7.4 (-8.7, -6.1) G2: -6.2 (-7.6, -4.9) G3: -2.0 (-3.3, -0.6) G1 vs. G3: *p*<0.001 G2 vs. G3: *p*<0.001	Withdrawals, *n* (%) G1: 18 (11) G2: 11 (7) G3: 8 (7) % calculated by reviewer Attendance as completion of every contact during 18–24 mo, %: G1: 24.6 G2: 39.2 G3: NR Attendance as those that did not speak to their counselors between 18 and 24 months,%: G1: 35.9 G2: 23.8 G3: NR
Rock et al. 2007 RCT, ITT is BOCF Weight is a	G1: Jenny Craig *Diet*: Jenny Craig, energy-reduced diet of 1200–2000	Duration: 12 mo Treatment: 0–12 mo Follow-up: NR	Adults, ages ≥18 yr, with initial BMIs >25 and a minimum of 15 kg	**At 6 mo** Weight change, % (SD) G1: -7.8 (7.2)	**At 12 mo** Weight change, % (SD) G1: -7.1 (10.8)	NR	Withdrawals, *n* (%) G1: 3 (9) G2: 2 (6)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
primary outcome US, electronic; school/ academic setting Fair	kcal/day, prepackaged prepared core foods that provide 35–68% of energy) *Physical Activity*: 30 min of physical activity/day 5 days/wk *Behavior*: Cognitive aspects of promoting weight loss and maintenance, including self-acceptance, improved body image, and interpretation of one's attitudes, behavior, and thinking patterns Comparator G2: Usual Care *Diet*: Reduced energy diet with 500–1000 kcal/day deficit *Physical Activity*: None *Behavior*: individual consultations with written materials	Contacts: G1: 52 (group, phone, Web-based) G2: 2 (individual consultation) Provider: G1: Research staff dietitian and Jenny Craig corporate-trained counselors G2: Research staff dietitian	over ideal weight *n*'s: G1: 35 G2: 35 Weight, kg G1: 94.4 G2: 89.6 BMI, kg/m^2 G1: 34.2 G2: 33.8	G2: -0.3 (4.5) *p*<0.01 Weight change, kg (SD) G1: -7.2 (6.7) G2: -0.3 (3.9) *p*<0.01	G2: -0.7 (6.0) *p*<0.01 Weight change, kg (SD) G1: -6.6 (10.2) G2: -0.7 (5.5) *p*<0.01		% calculated by reviewer Attendance NR
Heshka et al., 2000 Heshkas et al., 2001 Heshka et al., 2003 RCT, block randomization, ITT is LOCF Change in body weight is a primary outcome US, community-based; 6 academic research centers Fair	G1: Weight Watchers *Diet:* Weight Watchers, moderate-deficit nutritionally balanced diet (food plan) *Physical Activity:* Activity plan *Behavior:* Cognitive restructuring behavior modification plan G2: Self Help *Diet:* Self-help and in-person consultations with a dietitian *Physical Activity:* None *Behavior:* Provision of self-help resources	Duration: 2 yr Treatment: 2 yr Follow-up: NR Contacts G1: 104 (weekly visits for 2 yr) G2: 2 (20-minute sessions at baseline and at wk 12) Provider G1: Program Graduate as role model G2: Dietitian	Adults, ages 18 – 65, with BMIs of 27–40; individuals with health problems for which weight reduction is a medically accepted therapy n's G1: 211 G2: 212 Weight, kg (SD): G1: 94.2 (13.1) G2: 93.1 (14.4) BMI, kg/m^2 (SD) G1: 33.8 (3.4) G2: 33.6 (3.7)	**At 26 wk** Weight change, kg (SD) G1: -4.8 (5.6) G2: -1.4 (4.7) *p*<0.001 Difference (95% CI) 2.6 (1.9, 3.3)	**At 1 yr** Weight change, kg (SD) G1: -4.3 (6.1) G2: -1.3 (6.1) *p*<0.001	**At 2 yr** Weight change, kg (SD) G1: -2.9 (6.5) G2: -0.2 (6.5) *p*<0.001	Withdrawals, % G1: 61 (29) G2: 53 (25) Attendance at week 104 sessions, median G1: 13 G2: NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Truby et al., 2006 RCT, unblinded, multicenter, ITT is BOCF Weight is a primary outcome UK, community Fair	G1: Rosemary Conley *Diet:* Low-fat diet *Physical Activity*: Weekly group exercise class *Behavior:* NR Comparators G2: Atkins diet *Diet:* Self-monitored low-carbohydrate eating plan--Book ("Dr. Atkins' New Diet Revolution") *Physical Activity*: NR *Behavior:* NR G3: Weight Watchers *Diet:* Energy-controlled diet with weekly group meetings *Physical Activity*: NR *Behavior:* NR G4: Slim-Fast *Diet:* Meal replacement–two meal replacements per day plus Slim Fast support pack (not described) *Physical Activity*: NR *Behavior:* NR G5: Control *Diet:* Usual diet pattern *Physical Activity*: Usual exercise pattern Behavior: NR	Duration: 12 mo Treatment: 6 mo Follow-up: 6 mo Contacts: G1 and 3: 24 weekly visits G2, 4 and 5: No contacts Provider: G1: Commercial program-trained instructors G2, 4 and 5: No provider G3: Commercial program counselor	Adults, ages 18–65 with self-reported BMIs of between 27 and 40 *n*'s G1: 58 G2: 57 G3: 58 G4: 59 G5: 61 Weight, kg (SD) G1: 89.8 (12.9) G2: 90.3 (12.3) G3: 88.8 (13.3) G4: 90.1 (14.1) G5: 87.9 (13.5) BMI, kg/m^2 (SD) G1: 31.6 (2.6) G2: 31.9 (2.2) G3: 31.2 (2.7) G4: 32.2 (3.0) G5: 31.5 (2.9)	**At 6 mo** Weight change, % (SD) G1: -7.0 (6.6) G2: -6.2 (6.2) G3: -7.3 (6.1) G4: -4.9 (5.5) G5: +0.6 (2.7) G1 vs. G5*: p*=0.001 (same for G2, G2, G3, G4 vs. G5*: p*=0.001) Weight change, kg (SD) G1: -6.3 (6.1) G2: -6.0 (6.4) G3: -6.6 (5.4) G4: -4.8 (5.6) G5: +0.6 (2.2) G1 vs. G2 vs. G3 vs. G4*: p*=NS (value NR); G1 vs. G5*: p*=0.001 (same for G2, G2, G3, G4 vs. G5*: p*=0.001)	Note: 12-mo follow-up results not reported because of treatment crossover and only 54% participation.	NR	Withdrawals, *n* (%) G1: 17 (29) G2: 11 (19) G3: 17 (29) G4: 17 (29) G5: 21 (34) % calculated by reviewer [CHECK FOR WITHDRAWAL RATES AT 6 MO AND REPORT IF AVAILABLE] Attendance at 6 mo, % G1: NR G2: 47 G3: NR G4: 47 G5: NR

NOTE: Deibert 2004 removed because it is a commercially available supplement but not a commercial program per se; Willaing 2004 not included because commercial information material provided, not a commercial program, per se; Womble 2004 and Gold 2007are presented in the Electronic Summary Table

Summary Table 4.7. Efficacy/Effectiveness of Very Low-Calorie Diets, as Used as Part of a Comprehensive Lifestyle Intervention in Achieving Weight Loss

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Evidence from Weight Loss Trials							
Weight Loss Outcome Data at 6 Months or Greater							
Kaukua, 2002 RCT, open, single center, age and BMI stratified randomization Weight included as a primary outcome Finland, outpatient medical setting Fair	G1: Nutrifast and LEARN *Diet*: Weight loss phase: 10 wk VLED (Nutrifast: 2200 kJ/day, 52g protein, 64g CHO, 8g fat); Weight maintenance phase: gradual return to normal diet *Physical Activity*: Mainly lifestyle exercise *Behavior*: LEARN Program for Weight Control (goal setting, nutrition (decrease in fat intake and increase in complex carbohydrates and fiber intake), exercise (mainly lifestyle exercise), self-monitoring, stimulus control, problem solving, cognitive restructuring, and relapse prevention Comparator G2: Control - weight maintenance without attempts to lose weight *Diet*: No intervention *Physical activity*: No intervention *Behavior:* No intervention	Duration: 32 wk Treatment: Weight loss: 0–11 wk Maintenance: 12–17 weeks Follow-up: 18–32 wk Contacts: G1: 68 (weekly 1.5 hour group sessions for 17 wk) G2: 0 Provider: G1: Clinical nutritionist and nurse G2: NA	Adult men, ages 18–60 yr, with BMIs ≥35 *n*'s G1: 19 G2: 19 Weight, kg: G1: 124.0 G2: 126.5 Mean BMI, kg/m^2 G1: 39.3 G2: 39.4	**At 11 wk** Weight change, % (SD) G1: -17.0 (7.4) G2: "weight stable" Weight change, kg (SD) G1: -21.0 (9.8) G2: -1.02 (2.9) *p*<0.001 **At 17 wk** Weight change, % (SD) G1: -17.0 (7.4) G2: "weight stable" Weight change, kg (SD) G1: -21.1 (9.9) G2: -1.3 (3.9) *p* <0.001	**At 32 wk** Weight change, % (SD) G1: -13.9 (7.8) G2: "weight stable" Weight regain from baseline, kg (SD) G1: -17.3 (10.2) G2: +0.2 (4.8) *p*<0.001	NR	Withdrawals, *n* (%) G1: 3 (16) G2: 2 (11) During VLED phase: G1: 1 G2: 2 Attendance NR
Stenius-Aarniala, 2000 RCT, open, 2 randomized parallel groups Body weight included as a primary	G1: Supervised weight reduction program *Diet:* 8 wk VLED diet (Nutrilett:1760 kJ/day); plus 6 wk for weight reduction program *Physical activity:* NR *Behavior*: Group counseling on weight reduction, asthma, and	Duration: 52 wk Run-in: -2 to 0 wk Treatment: 0–14 weeks Follow-up: wk 15–52 Contacts: G1: 12 (12 half hr group sessions over 14 wk)	Adults, ages 18–60 yr, with BMIs of 30–42, and previously diagnosed asthma *n*'s G1: 19 G2: 19 Weight, kg:	**At 14 wk** Weight change from pretreatment, % G1: -14.5 G2: -0.3 Weight change from pretreatment, kg (range)	**At 52 wk** Weight change from pretreatment, % G1: -11.3 G2: +2.2 Weight change, kg G1: -11.1 (1.1 to	NR	Withdrawals, *n* (%) G1: 0 (0) G2: NR Note: 2 discontinued VLED product and used

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
outcome Finland, outpatient medical setting Fair	allergies Comparator G2. Usual care *Diet:* None *Physical activity:* None *Behavior:* Group counseling on asthma and allergies Note: Randomized after 2 wk run-in for lung function and laboratory measurements	G2: same as G1 Provider: G1: Unclear G2: Same as G1	NR Mean BMI, kg/m^2: NR	G1: -14.2 (7.2 –22.1) G2: NR Weight reduction ≥15%, *n* of subjects G1: 9 G2: NR Weight reduction of 10–14.9%, *n* of subjects G1: 8 G2: NR Weight reduction of 5–9.9%, *n* of subjects G1: 2 G2: NR	22.5) G2: +2.3 (NR)		VLED diet and were retained in the study Attendance: NR
Evidence from Weight Maintenance Trials							
Weight Maintenance Outcome Data at 6 Months or Greater							
Borg, 2002 RCT, block randomization within 3 weight loss strata, completers analysis Weight regain included as a primary outcome Finland, academic setting Fair	Prior to randomization to weight loss maintenance, all participants received a 2-mo run-in group weight loss program, including 6 wk of VLED (Nutrilett: 2.1 mj/day; 500 kcal/day) and LED during first and last week (500 mj/day/1,200 kcal day); mean weight loss achieved prior to randomization 14.3 (-26.1 to -5.1) kg (range) with a mean baseline of 106.0 kg and 91.7 at 2 mo G1: Walking *Diet*: High-CHO, low-fat diet *Physical Activity*: 45 min/day 3 times/wk, 400 kcal/session; one weekly session supervised *Behavior:* Small group dietary counseling (including discussion of	Duration: 29 mo Run-in: -2 to 0 mo Treatment Maintenance: 0–6 mo Follow-up: 6 –29 mo Contacts: G1: 26 (weekly group meetings) G2: same as G1 G3: same as G1 Provider: G1: Dietitian/nutritionist and Exercise Instructor G2: same G1 G3: Dietitian/nutritionist	Men, age 35–50, with BMIs between 30 and 40 and WCs >100 cm *n*'s G1: 25 G2: 28 G3: 29 Weight, kg (SD): G1: 91.9 (9.3) G2: 90.8 (8.6) G3: 92.3 (10.5) *p*<0.05 Mean BMI before weight maintenance phase, kg/m^2 (SD), NR by group Overall: 28.5 (2.6)	Note: completers analysis data **At 6 mo** Weight change, kg G1: +1.8 G2: NR G3: +1.6 Difference in weight change between groups, kg (95% CI) G1 vs. G3: +0.3 (-2.2, 2.8) G2 vs. G3: -1.3 (-3.8, 1.1) G1 vs. G2: NR Overall*: p*=0.25 Weight, kg (SD) G1: 93.7 (10.7) G2: 91.1 (8.0)	NR	Note: data reported in article at 29 mo not eligible due to completers analysis with >10% attrition at this time point	Withdrawals at 8 mo, *n* (%) G1:5 (20) G2:6 (23) G3:7 (24) % calculated by reviewer Attendance as frequency by session duration, % G1: 82 G2: 66 G3: NR Attendance as session duration, % G1: 94 G2: 87

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	problems in following advice or relapses) with written educational material G2: Resistance Training *Diet*: Same as G1 *Physical Activity*: 45 min/day 3 times/wk, 300 kcal/session *Behavior:* Same as G1 Comparator G3: Control *Diet*: High-CHO, low-fat diet *Physical Activity*: Advised not to increase physical activity *Behavior:* Same as G1			G3: 93.9 (11.1) *p*=0.25			G3: NR
Weight Maintenance Outcome Data at 9 Months or Greater							
Fogelholm, 2000 RCT, block randomization within 3 weight loss strata, completers analysis Body weight included as a primary outcome Finland, outpatient clinic Fair	Prior to randomization to weight loss maintenance, all groups received 12 wk run-in group weight loss program, including 8 wk of VLED (Nutrilett), and 4 wk of LED (week 1, 10, 11, and 12), habitual physical activity levels, and group counseling; mean weight loss prior to randomization 13.1 (3.5) kg (SD) with weight reduction range of 4.5 to 20.8 kg G1. Walk-1 *Diet:* Low-fat diet with educational material on healthy diet *Physical Activity:* Walking program of 2 to 3 hr weekly (4.2 mj/wk); 1 session supervised per wk *Behavior:* Small group weekly meetings where problems in diet and prevention of relapse discussed	Duration: 33 mo Run-in: -12 to 0 wk Treatment: Maintenance: 0–40 wk Follow-up: 9–33 mo Contacts: G1: 40 (weekly small group) G2: same as G1 G3: same as G1 Provider: G1: Exercise Instructor G2: same as G1 G3: same as G1	Adult, pre-menopausal women, ages 30–45, with BMIs of 30–45 *n*'s at randomization G1: 26 G2: 27 G3: 29 Weight at beginning of weight maintenance intervention, kg (SD): G1: 78.0 (8.8) G2: 78.2 (11.6) G3: 80.0 (9.5) *P*=NR Mean BMI before weight loss, kg/m^2, NR by group	*N*	Note: Completers Analysis **At 9 mo** Difference in weight change between groups, kg (95% CI) G1 vs. G3: -2.7 (-5.2 to -0.2) G2 vs. G3: -2.6 (-5.1 to 0.0) *p*=0.06 Weight, kg (SD): G1: 77.3 (10.7) G2: 77.6 (11.1) G3: 82.0 (10.2) *p*=0.06	Note: Completers Analysis **At 33 mo** Difference in weight change between groups, kg (95% CI) G1 vs. G3: -3.5 (-6.8 to -0.2) G2 vs. G3: -0.2 (-3.6 to 3.1) *p*=0.07 Weight, kg (SD): G1: 83.9 (12.2) G2: 87.4 (15.3) G3: 89.7 (9.6) *p*=0.07	Withdrawals from maintenance program, *n* (%) G1: 1 (4) G2: 0 (0) G3: 1 (3) % calculated by reviewer Withdrawals from maintenance program and follow-up, *n* (%) G1: 2 (8) G2: 4 (15) G3: 2 (7) % calculated by reviewer

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	G2. Walk-2 *Diet:* Same as G1 *Physical Activity:* Walking program 4–6 hours weekly (8.4 mj/week) 1 supervised session per week *Behavior:* Same as G1 Comparator G3. Control - diet counseling only *Diet:* Same as G1 *Physical Activity:* No increase in habitual exercise *Behavior:* Same as G1		Overall: 34.0				Attendance: NR

Summary Table 4.8. Efficacy/Effectiveness of Comprehensive Lifestyle Interventions in Maintaining Lost Weight

Trials are organized by onsite vs. electronic programs as the primary intervention, then by first outcome time period reported, then by greatest weight loss (with completers analysis data, or data not presented as kg or % being listed last)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Onsite Interventions							
Outcome Data at 6 Months or Less as the First Time Period Reported							
Wing et al., 2006 Weight maintenance trial RCT, two phase, implied	Prior to randomization to weight loss maintenance, all participants were required to have lost at least 10% of body weight during prior 2 yr; mean weight loss of 19.3 kg prior to randomization G1: Face-to-Face	Duration: 18 mo Treatment: 0–18 mo Follow-up: None Contacts G1: 21 (in-person, weekly group meetings for first	Adults who had lost ≥10% of their body weight over the prior 2 yr *n*'s G1: 105 G2: 104	At 6 mo Weight change, kg (SD) G1: - 0.02 (4.3) G2: +1.2 (4.2) G3: +1.5 (3.6) G1 vs. G3*: p*=0.02	At 12 mo Weight change, kg (SD) G1: +1.3 (6.0) G2: +3.1 (7.5) G3: +3.0 (5.7) *p*=NR	At 18 mo Weight change, kg (SD) G1: +2.5 (6.7) G2: +4.7 (8.6) G3: +4.9 (6.5) G1 vs. G3*: p*=0.05	Withdrawals, *n* (%) G1: 13 (12) G2: 3 (3) G3: 7 (7) % calculated by reviewer

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
ITT with imputed regain of 0.3 kg/month for dropouts Weight gain is a primary outcome US, academic medical center Good	*Diet*: When participant had a gain ≥2.3 kg, low-calorie, low-fat diet prescribed and meal replacements provided *Physical Activity*: Prescribed 60 min/day *Behavior:* Given scale, required to report weight weekly via telephone; different prescriptions based on weight change (i.e., green, yellow, or red zone); in-person support and group support via chat) G2: Internet *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 but required to report weight weekly via Internet G3: Control *Diet*: None *Physical Activity*: None *Behavior:* Quarterly newsletter with information on diet, exercise and weight control, no intervention contact	month, then monthly) G2: 21 (weekly via Internet for first month, then monthly contacts via Internet) G3: No contacts Provider G1: Nutritionists, exercise physiologists, and clinical psychologists with master's or PhD G2: Same as G1 G3: None	G3: 105 Weight, kg (SD) G1: 78.6 (17.1) G2: 76.0 (16.4) G3: 78.8 (14.8) BMI, kg/m^2 (SD) at randomization to maintenance/post weight loss G1: 29.1 (5.0) G2: 28.1 (4.6) G3: 27.7 (4.7)			Weight gain of ≥ 2.3 kg, % G1: 45.7 G2: 54.8 G3: 72.4 G1 vs. G3: p<0.001 G2 vs. G3: p=0.008 G1 vs. G2: p=0.19	Attendance at mo 1–6 sessions, % G1: 78.7 G2: 65.7 G3: NR Attendance at mo 7–12 sessions, % G1: 53.5 G2: 41.2 G3: NR Attendance at months 13–18 sessions, % G1: 41.5 G2: 34.2 G3: NR G1 vs. G2: p= 0.005 (over entire study period)
Leermakers et al., 1999 Weight maintenance trial RCT, ITT is BOCF Weight is the primary outcome US, school/ university	Run-in for all groups: 6 mo weight loss program prior to extended therapy; weight loss at end of 6 mo: G1 8.5 (SD: 6.2) and G2: 9.0 (SD: 4.6); randomization prior to extended therapy described below G1: Weight-focused Program *Diet:* 1,200 kcal/day women (1,500 kcal/day men), <30% fat *Physical Activity:* Walking 30 min/day 5 x/wk *Behavior:* Therapist-led group discussions on maintenance of	Duration: 18 mo Run-in (Weight loss phase): -6 to 0 months Treatment Maintenance: 0 to 6 mo Follow-up: 6–12 mo Contacts G1: 12 (biweekly group sessions) G2: 12 (biweekly group exercise and	NR, but baseline characteristics: 80% women, mean age of 50.8 (SD: 11.1), mean BMI of 30.8 (SD: 4.5) and mean weight of 85.2 kg (SD: 15.9) *n*'s G1: 29 G2: 38 Weight, kg: G1: NR	At 6 mo Weight change, kg (SD) G1: +0.9 (3.6) G2: +2.8 (4.3) p<0.05	At 12 mo Weight change from 6–12 mo, kg (SD) G1: +2.2 (4.9) G2: +2.4 (3.2) p=NR	NA	Withdrawals: G1: 3 (10) G2: 7 (18) Attendance, % G1: 70.8 G2: 73.1 p=0.2

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Fair	weight loss (issues addressed determined by participants), group problem solving of weight-related difficulties (as presented by participants) with major emphasis on coping strategies with obstacles Comparators G2: Exercise-focused Program *Diet:* Same as G1 *Physical Activity*: Walking 30 min/day 5 x/wk; supervised group exercise sessions *Behavior:* Individual monetary contingencies for meeting exercise goals; intergroup competitions and prizes based on group exercise completion; and comprehensive training in relapse prevention strategies targeted at avoiding or coping with lapses in exercise	training sessions) Provider G1: Graduate students in clinical psychology G2: Same as G1	G2: NR BMI, kg/m^2 G1: NR G2: NR				
Borg et al 2002 Weight maintenance trial RCT, block randomization within 3 weight strata, completers analysis Finland, academic setting Fair	Prior to randomization to weight loss maintenance, all participants received a 2 mo run-in group weight loss program, including 6 wk of VLCD (500 kcal/day)); mean weight loss achieved prior to randomization 14.3 (-26.1 to -5.1) kg (range) with a mean baseline of 106.0 kg and 91.7 at 2 mo G1: Walking *Diet*: High-CHO, low-fat diet *Physical Activity*: 45 min/day 3 times/wk, 400 kcal/session; one weekly session supervised *Behavior:* Small group dietary counseling (including discussion of problems in following advice or relapses) with written educational	Duration: 29 mo Run-in: -2 to 0 mo Treatment: Maintenance: 0–6 months Follow-up: 6–29 mo Contacts G1: 26 (weekly group meetings) G2: Same as G1 G3: Same as G1 Provider G1, G2: Dietitian/ nutritionist and Exercise Instructor G3:	Adult men, ages 35–50 yr with BMIs 30–40 and WCs >100 cm *n*'s G1: 25 G2: 28 G3: 29 Mean weight loss prior to randomization 14.3 kg Weight, kg: G1: 91.9 (9.3) G2: 90.8 (8.6) G3: 92.3 (10.5) *p*<0.05 Mean BMI before weight maintenance	*Note: completers analysis* At 6 mo Weight change, kg G1: +1.8 G2: NR G3: +1.6 *p*=NS (value NR) Difference in weight change between groups, kg (95% CI) G1 vs. G3: +0.3 (-2.2, 2.8) G2 vs. G3: -1.3 (-3.8, 1.1)	NR	Note: data at 29 mo are not eligible due to high attrition at this time point and completers analysis	Withdrawals, *n* (%) G1: 5 (20) G2: 6 (23) G3: 7 (24) % calculated by reviewer Attendance as frequency by session duration, % G1: 82 G2: 66 G3: NR Attendance, as session duration, %

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	material G2: Resistance Training *Diet*: Same as G1 *Physical Activity*: 45 min/day 3 times/wk, 300 kcal/session *Behavior:* Same as G1 Comparator G3: Control *Diet*: High-CHO, low-fat diet *Physical Activity*: Advised not to increase physical activity *Behavior:* Same as G1	Dietitian/nutritionist	phase, kg/m^2 (SD), NR by group Overall: 28.5 (2.6)	G1 vs. G2: NR Overall*: p*=0.25 Weight, kg (SD) G1: 93.7 (10.7) G2: 91.1 (8.0) G3: 93.9 (11.1) *p*=0.25			G1: 94 G2: 87 G3: NR
PRIDE (Program to Reduce Incontinence by Diet and Exercise) West et al., 2011 Weight maintenance trial RCT, 2:1 randomization to intervention vs. control; then intervention subjects further randomized to either Skill-based or Motivation-focused arms; then within each intervention	Run-in: 6 mo weight loss induction phase where intervention arms received a reduced calorie balanced diet with meal replacements (Slim Fast) coupons to replace 2 meals and 1 snack; exercise goals and pedometers; and a behavior program modeled after the DPP and Look AHEAD lifestyle interventions. Though randomization for the two maintenance interventions took place before initial weight loss phase, it was not revealed until after that phase was completed. Weight Maintenance Phase G1: Skills-based Behavioral Lifestyle Weight Loss Program *Diet:* Reduced calorie goals recommended until 10% weight loss goal achieved, then dietary intake goals focused on weight stability; meal replacements coupons for 1 meal and 1 snack provided *Physical Activity*: Exercise goals remained at to 200 min/week or more	Duration: months Run-in (Weight Loss): -6 to 0 mo Treatment: Maintenance: 0–12 mo Follow-up: NR Contacts G1: 26 (bi-weekly group meetings on weight maintenance) G2: Same as G1 G3: 7 education sessions Provider G1 and 2: dietitians, exercise physiologists, nurses 3nd psychologists G2: NR	Adults, at least 30 yr, with BMIs of 25–50, and reported 10 or more episodes of urinary incontinence *n*'s: G1 and 2: 226 (113 randomized after initial weight loss phase to skills-based maintenance and 113 to motivational maintenance program) G2: 112 Mean weight at start of maintenance phase NR Weight change at end of weight loss induction phase, kg (95% CI) G1: -7.64 (-9.26,-6.03) G2: -7.82 (-9.07, 6.57) G3: -1.45 (-2.55, -0.35) G1 vs. G3: p < 0.05	*Note: completers analysis* 6 mo Weight change, % (95% CI) G1: 0.73 (-0.33, 1.76) G2: 0.67 (-0.71, 2.06) G3: -0.74 (-1.77, 0.28) *p*=NS (value NR) Weight change, kg (95% CI) G1: -0.73 (-0.29, 1.76) G2: 0.69 (-0.51, 1.88) G3: -0.66 (-1.58, 0.26) *p*=NS (value NR) Weight loss of ≥5% or greater, *n* (%)	*Note: completers analysis* At 12 mo Weight change, % (95% CI) G1: 2.75 (1.41, 4.09) G2: 2.83 (1.09, 4.57) G3: -0.37 (-1.85, 1.12) G1 vs. G3: p < 0.05 G2 vs. G3: p < 0.05 Weight change, kg (95% CI) G1: 2.66 (1.41, 3.90) G2: 2.55 (1.02, 4.08) G3: -0.31 (-1.68, 1.06) G1 vs. G3*: p*<0.05	NR	Withdrawals at 12 mo (end of weight mainten-ance), % G1: 8 G2: 5 G3: 4 % calculated by reviewer Attendance at group sessions, % G1: 52 G2: 45 G3: NR G1 vs. G2: *p*=0.05

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
group further randomized to 18 clusters for group cohesion and social support that would carry through from the weight loss phase to maintenance phase Primary outcomes: weight at 16 and 18 mo US, academic medical setting Fair	of moderate physical activity *Behavior:* Standard behavioral weight maintenance program reflected current lifestyle program and focused on reviewing and refining behavioral skills in problem solving, goal setting, social support and relapse prevention; new skill development topics included reversing small weight gains, improving body image and self-esteem, and expanding exercise options G2: Motivation-focused Behavioral Lifestyle Weight Loss Program *Diet:* Same as G1 *Physical Activity*: Same as G1 *Behavior:* Program focused on increasing and sustaining motivation to use dietary, physical activity, and behavioral skills introduced during the weight loss phase; behavior goals same as in G1, but goals are promoted using strategies from motivational theories and methods G3: Educational Control *Diet:* None *Physical Activity*: None *Behavior:* Seven education sessions providing general information about physical activity, healthy eating habits, and weight loss, following a structured protocol		G2 vs. G3: p < 0.05 Weight change at end of weight loss induction phase, % (95% CI) G1: -7.98 (-9.64,-6.33) G2: -7.98 (-9.22, 6.73) G3: -1.48 (-2.59, -0.37) G1 vs. G3: p < 0.05 G2 vs. G3: p < 0.05 Weight loss of ≥ 5% or greater from the weight loss induction phase, n (%) G1: 77 (43.24) G2: 76 (42.37) G3: 26 (14.39) G1 vs. G3: p < 0.05 G2 vs. G3: p < 0.05 Mean BMI, kg/m^2 (SD) NR by group Overall: 36 (6)	G1: 72 (43.32) G2: 67 (40.40) G3: 27 (16.29) G1 vs. G3: *p*=0.05 G2 vs. G3: *p*=0.05	G2 vs. G3: *p*<0.05 Weight loss of ≥5% or greater, *n* (%) G1: 57 (39.79) G2: 55 (38.35) G3: 31 (21.86) G1 vs. G3: *p*=0.05 G2 vs. G3: *p*=0.05 Weight change from 6 mo, kg (95% CI) G1: 1.94 (1.13, 2.75) G2: 1.88 (1.09, 2.66) G3: 0.33 (-0.58, 1.24) G1 vs. G3: *p*<0.05 G2 vs. G3: *p*<0.05 Weight change from 6 mo, % (95% CI) G1: 1.99 (1.14, 2.84) G2: 2.17 (1.31, 3.02) G3: 0.35 (-0.65, 1.35) G1 vs. G3: *p*<0.05 G2 vs. G3: *p*<0.05		
Outcome Data at 6 Months or Greater as First Time Period Reported							
Perri et al., 2008 Weight maintenance	Run-in for all groups: DPP-based program (low-calorie, 1,200 kcal/day diet), 30 min/day of walking lifestyle modification, group counseling; weight change at end of 6 mo: G1:	Duration: 18 mo Run-in: -6 to 0 mo Treatment Maintenance: 0–12	Adult women, ages 50–75 years, with BMIs >30 and weight <159.1 kg	NR	At 12 mo Weight change from 0–12 months, kg (SD)	NA	Withdrawals: G1: 2 (2.8) G2: 8 (9.6) G3: 4 (5.1)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
trial RCT, ITT used a 0.3 kg/mo for missing values Weight is the primary outcome US, school/ university Good	-9.4 (SE: 0.6), G2: -10.1 (0.6), G3: -10.5 (0.6); randomization took place following initial lifestyle treatment G1: Telephone counseling *Diet:* Unclear if initial diet plan continued *Physical Activity:* Unclear if initial physical activity plan continued *Behavior:* Lifestyle modification with telephone counseling sessions to address barriers to maintaining eating and exercise behaviors required for sustaining weight loss Comparators G2: Face-to-face counseling *Diet:* Unclear if initial diet plan continued *Physical Activity:* Unclear if initial physical activity plan continued *Behavior:* Lifestyle modification with face-to-face counseling sessions to address barriers to maintaining eating and exercise behaviors required for sustaining weight loss G3: Educational Control *Diet:* Unclear *Physical Activity:* Unclear *Behavior:* Education via newsletters with tips for maintaining weight loss progress and recipes for low-calorie meals	mo Follow-up: NR Contacts G1: 26 (biweekly sessions via telephone) G2: 26 (biweekly sessions via face-to-face) G3: None Provider G1: Family and consumer sciences agents or individuals with Bachelors or Masters degrees in nutrition, exercise science, or psychology G2: Same as G1 G3: No provider	*n*'s G1: 72 G2: 83 G3: 79 Weight, kg: G1: 96.4 G2: 97.8 G3: 95.0 BMI, kg/m^2 G1: 36.9 G2: 37.1 G3: 36.2		G1: +1.2 (0.7) G2: +1.2 (0.6) G3: +3.7 (0.7) G1 vs. G3*: p* =0.03 G2 vs. G3*: p* =0.02		Attendance NR
Fogelholm, 2000 Weight maintenance trial	Prior to randomization to weight loss maintenance, all groups received 12 wk run-in group weight loss program, including 8 wk of VLED (Nutrilett), and 4 wk of LED (wk 1, 10, 11, and 12), habitual physical activity levels,	Duration: 33 mo Run-in: -12 to 0 weeks Treatment: Maintenance:	Adult, pre-menopausal women, ages 30–45, with BMIs of 30–45 *n*'s at randomization G1: 26	NR	*Note: Completers analysis* At 9 mo Difference in weight change	*Note: Completers analysis* At 33 mo Difference in weight change	Withdrawals from maintenance program, *n* (%) G1: 1 (4)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
RCT, block randomization within 3 weight loss strata, completers analysis Body weight included as a primary outcome Finland, outpatient clinic Fair	and group counseling; mean weight loss prior to randomization 13.1 (3.5) kg (SD) with weight reduction range of 4.5 –20.8 kg G1. Walk-1 *Diet:* Low-fat diet with educational material on healthy diet *Physical Activity:* Walking program of 2–3 hours weekly (4.2 mj/week); 1 session supervised per week *Behavior:* Small group weekly meetings where problems in diet and prevention of relapse discussed Comparators G2. Walk-2 *Diet:* Same as G1 *Physical Activity:* Walking program 4–6 hr weekly (8.4 mj/wk) 1 supervised session per week *Behavior:* Same as G1 G3. Control - diet counseling only *Diet:* same as G1 *Physical Activity:* No increase in habitual exercise *Behavior:* Same as G1	0–40 wk Follow-up: 9–33 mo Contacts G1: 40 (weekly small group) G2: Same as G1 G3: Same as G1 Provider G1: Exercise Instructor G2: Same as G1 G3: Same as G1	G2: 27 G3: 29 Weight at beginning of weight maintenance intervention, kg (SD): G1: 78.0 (8.8) G2: 78.2 (11.6) G3: 80.0 (9.5) *p*=NR Mean BMI before weight loss, kg/m^2, NR by group Overall: 34.0		between groups, kg (95% CI) G1 vs. G3: -2.7 (-5.2 to -0.2) G2 vs. G3: -2.6 (-5.1 to 0.0) *p*=0.06 Weight, kg (SD): G1: 77.3 (10.7) G2: 77.6 (11.1) G3: 82.0 (10.2) *p*=0.06	between groups, kg (95% CI) G1 vs. G3: -3.5 (-6.8 to -0.2) G2 vs. G3: -0.2 (-3.6 to 3.1) *p*=0.07 Weight, kg (SD): G1: 83.9 (12.2) G2: 87.4 (15.3) G3: 89.7 (9.6) *p*=0.07	G2: 0 (0) G3: 1 (3) % calculated by reviewer Withdrawals from maintenance program and follow-up, *n* (%) G1: 2 (8) G2: 4 (15) G3: 2 (7) % calculated by reviewer Attendance: NR
Dale et al., 2009 Group-randomized trial New Zealand, unclear Good	G1: *Diet*: High CHO diet (55% CHO, 15–20% protein, 25–30% fat, low glycemic index foods, 30 g/day fiber, 8% SF, 6% PUFA); and intensive support *Physical Activity*: Supervised circuit-type resistance training sessions *Diet:* High monounsaturated fatty acid (MUFA) (25% protein; 21% MUFA; 40% CHO; 8% SF, 6% PUFA,	Duration: Treatment: 2 yr Follow-up: NR Contacts: G1: 224 G2: 224 G3: 133 G4: 133 Provider: G1: Dietician/ nutritionist, exercise	Women 25–70 yr - lost at least 5% of their initial body weight in the previous 6 mo and have or have had a BMI ≥27 *n*'s G1: 49 G2: 51 G3: 51 G4: 49	NR	Weight, kg (SD): At 1 yr G1&2: 85.0 (14.8) G3&4: 83.3 (15.9) *p*=0.95 BMI (SD): At 1 yr G1&2: 31.5 (5.2) G3&4: 30.9 (5.5) *p*=0.95	Weight, kg (SD): At 2 yr G1&2: 84.3 (14.4) G3&4: 83.0 (15.2) *p*=0.95 BMI (SD): At 2 yr G1&2: 31.2 (5.1) G3&4: 30.8 (5.1) *p*=0.95	Withdrawals G1: 7 G2: 6 G3: 4 G4: 9

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	30 g/day fiber) and intensive support *Physical Activity*: Supervised circuit-type resistance training sessions *Behavior* G3: *Diet* : High CHO diet (55% CHO, 15-20% protein, 25-30% fat, low GI foods, 30 g/d fiber, 8% SF, 6% PUFA); and nurse support *Physical Activity*: Discussion of physical activity-related topics Behavior G4: *Diet*: High monounsaturated-fat diet (25% protein; 21% MUFA; 40% CHO; 8% SF, 6% PUFA, 30 g/day fiber); and nurse support *Physical Activity*: Supervised circuit-type resistance training sessions	consultant, general practitioner G2: Dietician/ nutritionist, exercise consultant, general practitioner G3: Dietician/ nutritionist, exercise consultant, general practitioner G4: Dietician/ nutritionist, exercise consultant, general practitioner	Baseline Weight: Intensive support (G1+G2): 86.6 (14.1) Nurse support (G3+G4): 85.1 (15.1)				
Outcome Data at Greater Than 12 Months as the First Time Period Reported							
Perri et al., 2001 RCT, ITT is BOCF Weight is the primary outcome US, Unclear setting Fair	Original weight loss part of the trial for all groups: Low-calorie, low-fat diet (1200 kcal/day, 25% fat), home-based walking program (30 min/day 5 days/wk), standard behavioral weight management techniques taught in didactic fashion (self-monitoring, goal setting, stimulus control); randomization took place prior to weight loss treatment phase (20 wk); weight losses at end of 5 mo: G1: -9.09 (4.97), G2: -8.42 (4.70), G3: -8.77 (4.77) G1: Behavioral Treatment + Relapse Prevention Training *Diet*: Weight loss phase:	Duration: 12 mo Treatment: Weight Loss for all groups: 0–6 mo Weight maintenance for G1 and G2 only: 6–17 mo Follow-up: NR Contacts: G1: 46 (weekly group sessions for first 20 wk, then 26 biweekly sessions for maintenance phase) G2: Same as G1	Adults, ages 21–60, with BMIs of 27–40, in good health and physician's approval to participate *n*'s: G1: 28 G2: 34 G3: 18 Weight, kg: G1: 96.95 G2: 97.96 G3: 94.67 BMI, kg/m^2 G1: 35.00 G2: 36.10	NR	NR	At 17 mo Weight loss ≥10%, *n* (%) G1: 6 (21.4) G2: 12 (35.3) G3: 1 (5.6) G2 vs. G3: *p*=0.025 G1 vs. G3: *p*=0.10 G2 vs. G1: *p*=0.10 Weight loss of 5–9.9%, *n* (%) G1: 6 (21.4) G2: 6 (17.6) G3: 6 (33.3) *p*=NR Weight loss of 1–	Withdrawals, *n* (%) G1: 8 (29) G2: 11(32) G3: 3 (17) Attendance at sessions NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Low-calorie, low-fat diet (1,200 kcal/day, 25% fat); Weight maintenance phase: unclear *Physical Activity*: Weight loss phase: home-based walking program (30 min/day 5 days/wk); Weight maintenance phase: unclear *Behavior*: Weight loss phase: standard behavioral weight management techniques taught in didactic fashion (self-monitoring, goal setting, stimulus control); Weight maintenance phase: relapse prevention training (psycho-educational training sessions based on 24 relapse prevention training modules designed to teach participants cognitive and behavioral skills for anticipating, avoiding, or coping with lapses in diet and exercise) Comparators G2: Behavioral Treatment + Program Solving Therapy *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior*: Weight loss phase: same as G1; Weight maintenance phase: Problem- solving training (group members report on eating or exercise related difficulties, led in group problem solving with goal of generating a solution plan for dealing with one problem situation using 5-stage problem-solving model); no formal instruction or handouts on problem solving techniques G3: Behavioral Treatment *Diet*: Same as G1	G3: 20 (weekly group sessions for first 20 wk) Provider G1: Pairs of clinical psychology graduate students during weight loss phase, no provider during maintenance phase G2: Pairs of clinical psychology graduate students for entire study	G3: 36.37			5%, *n* (%) G1: 12 (42.9) G2: 13 (38.2) G3: 9 (50) *p*=NR Weight gain, n (%) G1: 4 (14.3) G2: 3 (8.8) G3: 2 (11.1) *p*=NR	

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Physical Activity: Same as G1 *Behavior*: Weight loss phase same as G1; Weight maintenance phase: no counseling						
Electronic Interventions							
Outcome Data at 6 Months or Less as First Time Period Reporting							
WLM (Weight Loss Maintenance Trial) Svetkey et al. 2008 Weight maintenance trial RCT, two phase, multicenter Primary outcomes: weight change from randomization to end of study, weight maintenance, weight reduction from entry, and no more than 3% weight gain from randomization US, Outpatient medical setting - clinic	Prior to randomization to weight loss maintenance, all received group-based behavioral intervention (20 sessions over 6 mo) and had to lose ≥4kg to be eligible for randomization (8.5 kg mean weight loss achieved) G1: Interactive technology-based intervention *Diet:* Reduced caloric intake following DASH dietary pattern *Physical Activity*: Increasing moderate physical activity from 180–225 min/wk , unsupervised *Behavior:* Unlimited access to interactive Web site (encouraged to log-on ≥1 time/wk) with monitoring of weight, diet, and activity, with other lifestyle change; reinforced key theoretical constructs such as motivation, support, problem solving, relapse prevention, etc. covered in weight loss phase Comparators G2: Personal contact intervention *Diet:* Same as G1 *Physical Activity*: Same as G1 *Behavior:* Traditional lifestyle change; reinforced key theoretical constructs such as motivation, support, problem solving, relapse	Duration: 30 mo Run-in (Weight Loss): -6 to 0 mo Treatment: Maintenance: 0–30 mo Follow-up: NR Contacts: G1: 50 (no personal counseling; contacted via e-mail, automated calls and personal calls if failed to log on) G2: 37 (monthly, 5–15 min calls to reinforce adherence to lifestyle changes; 45–60 minute in-person meetings every 4th month) G3: 2 (brief face-to-face meeting at baseline and at mo 12) Provider: G1: Trained Interventionist G2: Same as G1 G3: Same as G1	Adults, with BMIs of 25–45, taking medication for hypertension, dyslipidemia, or both, no active CVD *n*'s: G1: 348 G2: 342 G3: 342 Mean weight at randomization/post weight loss, kg (SD) G1: 88.6 (15.4) G2: 88.7 (16.9) G3: 87.4 (15.3) Mean BMI, kg/m^2 (SD) at randomization to maintenance (post weight loss) G1: 34.2 (4.8) G2: 34.2 (4.9) G3: 34.0 (4.8)	At 6 mo Difference in weight change between groups, kg G1 vs. G3: -0.8 *p*=0.003 G1 vs. G2: -0.1 *p*=0.73 G2 vs. G3: -0.9 *p*=0.001	At 12 mo Difference in weight change between groups, kg G1 vs. G3: -1.0 *p*=0.005 G1 vs. G2: -0.6 *p*=0.11 G2 vs. G3: -1.6 *p*<0.001	At 18 mo Difference in weight change between groups, kg G1 vs. G3: -1.1 *p*=0.003 G1 vs. G2: -0.7 *p*=0.08 G2 vs. G3: -1.8 *p*<0.001 At 30 mo Weight change from randomization, kg (SD) G1: +5.2 (0.3) G2: +4.0 (0.3) G3: +5.5 (0.3) *p*<0.001 Difference in weight change between groups, kg (95% CI) G1 vs. G3: -0.3 (-1.2–0.6*), p*=0.51 G1 vs. G2: -1.2 (2.1–0.3*) p*= 0.008 G2 vs. G3: -1.5 (-2.4 to -0.6*)* *p*=0.001 Weight reduction	Withdrawals, *n* G1: 21 (6) G2: 25 (7) G3: 22 (6) % calculated by reviewer *Note: 1 death per group, not included in the ITT analysis* Attendance, as % of contacts G1: 77 (mo with ≥1 contact) G2: 91 (completed monthly intervention contacts) G3: NR Overall: 94%

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Good	prevention, etc. covered in weight loss phase G3: Self-directed minimal intervention *Diet:* Same as G1 *Physical Activity*: Same as G1 *Behavior:* Received printed lifestyle guidelines with diet and physical activity recommendations at start, two brief meetings with an interventionist					≥5% from entry weight, % G1: 35.3 G2: 42.2 G3: 33.9 G2 vs. G3*: p*=0.02	
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
Harvey-Berino et al., 2004 Weight maintenance trial RCT, two phase, ITT is BOCF US, 10 interactive television sites around University of Vermont Fair	Prior to randomization to weight maintenance, all participants received 24 sessions over 6 mo of group behavioral weight loss program (prescribed 1,000 to 2,500 kcal/day diet based on body weight, increase in programmed and lifestyle activity, and behavior modification skills). Mean weight loss achieved of kg (SD): G1: 8.4 (6.1); G2: 7.6 (4.9); G3: 7.6 (5.0*); p*=0.33 G1. Internet support *Diet*: Reduced calorie intake (4,186, 10,465\kJ/day) *Physical Activity*: Programmed unsupervised activity (walking) 1,000 kcal/wk *Behavior:* Group counseling via interactive television; Web-based program with online self-monitoring and 26 biweekly therapist-led chat room discussions of eating, activity, and behavioral goals for weight loss maintenance Comparators G2. Minimal in-person support *Diet*: Same as G1	Duration: 18 mo Run-in (Weight loss): -6 to 0 mo Treatment Maintenance: 0–12 months Follow-up: NR Contacts G1: 52 (26 biweekly chat room discussion, 26 biweekly e-mails) G2: 6 monthly meetings G3: 52 (26 biweekly group sessions, 26 biweekly phone sessions) Provider G1: Therapist for treatment sessions, health educators, and dietitians (site facilitators) G2: Same as G1 G3: Same as G1	Adults, age >18 yr, with BMIs ≥25 *n*'s G1: 77 G2: 78 G3: 77 Weight, kg (SD) G1: 82.7 (16.3) G2: 80.5 (14.4) G3: 81.2 (14.2) BMI, kg/m^2 (SD) G1: 28.9 (3.8) G2: 29.3 (5.2) G3: 29.0 (4.3)	NR	At 12 mo Weight change, kg (SD): G1: -4.7 (6.9) G2: -4.2 (7.9) G3: -3.9 (5.9) *p*=0.77 *Note: completers data not shown due to high attrition at end of study*	NA	Withdrawals, *n* (%) G1: 25 (32) G2: 15 (19) G3: 16 (21) % calculated by reviewer Attendance at meetings, *n* (SD) G1: 7.7 (5.3) G2 excluded because of minimal contact G3: 10 (5.1) *p*=0.02 Attendance at meetings, *n* (SD) G1: 7.7 (5.3) G2 excluded because of minimal contact G3: 10 (5.1) *p*=0.02

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Physical Activity: Same as G1 *Behavior:* Group counseling via interactive television, Maintenance: 6 monthly group onsite counseling sessions that discussed eating, activity, and behavioral goals for weight loss maintenance G3. Frequent in-person support: *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Group counseling via interactive television Maintenance: 26 biweekly group onsite counseling sessions that discussed eating, activity, and behavioral goals for weight loss maintenance						
Healthy Weight for Life Cussler et al., 2008 Weight maintenance trial RCT, two phase, ITT is BOCF Weight regain a primary outcome US, school/ university setting Good	Randomized after a 4–mo behavioral weight loss program of an energy deficit of 300–500 kcal/day, general exercise advise with individualized goals for energy intake and expenditure, group counseling where sessions dealt with 4 components of behavior change: physical activity, nutrition and healthy eating, social support and the mind/body connection; Achieved weight loss at 4 mo: G1: 5.3 kg, G2: 5.2 kg, no significant differences between groups G1: Internet *Diet*: Usual diet *Physical Activity*: Usual activity *Behavior:* Internet support (private mail, bulletin board, chat rooms, curriculum materials, links to other	Duration: 12 mo Run-in (Weight Loss): -4 to 0 mo Treatment: Maintenance: 0–12 mo Follow-up: NR Contacts: G1: Unknown (self-directed Internet use that allowed contact with study staff) G2: 0 (no further contact) Provider: G1: Intervention team G2: Same as G1	Adult perimenopausal women, ages 40–55 yr, with BMIs of 25–38 *n*'s G1: 66 G2: 69 Weight, kg (SD) G1: 84.6 (12.9) G2: 82.8 (10.7) BMI (SD) G1: 31.0 (3.9) G2: 30.4 (3.3)	NR	At 12 mo Weight, kg (SD) G1: +0.4 (5.0) G2: +0.6 (4.0) *p*=NS (value NR)	NA	Withdrawals, *n* (%) G1: 14 (21) G2: 10 (14) Attendance NR by group Overall: 90.8%

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Web sites of interest), support groups encouraged to meet once a week Comparator G2: Self-directed weight maintenance intervention *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 but without Internet though subjects permitted to continue to meet and practice the principles learned during months 1–4						
Comprehensive Weight Loss or Weight Loss Maintenance Trials That Reported Percentage of Participants who Achieved A Loss ≥5% of Initial Weight at ≥2 Years Post-Randomization							
Look AHEAD (Action for Health in Diabetes) Wadden et al., 2011 RCT, completers analysis Weight is not listed in evidence table as a primary or secondary outcome US, outpatient medical setting Fair	G1: Intensive Lifestyle *Diet*: Mo 0–6: ≤30% fat, ≤10% saturated fat, 1200–1500 kcal/day <250 lbs, 1500–1800 kcal/day >250 lbs with use of meal replacements; Mo 6–12: Personalized calorie target, optional 500 kcal/day deficit with use of meal replacements; *Physical Activity*: Goal of 175 min of moderate intensity physical activity per wk; although walking encouraged, participants allowed to choose other types of moderate-intensity physical activity *Behavior*: Behavior change curriculum including self-monitoring of food intake and physical activity; "toolbox" approach of DPP to help participants achieve and maintain the study's weight loss and activity goals including problem solving and motivational interviewing Comparator G2: Diabetes Support and	Duration: 4 yr Treatment: 4 yr Follow-up: NR Number of contacts: G1: 42 (Mo 0–6: 3 group weekly meetings (60–75 min) and 1 (20 min individual meeting per mo; Mo 7–12: 2 group and 1 individual meeting per mo; Mo 13–48: minimum of 1 onsite contact/month and 1 telephone or e-mail contact/mo; optional monthly group treatment and refresher and campaign groups G2: 4 (group educational/social support sessions) Provider:	Adults, ages 45/55–74 yr (changed during 2nd yr of recruitment) with BMIs >25 or >27 if currently taking insulin; with HbA1c s <11%; SBPs <160 and DBPs <100 mm Hg ; Triglycerides <600 mg/dL and CVD history *n*'s G1: 2,570 G2: 2,575 Weight, kg (SD) Women G1: 94.8 (17.9) G2: 95.4 (17.3) Men G1: 108.9 (19.0) G2: 109.0 (18.0) BMI, $kg/^2$ (SD) Women G1: 36.3 (6.2)	NR	*Note: Completers data* At 12 mo Weight change, % (SD) G1: -8.6 (6.9) G2: -0.7 (4.8) *p*<0.001 Weight change, kg (SD) G1: -8.6 (8.2) G2: -0.7 (5.0) *p*<0.001 Proportion lost ≥10% baseline weight, % G1: 37.8 G2: 3.2 *p*<0.001 Proportion lost ≥7% baseline weight, % G1: 55.2 % G2: 7.0	*Note: Completers data* At 4 yr Weight change, % (SD) G1: -4.7 (0.2) G2: -1.1 (0.2) *p*<0.0001 Weight change, kg (SD) NR Proportion lost ≥10% baseline weight, % G1: 23 G2: 10 *p*<0.0001 Proportion lost ≥ 7% baseline weight, % G1: 35 G2: 18 P < 0.0001	Withdrawals, *n* (%) G1: 74 (3) G2: 112 (4) % calculated by reviewer Attendance, *n* (%) G1: 35.4 (7.3) G2: NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Education *Diet:* None *Physical Activity*: None *Behavior*: General support and education (discussing topics related to diet, physical activity, and social support; received no counseling in behavioral strategies for changing diet and activity	G1: Lifestyle counselor G2: Unclear	G2: 36.6 (6.0) Men G1: 35.3 (5.7) G2: 35.1 (5.2)		*p*<0.001 Proportion lost ≥5% baseline weight, % G1: 68.0 G2: 13.6 *p*<0.001	Proportion lost ≥5% baseline weight, % G1: 46 G2: 25 *p*<0.0001	
Rock et al., 2010 RCT, ITT is BOCF US, academic Weight loss over time based on an interaction between treatment group and time is the primary outcome Fair	G1: Center-Based Jenny Craig *Diet:* Low-fat, 1,200–2,000 kcal/day diet including prepackaged prepared food items delivered to participants door *Physical Activity*: Prescribed goal of 30 min ≥5 days/wk *Behavior:* Brief, weekly individual contacts with an in-person counselor, as provided in the Jenny Craig program Comparators G2: Telephone-based Jenny Craig *Diet:* Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1, but provided via telephone contacts G3. Usual Care *Diet:* Deficit of 500–1000 kcal/day, provided sample meal plans by dietetic professional *Physical Activity*: Increased physical activity recommended *Behavior:* Two 1-hr sessions, combined with monthly check-in via e-mail and telephone, provided with publicly available print material on	Duration: 24 mo Treatment: 0–18 mo Follow-up: 18–24 mo Contacts: G1: 104 (brief individual contact, weekly for 2 years) G2: Same as G1 but via telephone G3: 2 (2 individual visits in 2 yr) Deliverer: G1: Jenny Craig consultant G2: Same as G1 G3: Dietetic professional	Overweight and obese women, ages 18–69 *n*'s G1: 169 G2: 164 G3: 113 Post randomization exclusions: G1: 2 G2: 0 G3: 2 Weight, kg (95% CI) G1: 92.2 (90.7, 93.7) G2: 92.9 (91.1, 94.7) G3: 91.0 (89.0, 92.9) BMI, kg/m^2 (95% CI) G1: 33.8 (33.3, 34.4) G2: 33.8 (33.3, 34.3) G3: 34.0 (33.4, 34.6)	At 6 mo Weight change, kg (95% CI) G1: -9.2 (-9.9, -8.4) G2: -8.3 (-9.1, -7.5) G3: -2.9 (-3.8, -2.0) *p*<0.001 for G1 vs. G3 and G2 vs. G3	At 12 mo Weight change, % (95% CI) G1: -10.9 (-9.7, -12.1) G2: -9.2 (-7.8, -10.6) G3: -2.6 (-1.4, -3.8) Weight change, kg (95% CI) G1: -10.1 (-11.2, -9.0) G2: -8.5 (-9.7, -7.2) G3: -2.4 (-3.6, -1.2) *p*<0.001 for G1 vs. G3 and G2 vs. G3	At 24 mo Weight change, % (95% CI) G1: -7.9 (-6.5, -9.3) G2: -6.8 (-5.2, -8.4) G3: -2.1 (-0.7, -3.5) Weight change, kg (95% CI) G1: -7.4 (-8.7, -6.1) G2: -6.2 (-7.6, -4.9) G3: -2.0 (-3.3, -0.6) P<0.001 for G1 vs. G3 and G2 vs. G3 Proportion lost ≥5% baseline weight, *n* (%) G1: 103 (62) G2: 91 (56) G3: 32 (29) *p*<0.001 for G1 vs. G3 and G2 vs. G3	Withdrawals, *n* (%) G1: 18 (11) G2: 11 (7) G3: 8 (7) % calculated by reviewer Attendance as completion of every contact during 18–24 mo, %: G1: 24.6 G2: 39.2 G3: NR Attendance as those that did not speak to their counselors between 18 and 24 mo,%: G1: 35.9 G2: 23.8 G3: NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	diet and physical activity						
POWER (Practice-based Opportunities for Weight Reduction) – 1 of 3 independent trials Appel et al., 2011 RCT, ITT Weight change from baseline to 24 mo is the primary outcome US, primary care practices Good	G1: Remote Support Diet: Recommended reduced calorie intake as part of DASH diet Physical Activity: Recommended increased exercise (no further detail provided) Behavior: Social cognitive theory framework incorporating behavior self-management approaches to set weight-related goals, self-monitor weight and weight-related behaviors (exercise and reduced calorie intake), increase self-efficacy and social support, problem solving, included motivational interviewing, encouraged to lose 5% of weight; received Web-based support of learning modules, tools and reminders to record weight so can get feedback regarding weight loss progress G2: In-person Support Diet: Same as G1 Physical Activity: Same as G1 Behavior: Same as G1 but no motivational interviewing Comparator G3: Control Diet: None Physical Activity: None Behavior: Given brochures and a list of recommended Web sites promoting weight loss; met with a weight-loss coach at the time of randomization and, if desired, after the final data collection visit	Duration: 24 mo Treatment: 0–12 mo Follow-up: 12 mo Contacts: G1: 33 (12 weekly calls for the first 3 months; one monthly call for next 3 mo; next 18 mo offered monthly calls; encouraged to log in to Web site on a weekly basis G2: 57 (nine 90-min group sessions and three 20-min individual sessions during first 3 mo [weekly]; one 90-min group session and 2 20-min individual sessions during each of the following 3 mo [< weekly]; next 18 mo offered 2 monthly contacts – 1 group session and 1 individual session [biweekly], with the latter conducted either in person or by telephone); also encouraged to log in to Web site on a weekly basis G3: 4 (baseline visit to collect data and meet with weight loss coach, and at 6, 12,	Adults, age ≥21 with one or more CV risk factor (hypertension,, hypercholesterolemia or diabetes) *n*'s G1: 139 G2: 138 G3: 138 Weight, kg (SD) G1: 102.1 (13.9) G2: 105.01 (13.9) G3: 104.4 (18.6) BMI, kg/m2 (SD) G1: 36.0 (4.7) G2: 36.8 (5.2) G3: 36.8 (5.14)	At 6 mo Weight change, % G1: -5.0 G2: -5.2 G3: -1.1 *p*=NS (value NR) Proportion lost ≥5% baseline weight, n (%) G1: 68 (52.7) G2: 57 (46.0) G3: 16 (14.2) G2 vs. G1*:* *p*<0.001 G3 vs. G2*:* *p*<0.001 G1 vs. G2*:* *p*=0.23 Proportion lost ≥10% baseline weight, *n* (%) G1: 30 (23.3) G2: -31 (25) G3: 4 (3.5) G2 vs. G1*:* *p*<0.001 G3 vs. G2*:* *p*<0.001 G1 vs. G2*:* *p*=0.92	NR	At 24 months Weight change, % G1: -5.0 G2: -5.2 G3: -1.1 P = NS (value NR) Weight change, kg (SE) G1: -4.6 (0.7) G2: -5.1 (0.8) G3: -0.8 (0.6) P = NS (value NR) Proportion lost ≥ 5% baseline weight, n (%) G1: 50 (38.2) G2: 55 (41.4) G3: 24 (18.8) G2 vs. G1*:* *p*<0.001 G3 vs. G2*:* *p*<0.001 G1 vs. G2*:* *p*=0.73 Proportion lost ≥10% baseline weight, *n* (%) G1: 24 (18.3) G2: 26 (19.5) G3: 11 (8.6) G2 vs. G1*:* *p*=0.02 G3 vs. G2*:* *p*=0.01 G1 vs. G2*:* *p*=0.69	Withdrawal NR (Note: those without weight measurements at 24 mo: G1: 5%; G2: 4%; G3: 7% (% calculated by reviewer) Attendance at in-person visits, median Treatment G1: 14/15 G2: 14/21 G3: NA Follow-up G1: 16/18 G2: 16/36 G3: NA

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, n Baseline weight Baseline BMI	≤ 6 month mean weight loss (kg/% change)	> 6 and ≤ 1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
		and 24 mo follow-up visits for measurements only and 1 additional meeting with weight loss coach, if desired) Provider: G1: Weight loss coach and PCP (provided encouragement to work with coach) G2: Same as G1 G3: Weight loss coach					

Summary Table 4.9. Characteristics of Lifestyle Intervention Delivery that May Affect Weight Loss: Intervention Intensity

*Moderate intensity is defined as providing 6–13 intervention sessions in the first 6 months; low intensity is defined as providing 1–5 intervention sessions in 6 months.

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Moderate Intensity Interventions							
Outcome Data at 6 Months or Less as First Time Period Reporting							
POWER (Practice-based Opportunities for Weight Reduction) – 1 of 3 independent trials Wadden et al., 2011b RCT, ITT Change in body weight is the primary outcome US, primary care practices Good	G1: Brief Lifestyle Counseling *Diet*: Diets prescribed based on weight: <113.4 kg (balanced diet of 1,200–1,500 kcal/day), ≥113.4 kg (1,500–1,800 kcal/day diets of 15–20% kcal protein, 20–35% fat, rest from carbohydrate); give a calorie-counting book *Physical Activity*: Instructed to gradually increase physical activity to 180 min/wk; given a pedometer *Behavior:* Given Aim for A Healthy Weight handouts; during quarterly visits to own PCP for diabetes, also get monthly brief counseling sessions (following DPP approach) with an auxiliary health care provider (included weigh in, review of food records, goals) Comparator G2: Usual Care *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Received same Aim for A Healthy Weight handout; as part of usual medical care with own PCP, weight recommendations were provided by the PCP during the quarterly scheduled visits, no specific behavioral strategies for	Duration: 24 mo Treatment: 24 mo Follow-up: NR Contacts G1: 33 (quarterly visits with PCP for 24 mo, plus monthly brief [10–15 min.] counseling sessions, plus 1 more counseling visit in mo 1. In year 2, phone contact allowed every other month in lieu of in-person contact) G2: 8 (quarterly visits with PCP) Provider G1: Medical Assistant (Lifestyle Coach) G2: Primary Care Physician	Adults, ≥21 yr,, with BMIs 30–50, with at least 2 of 5 criteria for metabolic syndrome (elevated WC, elevated BP, impaired fasting glucose, elevated triglycerides, low HDL-C) *n*'s G1: 131 G2: 130 Weight, kg (SD): G1: 106.3 (17.3) G2: 111.2 (20.0) BMI, kg/m^2 (SD) G1: 37.8 (4.7) G2: 39.0 (4.8)	**At 6 mo** Weight change, % (SD) G1: -3.5 (0.5) G2: -1.8 (0.5) G2 vs. G1*: p*=0.004 Weight change, kg (SD) G1: -3.5 (0.5) G2: -2.0 (0.5) G2 vs. G1*: p*=0.023	**At 12 mo** Weight change, % (SD) G1: -3.5 (0.6) G2: -2.1 (0.6) G2 vs. G1: *p*=0.078 Weight change, kg (SD) G1: -3.4 (0.6) G2: -2.3 (0.6) G2 vs. G1: *p*=0.208	**At 18 mo** Weight change, % (SD) G1: -3.1 (0.6) G2: -1.7 (0.6) G2 vs. G1*:* *p*=0.100 Weight change, kg (SD) G1: -3.0 (0.7) G2: -1.9 (0.7) G2 vs. G1*:* *p*=0.210 **At 24 mo** Weight change, % (SD) G1: -2.9 (0.7) G2: -1.6 (0.6) G2 vs. G1*:* *p*=0.130 Weight change, kg (SD) G1: -2.9 (0.7) G2: -1.7 (0.7) G2 vs. G1*:* *p*=0.230	Withdrawals, *n* (%) G1: 19 (15) G2: 20 (15) % calculated by reviewer Attendance at PCP sessions, % (SD) G1: 69.0 (29.1) G2: 71.8 (28.6) Attendance at weight loss coaching sessions, % (SD) G1: 56.1 (28.8) G2: NA

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	changing eating and activity habits were provided Note: Enhanced Brief Lifestyle Counseling Intervention arm not reported here because weight loss medications are offered						
Greaves et al., 2008 RCT, ITT is LOCF Weight is a secondary outcome, but proportion of participants meeting predefined targets for weight loss (5%) and moderate physical activity (150 min/wk) after 6 mo UK, community setting (fitness centers etc.) Good	G1: Motivational interviewing techniques *Diet*: reduced calorie intake, reduced portion size, reduced overall fat intake, reduced SF intake, increased fiber intake *Physical Activity*: increased physical activity within the context of the individual's existing life *Behavior*: motivational interviewing (supporting behavior changes, diet and physical activity recommendations); received Comparator G2. Control *Diet*: none *Physical Activity*: none *Behavior*: standardized information packet promoting diet and physical activity recommendations similar to G1	Duration: 6 mo Treatment: 6 mo Follow-up: NR Contacts G1: ≤11 (individual counseling sessions, a mixture of one-to-one contacts and telephone contacts with a mean 34 min/contact) G2: 0 Provider G1: Health promotion counselors (health visitor, rehabilitation nurse, postgraduate students in sports and health science) G2: same as G1	Adults, age ≥18, with BMIs of ≥28 *n*'s G1: 72 G2: 69 Weight, kg (SD): G1: 91.6 (13.3) G2: 94.4 (14.2) BMI, kg/m^2 NR	**At 6 mo** Weight, kg (SD) G1: 91.3 (13.7) G2: 92.6 (15.0) *p*=NR Difference between groups, kg (95% CI) G2 vs. G1: 1.3 (0.2, 2.4) Weight reduction of 5% since baseline, *n* (%) G1: 17 (23.6) G2: 5 (7.2) *p*=NR OR (95% CI): 4.0 (1.4, 11.4)	NA	NA	Withdrawals, *n* (%) G1: 14 (19.3) G2: 12 (17.3) Attendance at sessions G1: median 8 individual sessions and median 1.5 telephone contacts. G2: NR Note: 96% of intervention subjects attended at least 3, and 79% received ≥6 sessions
Outcome Data at Greater Than 6 Months as First Time Period Reporting							
PREDIAS (Prevention of diabetes self-management program) Kulzer et al., 2009 RCT, block	G1: Lifestyle Intervention based on Self-management Theory *Diet:* Not clear but appears to be to reduce fat and increase fiber *Physical activity:* Not clear but appears to be to increase physical activity and use of pedometer	Duration: 1 yr Treatment: 10 mo (not clear what happened during last 2 mo) Follow-up: NR Contacts G1: 12 (8 weekly small	Adults, ages 20–70, with BMIs of ≥26, impaired glucose tolerance or impaired fasting glucose, elevated diabetes risk based on a high score	NR	**At 12 mo** Weight change, % (SD) G1: -4.0 (5.4) G2: -1.6 (4.1) *p*=0.002 Weight change, kg	NA	Withdrawals, *n* (%) NR by group Overall: 17 (9.3) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
randomization; ITT is BOCF Weight is a primary outcome Germany outpatient medical setting Fair	*Behavior:* Diabetes prevention program (including book on diet, exercise, and diabetes, 12 lessons conducted in small groups based on self-management theory), includes stress management, dealing with failure and maintaining new lifestyle Comparator G2: Control *Diet:* None *Physical Activity*: None *Behavior*: Received G1 PREDIAS written information and patient materials	group sessions, 4 bimonthly sessions over next 10 mo, all sessions 90 min each) G2: 0 Provider G1: Diabetes educators or psychologists G2: None	(>10) on the Diabetes Risk Score or according to PCP, ability to read and understand German *n*'s: G1: NR G2: NR *Overall N*=182 Weight, kg (SD) G1: 92.1 (16.5) G2: 93.6 (19.3) BMI, kg/m^2 (SD) G1: 31 (4.7) 4. G2: 32 (5.7)		(SD) G1: -3.6 (5.1) G2: -1.3 (3.9) *p*<0.001 Weight, kg (SD): G1: 88.3 (15.9) G2: 92.2 (19.4) *p*=NR		
ICAN (Improving Control with Activity and Nutrition) Wolf et al., 2004 RCT, block randomization, ITT – unclear method of imputation for missing values Weight is a primary outcome US, school/ university	G1: Case management *Diet:* Goals tailored but based on national dietary recommendations for people with type 2 diabetes and obesity - modest weight loss (5% of initial weight) *Physical activity:* Goal for physical activity reflecting national recommendations *Behavior:* Individual and group education, support, and referral by registered dietitians Comparator G2: Usual care *Diet:* None *Physical Activity*: None *Behavior*: Received educational material and were free to join other	Duration: 12 mo Treatment: 0–12 mo Follow-up: NR Contacts G1: 12 –24 (6 individual sessions throughout year totaling 4 hr, 6 one-half hour small group sessions and brief monthly phone contacts) G2: Unclear/NR Provider: G1: Registered dietitian case manager G2: No provider	Adults, ages ≥20, with BMIs ≥27, treated with medication for T2D *n*'s G1: 74 G2: 73 Weight, kg: G1: 107.1 G2: 106.7 From completers data (*n*'s: G1: 73, G2: 71) BMI, kg/m^2 G1: 37.6 G2: 37.5 From completers data (*n*'s: G1: 73,	NR	**At 12 mo** Weight, kg (95% CI) G1: -2.4 (-4.1, -0.6) G2: +0.6 (-1.0, 2.2) G2: -3.0 (-5.4, -0.6) *p*<0.001 Weight reduction ≤5% since baseline, % G1: 53 G2: 32 *p*=NR Weight reduction ≥5% since baseline, % G1: 20 G2: 14 *p*=0.03	NA	Withdrawals, *n* (%) G1: 19 (26) G2: 10 (14) Attendance at individual classes, % G1: 100 G2: NR Attendance at group classes, % G1: 78 G2: NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Good	weight management or diabetes care programs		G2: 71)				
Finnish Diabetes Prevention Study Tuomilehto et al., 2001 Lindstrom et al, 2003 RCT, states ITT but weight is completers analysis Weight is not a specified outcome of interest Finland, outpatient medical clinic Good	G1: Intervention *Diet:* <30% of energy from fat, increase in fiber, 50% CHO, 1 g/kg ideal body weight/day protein (20% used some type of VLCD or partial meal replacement for a short period of time to boost weight loss) *Physical Activity:* Tailored, moderate intensity and medium- to high volume programs including endurance exercise (recommended) with supervised resistance training; exercise competition *Behavior:* Detailed dietary and physical activity topic sessions including problem solving; offered voluntary group sessions, lectures, cooking lessons, between visit phone calls and letters Comparator G2: Control *Diet*: None *Physical Activity*: None *Behavior*: Oral and written information about diet (a two-page leaflet) and exercise; no specific individualized programs were offered; completed a 3-day food diary, using a booklet illustrating the sizes of portions of food	Duration: 4.2 yr Treatment: 1 yr Follow-up: average 3.2 yr Contacts– G1: ~ 15 (7 sessions during the first year, plus 1 session every 3 mo thereafter G2: ~ 3 (annual visits) Provider G1: Nutritionist for diet advice, unclear for resistance training G2: Nutritionist	Adults, age 40–65 yr, with BMIs ≥25, and impaired glucose tolerance *n*'s 1: 265 2: 257 Weight NR BMI, kg/m^2 G1: 31.3 G2: 31.0	NR	*Note: completers data* **At 1 yr** Weight change, % (SD) G1: -4.7 (5.4) G2: -0.9 (4.2) *p*<0.001 Weight change, kg (SD) G1: -4.2 (5.1) G2: -0.8 (3.7) *p*<0.001 Weight reduction > 5% since baseline, % G1: 43 G2: 13 *p*=0.001	*Note: completers data* **At 2 yr** Weight change, kg (SD) G1: -3.5 (5.5) G2: -0.8 (4.4) *p*<0.001	Withdrawals at 1 yr, *n* (%) G1: 23 (9) G2: 17 (7) Attendance at diet sessions at 1 yr: NR Attendance at exercise sessions at 1 yr, % G1: 86 G2: 71
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
Esposito et al., 2004 RCT,	G1: Intervention *Diet*: Tailored advice on >10% weight reduction (1,700 kcal goal	Duration: 2 yr Treatment: 2 yr Follow-up: NR	Adult, obese sedentary males, ages 35–55, with evidence of erectile	NR	NR	**At 2 yr** Weight change, kg G1: -15.0	Withdrawals, *n* (%) G1: 19 (23) G2: 16(20)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
intervention staff not blinded, ITT but how missing values imputed is unclear Weight is a secondary outcome Italy, school/ university Good	for 1st year, 1,900 in yr 2), dietary regimen per 1,000 kcal: 50–60% CHO, 15–20% protein, <30% fat, <10% SF, 10–15% MUFA, 5–8% PUFA, 18 g fiber *Physical Activity*: Recommendations for increasing the level of physical activity (walking, swimming, aerobic); individual guidance *Behavior*: Behavioral and psychological counseling, plus instruction on reducing caloric intake, setting goals, and self-monitoring (food diaries) through a series of monthly small group sessions Comparator G2: Control *Diet*: No specific individualized program *Physical Activity*: No specific individualized program *Behavior*: General oral and written information about healthy food choices and exercise	Contacts G1: 18 (monthly sessions with the nutritionist and exercise trainer for the first year and bimonthly sessions for the second year) G2: same as G1 Provider G1: Nutritionist and exercise trainer G2: Dietitian/ nutritionist	dysfunction n's G1: 55 G2: 55 Weight, kg (SD) G1: 103.0 (9.4) G2: 101.0 (9.7) BMI, kg/m^2 (SD) G1: 36.9 (2.5) G2: 36.4 (2.3)			G2: - 2.0 *p*=NR Weight change corrected difference between groups, kg (95% CI) -13.0 (-18.0, -11.0) *p*=0.007 Weight, kg (SD) G1: 88.0 (8.5) G2: 99.0 (9.2) *p*=NR	G3: 18 (24) G4: 11 (14) % calculated by reviewer Attendance at sessions, % G1: 72 G2: 60 G3: 64 G4: 73
Esposito et al., 2003 RCT, intervention staff not blinded, ITT but how missing values imputed is unclear Weight is a secondary outcome	G1: Intervention *Diet*: Tailored advice on ≥10% weight reduction, mean kcal goals: 1,300 yr 1, 1,500 yr 2, recommended composition: 50–60% CHO, 15–20% protein, <30% fat, <10% saturated fat, 10–15% MUFA, 5–8% PUFA, 18 g fiber/1,000 kcal (similar to Mediterranean-style Step I diet) *Physical Activity*: Individual guidance on increasing physical activity (walking, swimming or	Duration: 2 yr Treatment: 2 yr Follow-up: NR Contacts G1: 18 (monthly sessions with the nutritionist and exercise trainer for the first yr and bimonthly sessions for the second yr) G2: same as G1	Adult, obese, premenopausal, sedentary females who had not participated in a diet reduction program in past 6 mo *n*'s G1: 60 G2: 60 Weight, kg (SD) G1: 95.0 (9.4)	NR	NR	**At 2 yr** Weight change, kg G1: -14.0 G2: -3.0 *p*=NR Weight change corrected difference between groups, kg (95% CI) -11.0 (-14.0, -8.0) *p*<0.001	Withdrawals, *n* (%) G1: 3 (5) G2: 5 (8) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Italy, outpatient medical setting Good	aerobic ball games) *Behavior*: Behavior and psychological counseling Comparator G2: *Diet*: No specific individualized program *Physical Activity*: No specific individualized program *Behavior*: General oral and written information about healthy food choices and exercise	Provider G1: Nutritionist and exercise trainer G2: Dietitian/ nutritionist	G2: 94.0 (9.2) BMI, kg/m^2 G1: 35.0 (2.3) G2: 34.7 (2.4)			Weight, kg (SD) G1: 81.0 (7.5) G2: 91.0 (9.0)	
REACH (Reasonable Eating and Activity to Change Health) Logue et al., 2005 RCT, parallel group trial, ITT is BOCF Weight change is the primary outcome US, outpatient medical setting – group practice Fair	G1: Transtheoretical Model *Diet*: Written dietary prescriptions based on the information from the dietary recalls (standard prescription to reduce calories, increase fruit and vegetables, reduce fat) *Physical Activity*: Increased activity and physical activity (prescription based on reported energy expenditure) *Behavior:* Transtheoretical model and chronic disease care program (patients mailed stage and behavior-matched workbooks that correspond to most recent stage of change profile; brief monthly telephone calls from trained weight loss advisor applying processes of change that correspond to patients profile Comparator G2: Augmented Usual Care *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Counseling based on	Duration: 2 yr Treatment: 24 mo Follow-up: NR Contacts G1: 36 (stage of change assessments every other month and monthly phone calls) G2: 0 Provider G1: Physician, dietitian, weight loss advisor Practitioner G2: Dietitian	Adults, ages 40–69, with BMIs >27 or waist-to-hip ratios > 0.950 in men or >0.800 in women *n*'s G1: 329 G2: 336 Weight, kg (SD): NR BMI, *n* by range (%) G1: 25–29.9: 59 (18) 30–34.5: 119(37) 35 –39.0: 69 (21) 40.0+: 79 (24) G2: 25–29.9: 73 (22) 30–34.5: 107(32) 35–39.0: 82 (24) 40.0+: 74 (22)	NR	NR	**At 24 mo** Weight change, kg (95% CI) G1: -0.39 (-1.1, 0.4) G2: -0.16 (-1, -0.7) *p*=0.50	Withdrawals, *n* (%) G1: 58 (18) G2: 70 (21) Attendance at sessions NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	USDA Food Guide Pyramid or a Soul Food Guide Pyramid						
Low-Intensity Interventions							
Outcome Data at 6 Months or Less as First Time Period Reporting							
No trials							
Outcome Data at Greater Than 6 Months as First Time Period Reporting							
GOAL (Groningen Overweight and Lifestyle study) ter Bogt et al., 2009 RCT, ITT is BOCF Weight included as a primary outcome The Netherlands, outpatient medical setting – private practices Fair	G1: Nurse Practitioner - Lifestyle *Diet*: No specific prescription but given diet advice *Physical Activity*: No specific prescription but given a pedometer *Behavior*: Lifestyle intervention including extensive conversation on history of slimming and motivation to change lifestyle/lose weight and development of a treatment plan, feedback on food diary, physical activity, attainability of goals and if necessary refer to dietitian Comparator G2: General Practitioner – usual care *Diet*: No intervention *Physical activity*: No intervention *Behavior:* Offered one visit to discuss from a screening and thereafter usual PCP care	Duration: 1 yr Treatment: 12 mo Follow-up: NR Contacts G1: 5 (4 individual visits, 1 feedback session by phone) G2: 1 (via phone to discuss screening results) Provider G1: Nurse Practitioner G2: General Practitioner	Adults, ages 40–70, BMIs 25–40, with hypertension and/or dyslipidemia *n*'s G1: 225 G2: 232 Weight, kg: NR BMI, kg/m^2 (SD) G1: 29.5 (3.1) G2: 29.6 (3.6)	NR	**At 1 yr** Weight change (adjusted for gender, age, BMI, weight change between screening and baseline), % (95% CI) G1: -1.9 (-2.5, -1.2) G2: -0.9 (-1.5, -0.2) *p*<0.05 BOCF Weight losers and stabilizers, % G1: 77 G2: 65 *p*<0.05	NA	Withdrawals (*n*): G1: 24 (11) G2: 17 (7.3) Attendance at sessions NR
Christian et al., 2008 RCT, ITT is LOCF Weight loss as fraction of subjects	G1: Lifestyle Change Pre-intervention computer-based assessment generated tailored plan to set self-management goals with feedback on barriers to improving diet, physical activity, planning guide for participants,	Duration: 1 yr Treatment: 52 wk Follow-up: NR Contacts: G1: 4 (once every 3 mo to review goal sheet with physician)	Latino/Hispanic adults in community health centers, ages 18–75, with BMIs of ≥25, a diagnosis of type 2 diabetes, uninsured or Medicaid eligible or	NR	**At 12 mo** Weight change, kg G1: -0.08 G2: +0.63 *p*=0.23 Note: converted from lb to kg by		Withdrawals G1: 14 (9) G2: 23(15) Attendance at sessions NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
achieving a clinically meaningful weight loss (5% reduction in body weight) included as a primary outcome US, outpatient clinic Good	companion report for physician counseling *Diet*: Individualized diet recommendations *Physical Activity*: Individualized physical activity recommendations *Behavior:* Motivational interviewing counseling during quarterly visits with physician to help patients make changes in dietary and physical activity behaviors, including discussing patient's tailored lifestyle change goal and encouragement in attaining goals; also provided with planning guide with supplemental information on diabetes and achieving a healthy lifestyle Comparator G2: Control *Diet*: None *Physical Activity*: None *Behavior:* Health educational materials on diabetes, diet, and exercise	G2: 4 (once every 3 mo to receive usual care) Provider G1: Physician G2: Physician	Medicare enrolled *n*'s G1: 155 G2: 155 Weight, kg G1: 93.15 G2: 90.09 Note: converted from pounds to kg by reviewer BMI, kg/m^2 G1: 35.4 G2: 34.8		reviewer, lb data: G1: - 0.18 (10.92) G2: +1.39 (10.60) *p*=0.23 Weight reduction of ≥ 5% since baseline, n (%) G1: 30 (21) G2: 14 (11) *p*=0.02		
Outcome Data at Greater Than 12 Months as First Time Period Reporting							
No trials							

Summary Table 4.10. Characteristics of Lifestyle Intervention Delivery that May Affect Weight Loss or Weight Maintenance: Onsite Vs. Electronically Delivered Interventions

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Randomized Comparison of High-Intensity Onsite vs. Electronically Delivered interventions							
Harvey-Berino et al., 2010 RCT, 3x3 repeated measures design, ITT is BOCF Weight loss is a primary outcome US, medical center and internet Fair	G1: Hybrid (Internet and in person) *Diet*: Calorie-restricted diet and given a dietary fat goal corresponding to ≤25% of calories from fat *Physical Activity*: Graded exercise goals progressing to 200 min/wk of moderate to vigorous exercise like walking; pedometers provided *Behavior:* Self-monitoring, stimulus control, problem solving, goal setting, relapse prevention and assertiveness training; all educational materials delivered electronically Comparators G2: Internet *Diet*: Same as G1 *Physical Activity*: same as G1 *Behavior:* Same as G1 with a new lesson each week online, access to an online database to help monitor calorie intake as well as online educational resources, a bulletin board for group communication, weekly tips and recipes, a BMI calculator, and local physical activity events) G3: In person *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 but received paper journal for monitoring dietary intake and	Duration: 6 months Treatment: 6 months Follow-up: NR Contacts: G1: 24 (1-hr weekly sessions, access to Internet treatment but once a month an in-person group meeting substituted for an online chat) G2: 24 (1-hr weekly group sessions in secure online chat room) G3: 24 (1-hr weekly group sessions) Provider: G1: Behaviorally trained graduate students, clinical psychologists, and registered dietitians with extensive weight management experience G2: same as G1 G3: same as G1	Adults, with BMIs between 25 and 50 n's G1: 161 G2: 158 G3: 162 Weight, kg (SD) G1: 96.5 (16) G2: 97.2 (18.7) G3: 97.4 (18.5) BMI, kg/m^2 (SD) G1: 35.6 (5.7) G2: 36/0 (5.7) G3: 35.6 (5.5)	**At 6 mo** Weight change, % (SD): G1: -6.0 (5.8) G2: -5.7 (5.4) G3: -7.9 (6.2) *p*<0.01 Note: G3 superior to G1 and G2 as determined by "pair-wise comparisons" *p* values not given for comparisons noted at significant by authors; also noted no significant differences between G1 and G2 Weight change, kg (SD): G1: -5.7 (5.5) G2: -5.5 (5.6) G3: -7.6 (5.2) *p*<0.01 Weight change ≥7%, % G1: 42.0 G2: 37.3 G3: 53.2	NA	NA	Withdrawals, *n* (%) G1: 8 (4.9) G2: 2 (1.2) G3: 8 (5.1) % calculated by reviewer Attendance at sessions, % (SD) G1: 72 G2: 76 G3: 71

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	physical activity, as well as a commercially available calorie and fat-counting book						
High-Intensity, Onsite Comprehensive Interventions							
Weight Loss Outcome, Data at 6 Months or Less							
PRIDE (The Program to Reduce Incontinence by Diet and Exercise Subak et al., 2009 RCT, block randomization, 2:1 ratio, ITT is BOCF Weight is a secondary outcome US, outpatient medical setting Good	G1: Weight Loss Program *Diet:* Standard reduced-calorie diet (1,200–1,500 kcal./d, ≤30% fat), sample meal plans, vouchers for 2 meal replacements per day in mo 1–4, and 1 meal replacement per day thereafter *Physical Activity*: Increased physical activity (brisk walking or activities of similar intensity) >200 min/wk *Behavior:* Behavioral skills (self-monitoring, stimulus control, and problem-solving) Comparator G2: Education *Diet:* No intervention *Physical Activity*: No intervention *Behavior:* Educational sessions on weight loss, physical activity, and healthy eating habits	Duration: 6 mo Treatment: 0–6 months Follow-up: NR Contacts G1: 24 (weekly sessions for 6 mo) G2: 4 (education sessions at mo 1, 2, 3, and 4) Provider G1: Experts in nutrition, exercise, and behavior change G2: Unclear	Women >30 yr, with BMIs 25–50, with baseline incontinence *n*'s: G1: 226 G2: 112 Weight, kg (SD): G1: 98 (17) G2: 95 (16) BMI, kg/m^2 (SD) G1: 36.0 (6) G2: 36.0 (6)	**At 6 mo** Weight change, % (95% CI) G1: -8.0 (9, -7) G2: -1.6 (-2.7, -0.4) *p*<0.001 Weight change, kg (95% CI) G1: -7.8 (NR) G2: -1.5 (NR) *p*<0.001 Weight, kg (SD) G1: 90.0 (17.0) G2: 94.0 (17.0) *p*=NR	NA	NA	Withdrawals, *n* (%) G1: 5 (2.2) G2: 15 (13.4) Attendance NR
Blumenthal et al., 2000 RCT, ITT, unclear if weight is BOCF Weight is a primary outcome US, outpatient medical setting Fair	G1: Weight Management *Diet*: 5,021 J/d (women), 6,276 J/d (men), 15–20% fat *Physical Activity*: Aerobic exercise 55 min 3–4 times/week *Behavior:* LEARN weight management program (lifestyle, exercise, attitudes, relationships, nutrition), self-monitoring of food intake and weight	Duration: 26 wk Treatment: 26 wk Follow-up: NR Contacts: G1: plus 26 (weekly group sessions – LEARN program) G2: 72–96 (weekly aerobic exercise sessions)	Adults, >29 yr, with BMIs of 25–37, and unmedicated high normal BP or stage 1 to 2 HTN *n*'s G1: 55 G2: 54 G3: 24 Weight, kg	**At 6 mo** Weight change, kg (SD) G1: -7.9 (6.0) G2: -1.8 (2.8) G3: +0.7 (3.3) G1 vs. G2*: p*=0.001 G1 + G2 vs. G3: *p*=0.001 Weight, kg (SD) G1: 85.4 (17.1)	NA	NA	Withdrawals, *n* (%) G1: 9 (16.3) G2: 10 (18.5) G3: 2 (8.3) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Comparators: G2: Exercise Only *Diet*: Usual diet *Physical Activity*: Same as G1 *Behavior:* No intervention G3: Usual care *Diet*: Usual *Physical Activity*: Usual *Behavior:* No intervention	G3: None Provider G1: Exercise Physiologist and unclear for diet and behavioral interventions G2: Exercise Physiologist G3: None	G1: 93.3 G2: 95.4 G3: 94.0 BMI, kg/m^2 G1: 32.1 G2: 32.8 G3: 32.6	G2: 93.6 (14.2) G3: 94.7 (17.9) G1 vs. G2*: p*=NR G1 vs. G3*: p*=0.001			
DPP (Diabetes Prevention Program) Knowler et al., 2002 West et al., 2008 Knowler et al., 2009 RCT, West data presented here is secondary analysis using all available data without imputation for missing values or deleting incomplete observations, includes only White, African American and	G1: Intensive Lifestyle Modification *Diet*: Low-calorie and low-fat (<25%) *Physical Activity*: Moderate-intensity physical activity (walking) 150 min/wk *Behavior*: 16 lesson core curriculum on strategies for weight loss and physical activity changes, including self-monitoring of food intake, physical activity, and weight Comparator G2: Usual care + Placebo *Diet*: Food Guide Pyramid and NCEP Step 1 *Physical Activity*: Encouraged to increase physical activity (walking) 150 min/wk *Behavior*: Standard lifestyle recommendations G3: Usual care + Metformin *Diet*: Food Guide Pyramid and	Duration: Average 2.8 yr Treatment: 30 mo Follow-up: NR Contacts: G1: 52 (16 individual sessions over 24 wk, followed by bimonthly individual or group sessions at minimum) G2: Annual 20–30 min meeting G3: Annual 20–30 min meeting Provider G1: Dietitians acted as Case Manager G2: same as G1 G3: same as G1	Adults, ≥25 yr with BMIs of ≥24 (22 in American Asians) and at high risk for diabetes *n*'s for White, African American, Hispanic participants G1: 962 G2: NR (1,082 for main study) G3: 985 Weight, kg (SD) G1: 94.1 (20.8) G2: 94.3 (20.2) G3: 94.3 (19.9) BMI, kg/m^2 G1: 33.9 G2: 34.2 G3: 33.9	**At 6 mo** Weight change, kg (SD) G1: -7.1 (5.8) G2: NR G3: -2.2 (4.0) *p*=NR Weight change of at least 7% from baseline, % G1: 50 G2: NR G3: NR	**At 12 mo** Weight change, kg (SD) G1: -7.1 (7.2) G2: NR G3: -2.8 (4.8) *p*=NR	**At average of 2.8 yr** Weight change, kg G1: -5.6 G2: -0.1 G3: -2.1 G1 vs. G3*:* *p*<0.001 G1 vs. G2*:* *p*<0.001 G2 vs. G3*:* *p*<0.001 At 10 yr *absolute weight change data not reported; data presented in Figure only	Withdrawals, *n* (%) G1: 107 (10) G2: 107 (10) G3: 106 (10) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Hispanic participants (Asian Americans and Native Americans excluded) Weight is listed as a primary outcome for the secondary analysis US, 27 medical clinics Good	NCEP Step 1 *Physical Activity*: Encouraged to increase physical activity (walking) 150 min/wk *Behavior*: Standard lifestyle recommendations						
POWER (Practice-based Opportunities for Weight Reduction) – 1 of 3 independent trials Appel et al., 2011 RCT, ITT is LOCF Weight change from baseline to 24 mo is the primary outcome US, primary care practices Good	G1: Remote Support *Diet*: Recommended reduced calorie intake as part of DASH diet *Physical Activity*: Recommended increased exercise (no further detail provided) *Behavior*: Social cognitive theory framework incorporating behavior self-management approaches to set weight-related goals, self-monitor weight and weight-related behaviors (exercise and reduced calorie intake), increase self-efficacy and social support, problem solving, included motivational interviewing, encouraged to lose 5% of weight; received Web-based support of learning modules, tools and reminders to record weight so can get feedback regarding weight loss progress Comparators G2: In-person Support *Diet*: Same as G1	Duration: 24 mos Treatment: 0–12 mo Follow-up: 12 mo Contacts: G1: 33 (12 weekly calls for the first 3 mo; one monthly call for next 3 mo; next 18 mo offered monthly calls; encouraged to log in to Web site on a weekly basis G2: 57 (nine 90-min group sessions and three 20-min individual sessions during first 3 mo; one 90-min group session and two 20-min individual sessions during each of the following 3 mo; next 18 mo offered 2 monthly contacts – 1 group session and 1 individual session, with	Adults, age ≥21 with one or more CV risk factors (hypertension, hypercholesterol-emia or diabetes) *n*'s G1: 139 G2: 138 G3: 138 Weight, kg (SD) G1: 102.1 (13.9) G2: 105.01 (13.9) G3: 104.4 (18.6) BMI, kg/m^2 (SD) G1: 36.0 (4.7) G2: 36.8 (5.2) G3: 36.8 (5.14)	**At 6 mo** Weight change, % G1: -5.0 G2: -5.2 G3: -1.1 *p*=NS (value NR) Weight change, kg (SE) G1: -6.1 (0.5) G2: -5.8 (0.6) G3: -1.4 (0.4) *p*=NS (value NR) Proportion lost ≥5% baseline weight, *n* (%) G1: 68 (52.7) G2: 57 (46.0) G3: 16 (14.2) G2 vs. G1*: p*<0.001 G3 vs. G2*: p*<0.001 G1 vs. G2*: p*=0.23 Proportion lost ≥10% baseline weight, *n* (%) G1: 30 (23.3) G2: -31 (25)	NR	**At 24 months** Weight change, % G1: -4.9 (0.8) G2: -5.2 (0.7) G3: -1.1 (0.6) G1 vs. G3: *P* <0.001 G2 vs. G3: *P* <0.001 G2 vs. G1: *P* =0.58 Weight change, kg (SE) G1: -4.6 (0.7) G2: -5.1 (0.8) G3: -0.8 (0.6) G1 vs. G3: p < 0.001 G2 vs. G3: p < 0.001 G2 vs. G1*: p*=0.77 Proportion lost ≥ 5% of baseline	Withdrawal NR (Note: those without weight measurements at 24 months: G1: 5%; G2: 4%; G3: 7% (% calculated by reviewer) Attendance at in-person visits, median Treatment G1: 14/15 G2: 14/21 G3: NA Follow-up G1: 16/18 G2: 16/36 G3: NA

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Physical Activity: Same as G1 *Behavior*: Same as G1 but no motivational interviewing G3: Control *Diet*: None *Physical Activity*: None *Behavior*: Given brochures and a list of recommended Web sites promoting weight loss; met with a weight loss coach at the time of randomization and, if desired, after the final data collection visit	the latter conducted either in person or by telephone); also encouraged to log in to Web site on a weekly basis G3: 4 (baseline visit to collect data and meet with weight loss coach, and at 6, 12, and 24 mo follow-up visits for measurements only and 1 additional meeting with weight loss coach, if desired) Provider: G1: Weight loss coach and PCP (provided encouragement to work with coach) G2: Same as G1 G3: Weight loss coach		G3: 4 (3.5) G2 vs. G1*: p*<0.001 G3 vs. G2*: p*<0.001 G1 vs. G2*: p*=0.92		weight, *n* (%) G1: 50 (38.2) G2: 55 (41.4) G3: 24 (18.8) G1 vs. G3*:* *p*<0.001 G2 vs. G3*:* *p*<0.001 G2 vs. G1*:* *p*=0.73 Proportion lost ≥10% of baseline weight, *n* (%) G1: 24 (18.3) G2: 26 (19.5) G3: 11 (8.6) G1 vs. G3*:* *p*=0.02 G2 vs. G3*:* *p*=0.01 G2 vs. G1*:* *p*=0.69	
TOHP-II (Trials of Hypertension Prevention, Phase II) Stevens et al., 2001 RCT Weight change is a primary outcome US, outpatient medical setting Good	G1: Weight Loss *Diet*: Reduced caloric intake; 1,500–1,200 kcal/day goals (men/women) *Physical Activity*: 30–45 min/day 4–5 days/wk; moderate exercise intensity (including brisk walking) *Behavior*: Self-directed behavior change, nutrition education, information on physical activity and social support for making and maintaining behavior changes (food diaries, graphs of activities, setting short term goals, developing action plans to achieve objectives, alternative strategies for trigger problem eating)	Duration: 3 yr Treatment: 3 yr Follow-up: NR Contacts G1: ≤32 (1 individual counseling session followed by 14 weekly group meetings, 6 biweekly and then monthly group meetings up until mo 18) G2: NR Provider G1: Dietitians or Health Educators G2: None	Adults, ages 30–45, with BMIs of 26.1–37.4 (men) 24.4–37.4 (women), with nonmedicated DBPs of 83–89 mmHg and SBP <140 mmHg n's G1: 595 G2: 596 Weight, kg (SD) G1: Men: 98.9 (12.3) Women: 84.1 (11.9) G2: Men: 98.5	*Note: completers data* **At 6 mo** Weight change, kg G1: -4.4 G2: +0.1 *p*<0.0001	NR	*Note: completers data* **At 18 mo** Weight change, kg G1: -2.0 G2: +0.7 *p*<0.0001 **At 36 mo** Weight change, kg G1: -0.2 G2: +1.8 *p*<0.0001	Withdrawals, *n* (%) G1: 48 (8) G2: 42 (7) % calculated by reviewer Attendance NR by group

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Comparator G2: Usual Care *Diet*: NR *Physical Activity*: NR *Behavior*: NR		(11.7) Women: 82.9 (10.9) BMI, kg/m^2 (SD) G1: Men: 31.0 (2.9) Women: 31.0 (3.6 G2: Men: 31.0 (2.9) Women: 30.8 (3.5)				
ORBIT (Obesity Reduction Black Intervention Trial) Stolley et al., 2009 Fitzgibbon et al 2010 RCT, completers analysis Weight is a primary outcome US, academic setting Fair	G1: Weight Loss and Maintenance *Diet:* Weight loss phase: Low-fat, high-fiber diet (<30% fat, ≥ 25 g fiber) (≥ 5 servings/d fruits and vegetables); Maintenance phase: unclear/NR *Physical Activity:* Weight loss phase: Exercising at moderate to vigorous level 3–4 times per week ≥ 30 min, including supervised exercise during group sessions; Maintenance phase: continued exercise during group sessions *Behavior:* Weight loss phase: discussion related to diet, physical activity and weight loss plus motivational interviewing sessions; Maintenance phase: unclear /NR Comparator G2: Control *Diet:* No intervention *Physical Activity:* No intervention *Behavior:* Weight loss phase: Newsletters and phone calls on general health and safety topics; Maintenance phase: unclear/NR continued newsletters/phone calls	Duration: 18 mo Treatment: 18 mo Weight loss: 0–6 mo Maintenance: 7–12 mo Follow-up: NR Contacts G1: 54 (2 sessions per week for 24 wk, then monthly motivational interviewing sessions either face-to-face or by phone) G2: 6 (monthly phone calls to discuss/clarify newsletter content) Provider G1: Trained interventionist G2: Staff member not affiliated with weight loss intervention	Adult, African American females, ages 30–65, with BMIs of 30–50 *n*'s: G1: 107 G2: 106 Weight, kg G1: 103.9 G2: 105.9 BMI, kg/m^2 G1: 38.7 G2: 39.k8	*Note: completers data* **At 6 mo** Weight change, kg (SD) G1: -3.0 (4.9) G2: +0.2 (3.7) *p*<0.001 Weight, kg (SD) G1: 101.3 (16.3) G2: 106.0 (17.5) *p*<0.001 Subjects losing ≥5% from baseline, % G1: 26 G2: 5 *p*= NR	NR	*Note: completers data* **At 18 mo** Weight change, kg (SD) G1: -2.3 (7.4) G2: +0.5 (5.7) *p*=0.003 Subjects losing ≥ 5% from baseline, % G1: 24 G2: 12 *p*=0.04	Withdrawals at 6 mo, *n* (%) G1: 7 (6.5) G2: 8 (7.5) Withdrawals for 7–18 mo G1: 7 G2: 0 Attendance at diet classes at 6 mo, % G1: 53.3 (31.5) G2: 52.5 (31.8) *p*=0.90 Attendance at diet classes from 7–18 mo, % G1: 27.1 (30.2) G2: NR
Weight Loss Outcome Data at Greater than 6 Months to 12 Months							

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Look AHEAD (Action for Health in Diabetes) Pi-Sunyer et al., 2007 Wadden et al., 2009 Wing et al., 2010 Wadden et al., 2011 RCT, completers analysis Weight is not listed in ET as a primary or secondary outcome US, outpatient medical setting Fair	G1:Intensive Lifestyle *Diet*: Mo 0–6: ≤30% fat, ≤10% saturated fat, 1200–1500 kcal/day <250 lb, 1500–1800 kcal/day >250 lbs with use of meal replacements; mo 6–12: Personalized calorie target, optional 500 kcal/day deficit with use of meal replacements; *Physical Activity*: Goal of 175 min of moderate intensity physical activity per week; although walking encouraged, participants allowed to choose other types of moderate-intensity physical activity *Behavior*: Behavior change curriculum including self-monitoring of food intake and physical activity; "toolbox" approach of DPP to help participants achieve and maintain the study's weight loss and activity goals including problem solving and motivational interviewing Comparator G2: Diabetes Support and Education *Diet:* None *Physical Activity*: none *Behavior*: General support and education (discussing topics related to diet, physical activity, and social support; received no counseling in behavioral strategies for changing diet and activity	Duration: 1 yr Treatment: 1 yr Follow-up: NR Number of contacts: G1: 42 (Mo 0–6: 3 group weekly meetings (60–75 min) and 1 (20 min individual meeting per month; Mo 7–12: 2 group and 1 individual meeting per month G2: 4 (group educational/social support sessions) Provider: G1: Lifestyle counselor G2: Unclear	Adults, ages 45/55–74 yr (changed during 2nd yr of recruitment) with BMIs >25 or >27 if currently taking insulin; with HbA1c s <11%; SBPs <160 and DBPs <100 mm Hg; Triglycerides <600 mg/dL and CVD history *n*'s G1: 2,570 G2: 2,575 Weight, kg (SD) Women G1: 94.8 (17.9) G2: 95.4 (17.3) Men G1: 108.9 (19.0) G2: 109.0 (18.0) BMI, $kg/^2$ (SD) Women G1: 36.3 (6.2) G2: 36.6 (6.0) Men G1: 35.3 (5.7) G2: 35.1 (5.2)	NR	*Note: Completers data* **At 12 mo** Weight change, % (SD) G1**:** -8.6 (6.9) G2: -0.7 (4.8) *p*<0.001 Weight change, kg (SD) G1**:** -8.6 (8.2) G2: -0.7 (5.0) *p*<0.001 ≥10% weight reduction, % G1: 37.8 G2: 3.2 *p*<0.001 ≥7% weight reduction from baseline, % G1: 55.2 % G2: 7.0 *p*<0.001	*Note: Completers data* **At 4 yr** Weight change, % (SD) G1**:** -4.7 (0.2) G2: -1.1 (0.2) *p*<0.001 Weight change, kg (SD) NR	Withdrawals, *n* (%) G1: 74 (3) G2: 112 (4) % calculated by reviewer Attendance, *n* (%) G1: 35.4 (7.3) G2: NR
Teixeira et al., 2010 RCT, ITT is BOCF Change in bodyweight is a	G1: Weight Loss *Diet:* Decrease daily caloric intake by 300–400 kcal *Physical activity:* No specific prescription but encouraged to find situations in their daily lives to	Duration: 2 yr Treatment: 52 wk Follow-up: 1 yr Contacts G1: 30 (face-to-face	Adult premenopausal females, ages 25–50 yr, with BMIs between 25–40, free from major illnesses, not	NR	**At 12 mo** Weight change, % (SD) G1: -7.1 (7.0) G2: -1.7 (4.9) G1 vs. G2*: p*=NR	**At 24 mo** Weight change, % (SD) G1: -4.9 (7.5) G2: -1.9 (6.9) G1 vs. G2*: p*=NR	Withdrawals NR by group Attendance at sessions NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
primary outcome Portugal, school/ university Fair	increase caloric expenditure; pedometer offered *Behavior:* Cognitive behavior group sessions (based on self-determination theory; included aspects such as identifying personal resistances, overcoming lapses, establishing adequate goals, and implementing self-monitoring; topics covered emotional and external eating, improving body acceptance and body image Comparator G2: Control *Diet:* None *Physical Activity*: None *Behavior*: General health education curriculum based on several educational courses on various topics (e.g., preventive nutrition, stress management, self-care, and effective communication skills)	120 min meetings in groups of 25 to 30 participants) G2: Unclear (article states that curriculum based on several 3–6 week-long educational topics; format not described) Provider G1: 6 PhD or MS level exercise physiologists, nutritionists/dietitians and psychologists G2: Unclear/NR	taking medications known to interfere with body weight regulation *n*'s G1: NR G2: NR Overall: 258 19 excluded from analyses due to medication to affect weight Weight, kg (SD) NR BMI, kg/m^2 Overall: 31.3 (4.1) Note: Demographic data not reported by treatment group, but article states intervention group did not differ from those in the control group in terms of BMI		Subjects with 5% weight loss from baseline, % G1: 61 G2: 16 G1 vs. G2: *p*<0.001 Subjects with 10% weight loss from baseline, % G1: 29 G2: 4 G1 vs. G2: *p*<0.001	Subjects with 5% weight loss from baseline, % G1: 45 G2: 19 G1 vs. G2*:* *p*<0.001 Subjects with 10% weight loss from baseline, % G1: 18 G2: 8 G1 vs. G2*:* *p*<0.001	
TONE (Trial of Non-pharmacologic Interventions in the Elderly) Whelton et al., 1998 Kumanyika et	G1: Sodium Reduction and Weight Loss *Diet*: Weight loss diet with sodium restriction diet (goal of achieving and maintaining a 24-hour dietary sodium intake of ≤80mmol (≤1,800 mg) and achieving and maintaining a weight loss of ≥4.5 kg (≥10 lb) by reducing calorie and fat intake *Physical Activity*: Frequency and duration of activity individualized, with walking recommended most frequently *Behavior*: Combination of small	Duration: 29 mo (median) Treatment (intensive): 4 mo Treatment (extended): 4 mo Maintenance: Unclear/NR Follow-up: 15–36 mo (range) 29 mo (median) Contacts: Treatment (intensive):	Adults age 60–80 yr, willing to participate, avg SBP <145mm Hg and DBP <85 mm Hg while taking a single antihypertensive medication or a single combination regimen consisting of a diuretic agent and a non-diuretic	NR	**At 9 mo** Mean Weight change, kg G1 & G2: -5.0 G3 & G4: -1.2 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.8 (3.1–4.5) G3 & G4: NR	**At 18 mo** Mean Weight change, kg G1 & G2: -4.4 G3 & G4: -0.8 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.6 (2.8–4.3) G3 & G4: NR **At 30 mo**	Withdrawals, *n* (%) G1: 16 (10.9) G2: 10 (6.8) G3: 30 (8.8)* G4: 27 (7.9)* % calculated by reviewer Attendance at sessions, *n* (%) 9 mo: 884 (91) 18 mo: 829 (86)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
al., 2002 RCT, factorial analysis Weight loss is a secondary outcome US, school/ university Good	group and individual meetings, (advised participants on ways to change eating patterns and increasing physical activity; food diaries used; primary goal was to provide participants with core knowledge and behavior skills necessary to achieve behavior change) G2: Weight Loss Only *Diet*: Same as G1 without sodium restriction *Physical Activity*: Same as G1 *Behavior*: Same as G1 without focus on sodium restriction Comparators G3: Sodium Reduction *Diet*: Sodium-restricted diet (goal of achieving and maintaining a 24-hr dietary sodium intake of ≤80mmol (≤1800 mg) or less) *Physical Activity*: None *Behavior*: Combination of small group and individual meetings (advised participants on ways to change eating patterns; primary goal was to provide participants with the core knowledge and behavior skills necessary to achieve and maintain their desired reductions in sodium intake) G4: *Diet*: None *Physical Activity*: None *Behavior*: No study-related counseling in lifestyle change techniques but were invited to meetings on topics unrelated to the goals of the trial	G1: 16 (weekly sessions) G2: 16 (weekly sessions) G3: 16 (weekly sessions) G4: NR/ Unclear Treatment (extended): G1: 8 (biweekly sessions) G2: 8 (biweekly sessions) G3: 8 (biweekly sessions) G4: NR/ Unclear Maintenance: G1: NR (monthly sessions) G2: NR (monthly sessions) G3: NR (monthly sessions) G4: Unclear/NR Provider: G1: Nutritionists and exercise counselors G2: Nutritionists and exercise G3: Nutritionists and exercise counselors G4: Nutritionists and exercise counselors	agent, stable health, independence in daily living, presumed capacity to alter diet and exercise as required by the study *n*'s G1: 147 G2: 147 G3: 144* G4: 147 Weight, kg G1: 86.0 G2: 87.0 G3: 88.0 G4: 86.0 BMI, kg/m^2 G1: 31.2 G2: 31.0 G3: 31.2 G4: 31.3 *Information reported here is for overweight subjects (*N*=585) only			Mean Weight change, kg G1 & G2: -4.7 G3 & G4: -0.9 Net Reduction in Weight, kg (95% CI) G1 & G2: -3.9 (2.7-5.1) G3 & G4: -0.9 (0.4 –1.3) *Mean weight loss in group 2 was 1.0 kg (95% CI -0.1-2.0) greater than in Group 1.	30 mo: 441 (86) *- Both overweight and not overweight participants
Weight Loss Outcome Data at Greater than 12 Months							

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
ADAPT (The Arthritis, Diet and Activity, Promotion Trial) Messier et al., 2004 RCT, 2x2 factoral design, ITT was computed missing values Weight loss is a secondary outcome US, school/ university Good	G1: Combined exercise and dietary weight loss *Diet*: 500 kcal/day deficit, nutrient intake NR, no food provided *Physical Activity*: 180 min/wk, aerobics and strength training *Behavior:* Behavior therapy of group dynamics and social cognitive theory Comparators G2: Dietary weight loss *Diet*: 500 kcal/day deficit, nutrient intake NR, no food provided *Physical Activity*: No exercise *Behavior:* Behavior therapy: group dynamics and social cognitive theory. Behavior change using self-regulatory skills including self-monitoring G3: Structured exercise *Diet*: Usual diet *Physical Activity*: 180 min/wk, aerobics and strength training *Behavior:* No guided behavioral therapy G4: Healthy Lifestyle Control *Diet*: None *Physical Activity*: No exercise *Behavior:* No guided behavioral therapy	Duration: 18 mo Treatment: 26 wk Follow-up: 6–18 mo Contacts G1: 70 (diet: see G1 and exercise: see G2) G2: 44 (16 weekly sessions in mo 1–4, then group/individual sessions biweekly sessions in mo 5–6, then alternating every 2 wk meetings/phone contacts plus newsletters in mo 7_18 with the duration of each contact NR G3: 48 (exercise contacts: 3x/wk/60 min/session at facility in months 1–3, then option of doing home based, duration of contact NR G4: 12 (1-hr monthly meetings in mo 1–3, monthly phone calls in months 4–6, then bimonthly phone calls from mo 7–18) Provider G1: Both dietitian and exercise physiologist trained by health psychologist G2: Master's degree dietitian/ nutritionist Health Educator G3: Exercise	Adults, ≥60 yr, with BMIs ≥28, sedentary lifestyle, knee osteoarthritis with pain *n*'s G1: 76 G2: 82 G3: 80 G4: 78 Weight, kg (SEM) G1: 92 (0.2) G2: 95 (0.2) G3: 92 (0.2) G4: 96 (0.2) BMI, kg/m^2 (SD) G1: 34.0 (0.7) G2: 34.5 (0.6) G3: 34.2 (0.6) G4: 34.2 (0.6)	NR	NR	**At 18 mo** Weight change, % G1: -5.7 G2: -4.9 G3: -3.7 G4: -1.2 G1 vs. G4*:* *p*<0.05 G2 vs. G4*:* *p*<0.05 Weight change, kg (95% CI) G1: -5.20 (0.85, 9.55) G2: -4.61 (0.38, 8.84) G3: -3.46 (-0.77, 7.69) G4: 1.10 (-3.00, 5.20) G1 vs. G4*:* *p*<0.05 G2 vs. G4*:* *p*<0.05	Withdrawals, *n* (%) G1: 19 (23) G2: 16(20) G3: 18 (24) G4: 11 (14) % calculated by reviewer Attendance at sessions, % G1: 72 G2: 60 G3: 64 G4: 73

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
		Physiologist G4: Health Educator					
Comprehensive Electronically Delivered Interventions							
Evidence of Weight Loss in Comprehensive Electronic (Telephone) Interventions							
Compared with Usual Care, Minimal Control, or No Intervention (includes self-directed)							
Weight loss outcome data at greater than 12 months							
Haapala et al., 2009 RCT, ITT is BOCF or LOCF, whichever is greater Finland, unclear Weight is a primary outcome Fair	G1: Mobile Phone Weight Loss Program *Diet:* Reduction in caloric intake *Physical Activity*: Increase physical activity *Behavior:* Automated tailored text message responses to participants reporting, password protected Web site provides further information on attaining goals Comparator G2: Control group *Diet:* No intervention *Physical Activity*: No intervention *Behavior:* No intervention	Duration: 12 mo Treatment: 0–12 mo Follow-up: NR Contacts: G1: Varied by participant (mobile phone text messaging and Internet) G2: NR Provider: G1: Automated Weight Balance Mobile phone program G2: No provider	Adults, ages 25–44 yr, with BMIs of 25–36, and access to a mobile phone and Internet connection *n*'s G1: 62 G2: 63 Weight, kg (SD) G1: 87.5 (12.6) G2: 86.4 (12.5) BMI, kg/m^2 (SD) G1: 30.6 (2.7) G2: 30.0 (2.8)	NR	**At 12 mo** Weight, kg (SD) G1: - 3.1 (4.9) G2: - 0.7 (4.7) *p*=0.245	NA	Withdrawals, *n* (%) G1: 17 (27) G2: 22 (35) % calculated by reviewer Attendance NR Frequency of program usage faded from 8 wk to 3 or 4/wk by 12 mo
Evidence of Weight Loss in Comprehensive Electronic (Internet) Interventions							
Compared with Usual Care, Minimal Control, or No Intervention (includes self-directed)							
Weight Loss Outcome Data at 6 Months or Greater							
SHED-IT Morgan et al., 2009, 2010 RCT, parallel group, stratified by obesity level Body weight and % change from baseline are primary	G1: Internet-based *Diet:* Modification of dietary habits *Physical Activity:* Modification of physical activity habits, pedometers provided *Behavior:* Lifestyle modification information session, access to CalorieKing Web site to self-monitor weight, food intake, and activity; e-mail feedback from counselors	Duration: 6 mo Treatment: 0–3 mo Follow-up: 4–6 mo Contacts: G1: 8 (1 face-to-face information session, 7 feedback sheets provided by e-mail) G2: 1 (1 face-to-face	Adult men, ages 18–60 yr, with BMIs of 25–37 *n*'s: G1: 34 G2: 32 Weight, kg (SD) G1: 99.1 (12.2) G2: 99.2 (13.7)	**At 3 m** Weight change, kg (95% CI): G1: -4.8 (-6.4, -3.3) G2: -3.0 (-4.5, -1.4) *p*=NS (value NR) Weight reduction >5%, % G1: 55.6 G2: 28.0	NA	NA	Withdrawals, *n* (%) G1: 6 (17.6) G2: 5 (16.1) Attendance NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
outcomes US, military research center Good	Comparator G2: Wait list; Control: self-help *Diet:* No intervention *Physical Activity:* No intervention *Behavior:* Lifestyle modification information session, provided with program booklet	information session) Provider: G1: Member of research team G2: same as G1	BMI, mean kg/m^2 (SD) G1: 30.1 (3.0) G2: 30.6 (2.7)	*p*=0.04 **At 6 mo** Weight change, kg (95% CI): G1: -5.3 (-7.3, -3.3) G2: -3.5 (-5.5, -1.4) *p*=NS (value NR) Weight reduction >5%, % G1: 50.0 G2: 34.6 *p*=0.25			
Hunter et. al., 2008 RCT, two-group parallel design, ITT is BOCF US, military medical research center Body change (kg and % change from baseline) a primary outcome Good	G1: Behavioral Internet Treatment *Diet:* Calorie restriction of 1,200–1500 kcal/day; fat intake <30% of total kcal; food diaries *Physical Activity:* Increase physical activity until expenditure is at least 1,000 kcals/wk *Behavior:* 24 weekly self-taught weight loss behavior intervention lessons about 20–30 min each available on Web site (stimulus control, behavior modification, and stress management) with feedback from counselor, LEARN manual provided Comparator G2: Usual care *Diet:* No prescribed intervention (nutrition consultants, healthy cooking classes and annual diet assessments available) *Physical Activity*: Usual group workouts at least 3x/wk with fitness assessments available *Behavior:* No prescribed intervention (weight loss classes	Duration: 6 mo Treatment: 0–24 wk Follow-up: NR Contacts G1: 27 (1 in-person orientation, 24 weekly feedback, and brief motivational interviewing telephone calls scheduled at 4 and 8 wks post-baseline) G2: None Provider G1: Counselor (via Internet) G2: None	Adults, ages 18–65, whose weight is within 5 lb or above their maximum allowable weight for US Air Force (BMI ≥25 in women and ≥27.5) *n*'s G1: 224 G2: 222 Weight, kg (SD): G1: 87.4 (15.6) G2: 86.6 (14.7) BMI, kg/m^2 (SD) G1: 29.4 (3.0) G2: 29.4 (3.0)	**At 6 mo** Weight change, kg (SD) G1: -1.0 (3.7) G2: +0.5 (3.1) *p*=0.001 Weight reduction of 5%, % G1: 22.6 G2: 6.8 *p*<0.001	NA	NA	Withdrawals, *n* (%) G1: 34 (15) G2: 18 (8) % calculated by reviewer Attendance at 8 wk, as availability for motivational calls, *n* (%) G1: 176 (78.4) G2: NA Attendance through 6 mo, as Web site log-ins, mean (range) G1: 49.1 (1, 707) G2: NA

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	available)						
Compared with Comprehensive Electronic Interventions							
Weight Loss Outcome Data at 6 Months or Greater							
Gold et al., 2007 RCT, pilot, ITT is BOCF Weight is a primary outcome US, Web-based Fair	G1. VTrim (online weight loss and maintenance program) *Diet:* Calorie goals ranges from 1,200–2,200/day *Physical Activity*: Gradual increase in exercise energy expenditure with ≥1,000 calories/wk burn via aerobic activity (walking particularly encouraged) *Behavior*: Online therapist-led program with no structured curriculum although fundamental behavioral weight loss concepts presented online, but is interactive for consultation Comparator G2. eDiets.com (access to self-help commercial weight loss program) *Diet:* Reduced energy diet following U.S. Dietary Guidelines; 1,000 calories/day deficit (goal of 1–2 lb loss/wk, automated feedback based on self-reported weight *Physical Activity*: Encouraged exercise tailored to participants exercise abilities, likes and dislikes *Behavior*: Online therapist-led program of fundamental behavioral weight loss concepts, no structured behavioral curriculum	Duration: 12 mo Treatment: G1: Weight loss: 0–6 mo Weight maintenance: 6–12 mo G2: 0–12 mo Follow-up: NR Contacts: G1: 39 (weekly hour long online chats with therapist for weight loss phase, biweekly for maintenance phase) G2: same as G1 Provider: G1: Weight loss phase: online therapist; Maintenance phase: Web site only G2: Web site, online expert and peer support	Adults, ages >18 yr, with BMIs >25 but ≤ 39.9 *n*'s G1: 62 G2: 62 Weight, kg (SD) G1: 92.0 (15.7) G2: 90.2 (14.1) BMI, kg/m^2 (SD) G1: 32.3 (3.9) G2: 32.5 (4.2)	**At 6 mo** Weight change, % (SD) G1: -7.3 (7.8) G2: -3.6 (6.1) *p*=NR Weight change, kg (SD) G1: -6.8 (7.8) G2: -3.3 (5.8) *p*=0.005	**At 12 mo** Weight change, % (SD) G1: 5.5 (7.6) G2: 2.8 (5.5) *p*=NR Weight change, kg (SD) G1: +5.1 (7.1) G2: +2.6 (5.3) *p*=0.034	NA	Withdrawals, *n* (%) G1: 22 (31) G2: 14 (22) % calculated by reviewer Attendance at 6 mo, as logins to Web site, median (range) G1: 47 (25–65) G2: 193 (120–209) *p*<0.001 Attendance from 6–12 mo, as logins to Web site, median (range) G1: 14 (8–23) G2: 90 (21–154) *p*<0.001
Tate et al., 2006 RCT, ITT is BOCF	G1: Slim-Fast Web site and Computer-automated feedback *Diet:* Standard calorie-restricted diet of 1,200–1,500 kcal/day with	Duration: 6 mo Treatment: 0–6 mo Follow-up: NR	Adults, ages 20–65 with BMIs of 27–40 *n*'s:	**At 3 mo** Weight change, kg (SD) G1: -4.1 (4.3)	NA	NA	Withdrawals, *n* (%) G1: 17 (28) G2: 12 (19)

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Change in bodyweight is a primary outcome US, worksite Good	advice on use of structural meals and meal replacements (2 meal replacements/day encouraged) *Physical Activity*: Exercise recommendations of minimum of 1,050 kcal/wk exercise *Behavior:* Instructed on how to use the Slim-Fast Web site: weekly weight reporting, weekly diet tips, weight loss e-buddy system, plus weekly behavioral lessons similar to those in the DPP, and automated feedback to diary entries Comparators G2: Slim-Fast Web site and Human E-mail Counseling *Diet:* see G1 *Physical Activity*: see G1 *Behavior:* see G1 but with human e-mail feedback to diary entries G3: Slim-Fast Web site and no Counseling *Diet:* see G1 *Physical Activity*: See G1 *Behavior:* See G1 but with no feedback	Contacts: G1: 26 (weekly programmed feedback tailored to individual diary submission) G2: 26 (weekly e-mail feedback tailored to individual diary submission) G3: None Provider; G1: None (automated responses based on cognitive behavior therapy theory) G2: Weight loss counselor G3: None (Web site data only)	G1: 61 G2: 64 G3: 67 Weight, kg (SD) G1: 89.0 (13.2) G2: 89.0 (13.0) G3: 88.3 (13.9) BMI, kg/m^2 (SD) G1: 32.7 (3.5) G2: 32.8 (3.4) G3: 32.3 (3.7)	G2: -5.3 (4.2) G3: -2.3 (3.4) *p*=NR **At 6 mo** Weight change, kg (SD) G1: -3.5 (5.4) G2: -5.9 (6.2) G3: -2.3 (5.4) *p*=NR Weight loss of >5 %, % G1: 34 G2: 52 G3: 27 *p*=0.01			G3: 8 (12) % calculated by reviewer Attendance, as median logins to Web site, *n* G1: 2 G2: 9 G3: 20 *p*=0.001

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Weight Loss Outcome Data at 12 Months or Greater							
Tate et al., 2003 RCT, ITT is BOCF U.S., outpatient medical setting - hospital Change in body weight is a primary outcome Good	G1: Basic Internet Program and Behavioral Counseling *Diet:* 1,200 and 1,500 kcal/day, fat intake of 20% or fewer calories *Physical Activity*: Minimum of 1,000 kcal/wk exercise *Behavior:* Web site support with e-counseling, diet and exercise recommendations Comparator G2: Basic Internet Program *Diet:* see G1 *Physical Activity*: See G1 *Behavior:* Web site support without e-counseling	Duration: 1 yr Treatment: 1 yr Follow-up: NR Contacts: G1: 53 (1 face-to-face counseling session, weekly tips, plus weekly communications via e-mail with assigned weight loss counselor) G2: 1 (1 face-to-face counseling session) Provider; G1: Behavioral Counselor (all held master's or doctoral degrees in health education, nutrition, or psychology) G2: None	Adults with BMIs of 27–40, and one or more risk factors for T2D *n*'s: G1: 46 G2: 46 Weight, kg (SD) G1: 86.2 (14.3) G2: 89.4 (12.6) BMI, kg/m^2 (SD) G1: 32.5 (3.8) G2: 33.7 (3.7)	Note: 3 mo and 6 mo data NR here due to completers analysis and greater than 10% attrition	**At 12 mo** Weight change, % G1: -4.8 G2: -2.2 *p*=0.03 Weight change, kg (SD) G1: -4.4 (6.2) G2: -2.0 (5.7) *p*=0.04 Difference as 95% CI: -0.1 to 4.9; *p*=0.04	NA	Withdrawals, *n* (%) G1: 8 (17) G2: 7 (15) % calculated by reviewer Attendance at 12 mo assessment G1: NR G2: NR *p*=0.78 Overall: 84%
Compared with Other Comprehensive Interventions (includes Onsite and/or Electronic)							
Weight Loss Outcome Data at 4 Months or Greater							
Harvey-Berino et al., 2010 RCT, 3x3 repeated measures design, ITT is BOCF Weight loss is a primary outcome U.S., medical center and internet	G1. Hybrid (Internet and in person) *Diet*: Calorie-restricted diet and given a dietary fat goal corresponding to ≤25% of calories from fat *Physical Activity*: Graded exercise goals progressing to 200 min/wk of moderate to vigorous exercise like walking; pedometers provided *Behavior:* Unlimited access to an interactive Web site, includes self-monitoring, stimulus control, problem solving, goal setting,	Duration: 6 mo Treatment: 6 mo Follow-up: NR Contacts: G1: 24 (1-hr weekly sessions, access to Internet treatment but once a month an in-person group meeting substituted for an online chat) G2: 24 (1-hr weekly	Adults, with BMIs between 25–50 n's G1: 161 G2: 158 G3: 162 Weight, kg (SD) G1: 96.5 (16) G2: 97.2 (18.7) G3: 97.4 (18.5) BMI, kg/m^2 (SD) G1: 35.6 (5.7) G2: 36/0 (5.7)	**At 6 mo** Weight change, % (SD): G1: -6.0 (5.8) G2: -5.7 (5.4) G3: -7.9 (6.2) *p*<0.01 Note: G3 superior to G1 and G2 as determined by "pair-wise comparisons," *p* values not given for	NA	NA	Withdrawals, *n* (%) G1: 8 (4.9) G2: 2 (1.2) G3: 8 (5.1) % calculated by reviewer Attendance at sessions, % (SD) G1: 72 G2: 76 G3: 71

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
Fair	relapse prevention and assertiveness training; all educational materials delivered electronically Comparators G2. Internet *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 with a new lesson each week online, access to an online database to help monitor calorie intake as well as online educational resources, a bulletin board for group communication, weekly tips and recipes, a BMI calculator, and local physical activity events) G3. In person *Diet*: Same as G1 *Physical Activity*: Same as G1 *Behavior:* Same as G1 but received paper journal for monitoring dietary intake and physical activity, as well as a commercially available calorie and fat-counting book	group sessions in secure online chat room) G3: 24 (1-hr weekly group sessions) Provider: G1: Behaviorally trained graduate students, clinical psychologists, and registered dietitians with extensive weight management experience G2: same as G1 G3: same as G1	G3: 35.6 (5.5)	comparisons noted as significant by authors; also noted no significant differences between G1 and G2 Weight change, kg (SD): G1: -5.7 (5.5) G2: -5.5 (5.6) G3: -7.6 (5.2) $p<0.01$ Weight change ≥7%, % G1: 42.0 G2: 37.3 G3: 53.2			
Womble et al., 2004 RCT, ITT is LOCF Change in body weight is a primary outcome US, electronic, commercial Fair	G1: eDiets.com *Diet:* Diet of conventional foods matching participant's needs, likes, and lifestyle *Physical activity*: Personalized prescriptions of physical activity based on self-reported levels of CV endurance and muscular strength *Behavior*: NR G2: Weight loss manual *Diet:* Self-selected diet of conventional table foods	Duration: 52 wk Treatment: G1: Weight loss: 0–52 weeks G2: Weight loss: 0–16 wk; Weight maintenance: 16–36 wk Follow-up: NR Contacts: G1: 5 (individual meetings at baseline	Adult women, ages 18–65 with BMI's of 27 to 40 *n*'s G1: 23 G2: 24 Weight, kg (SD) G1: 93.4 (12.6) G2: 87.9 (10.8) BMI, kg/m^2 (SD) G1: 33.9 (3.2) G2: 33.0 (3.0)	**At 16 wk** Weight change, % (SD) G1: -0.9 (3.2) G2: -3.6 (4.0) $p=0.01$ Weight change, kg (SD) NR	**At 52 wk** Weight change, % (SD) G1: -1.1 (4.0) G2: -4.0 (5.1) $p=0.04$ Weight change, kg (SD) NR	NA	Withdrawals, *n* (%) G1: 8 (35) G2: 8 (33) Adherence as mean attendance at scheduled meetings, *n* (SD) G1: 7.6 (3.2) G2: 8.1 (3.4) Mean logons to

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Physical activity: Increased physical activity (walking up to 30 min/day) *Behavior:* LEARN manual, Weight Maintenance Survival Guide weight control behaviors (e.g., stimulus control, slowing eating, cognitive restructuring)	and at 8, 16, 26, and 52 wk) G2: 5 (individual meetings at baseline and at 8, 16, 26, and 52 wk) Provider G1: eDiets.com; psychologist G2: LEARN Manual; psychologist					Web site, *n* (SD) G1: 17.7 (21.1) G2: NR
Evidence of Weight Loss in Comprehensive Electronic (Interactive Equipment) Interventions							
Compared with Other Comprehensive Intervention (Internet or Onsite)							
Weight Loss Outcome Data at 4 Months or Greater							
Byrne et al., 2006 RCT, stratified by age, sex and BMI, ITT is LOCF Weight loss is the primary outcome Australia, outpatient medical setting - clinic Fair	G1: Personalized weight management program - electronic *Diet*: Ad librium low-fat and energy-reduced diet advice *Physical Activity*: Increase of physical activity *Behavior*: Received a transmitter belt, receiver watch, program user's manual, diet diary, tape measure, calorie-counting book; program calculates weight loss or maintenance goals based on information provided by subjects Comparator G2: Standard care *Diet*: Same as G1 *Physical Activity*: Increase of physical activity following the Australian National Physical Activity	Duration: 32 wk Treatment: 32 wk Follow-up: NR Contacts: G1: 1 (one training session and encouraged to e-mail staff with questions if there were problems with the program) G1: 1 (single consultation) Provider G1: Health professional with dual qualification in dietetics and exercise physiology G2: Same as G1	Adults, ages 30–45 yr, with BMI's of 27–32, sedentary and ready to change *n*'s G1: 33 G2: 41 Weight, kg: G1: 85.7 G2: 87.2 BMI, kg/m^2 G1: 29.3 G2: 29.3	**At 16 wk** Weight change, kg (SE) G1: -4.46 (0.5) G2: -2.35 (0.6) *p*=NS (value NR) **At 32 wk** Weight change from 16 wk, kg (SE) G1: -0.39 (0.5) G2: +0.12 (0.6) *p*=NS (value NR) Weight change from baseline, kg (SE) G1: -4.84 (0.5) G2: -2.19 (0.6) *p*<0.05	NA	NA	Withdrawals, *n* (%) G1: 9 (22) G2: 6 (18) Attendance at sessions NR

Study Cited, Design, Primary Outcome Setting, Quality Rating	Intervention Groups, Component Details	Treatment Duration, Follow-up Time Period Total Contacts	Sample Characteristics, Group Size, *n* Baseline weight Baseline BMI	≤6 month mean weight loss (kg/% change)	>6 and ≤1 year mean weight loss (kg/% change)	>1 year mean weight loss (kg/% change)	Attrition Attendance
	Guidelines *Behavior*: Consultation of simple advice to reducing energy intake and increase physical activity with clear directions that the goal should be to lose no greater than 1 kg/wk						

Critical Question 5

Summary Table 5.1. Component 1: Efficacy

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
Dixon et al, 2008 RCT Glycemic control University Obesity Research Center, G1 and G2 Australia Fair	G1: Subjects underwent placement of a LAGB via the pars flaccid technique by one of two experienced surgeons within 1 mo of randomization; plus all aspects of the conventional therapy program for G2 (below) G2: Lifestyle modification programs were individually structured to reduce energy intake, to reduce intake of fat (<30%) and saturated fats, and to encourage intake of low-glycemic index and	Inclusion criteria: Between 20–60 yr; BMI of 30–40; had been diagnosed with clearly documented T2D within previous 2 yr *N*'s at baseline G1: 30 G2: 30 Age, mean (SD): G1: 46.6 (7.4) G2: 47.1 (8.7) Sex, *n* (% male): G1: 15 (50) G2: 13 (43) BMI, mean (SD): G1: 37.0 (2.7) G2: 37.2 (2.5)	Mean weight loss at 2 yr, % (SD): G1: 20.0 (9.4) G2: 1.4 (4.9) *p*-value between groups <.001 Mean weight change at 2 yr, kg (SD): G1: -21.1 (10.5) G2: -1.5 (5.4) *p*-value between groups <0.001	Change in Systolic BP at 2 yr, mm Hg (SD): G1: -6.0 (17.9) G2: -1.7 (14.2) *p*–value between groups =.37 Change in Diastolic BP at 2 yr, mm Hg (SD): G1: -0.7 (11.1) G2: -0.9 (11.1) *p*–value between groups =.92 Change in Plasma Glucose at 2 yr, mg/dL (SD): G1: -51.2 (37.6) G2: -18.4 (41.2) *p*–value between groups =.002 Change in Plasma Insulin at 2 yr, µIU/mL (SD): G1: -12.4 (8.4) G2: -1.0 (14.8) *p*–value between groups <.001 Change in Total Cholesterol at 2 yr, mg/dL(SD):	Duration of follow-up: G1: 24 mo G2: 24 mo *n*'s (%), at 2 yr follow-up: G1: 29 (97) G2: 26 (87)

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
	high-fiber foods. Physical activity advice encouraged 10,000 steps/day and 200 min/wk of structured activity, including moderate intensity aerobic activity and resistance exercise			G1: 3.6 (51.6) G2: -0.4 (31.4) *p* –value between groups =.72 Change in triglyceride at 2 yr, mg/dL (SD): G1: -71.7 (92.9) G2: -2.1 (120.6) *p*–value between groups =.02 Change in HDL-C at 2 yr, mg/dL (SD): G1: 12.6 (9.8) G2: 2.6 (6.1) *p* –value between groups <.001 Change in total cholesterol to HDL-C ratio at 2 yr (SD): G1: -0.82 (1.9) G2: -0.14 (1.04) *p*–value between groups =.02 Remission of type 2 diabetes G1: 73% G2: 27% *p* –value between groups <.001 Conservative analysis assuming all four noncompleters in the conventional therapy group achieved remission; the only noncompleter in the surgical group did not.	
Ikonomidis et al, 2007 Prospective cohort study aortic elastic properties and cardiac function Outpatient medical setting – hospital (G1, G2, G3) Greece	Treatment Groups: G1. Surgical group G2. Nonsurgical Group Intervention: G1: Subjects underwent BPD with RYGB G2: Morbidly obese individuals who refused any surgical or medical intervention; maintained their weight over the course of the study	Inclusion Criteria: Not reported in detail *N*'s at baseline G1: 60 G2: 20 Age, mean (SD): G1: 35 (11) G2: 37 (12) Sex, Women, *n* (%) G1: 45 (75) G2: 16 (80) BMI, mean (SD):	BMI, mean kg/m^2 (SD): 3 yr G1: 32 (6) G2: 49.8 (5.8) *p*-value between groups <0.001 Weight, mean kg (SD): 3 yr G1: 87 (17) G2: 134 (23) *p*-value between groups <0.001	Plasma glucose level, mg/dl: 3 yr G1: 87 (13) G2: 106.5 (24) *p*-value between groups <0.001 Total Cholesterol, mg/dl: 3 yr G1: 147 (34) G2: 234 (29) *p*-value between groups <0.001 Triglycerides, mg/dl: 3 yr G1: 74 (24) G2: 148 (53)	*n*'s (%), at 3 yr follow-up: G1: 60 G2: 20 Duration of follow-up: G1: 3 yr G2: 3 yr

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
Fair		G1: 48.68 (7.8) G2: 48.57 (5.9)		*p*-value between groups <0.001 Hypertension, *n* (%) 3 mo G1: 8 (17) G2: 8 (40) 3 yr G1: 4 (9) G2: 10 (50) *p*-value between groups <0.001 Diabetes, *n* (%) 3 mo G1: 2 (3) G2: 4 (20) 3 yr G1: 1 (2) G2: 5 (25) *p*-value between groups <0.001	
Mingrone, 2012 Single-center, non-blinded, randomized, controlled trial Weight	1. Gastric bypass 2. BPD 3. Medical therapy	Inclusion Criteria: Age of 30–60 yr BMI of ≥35; history of type 2 diabetes of at least 5 yr; a glycated hemoglobin level of ≥7.0% (as	% Change in Weight loss (from baseline), 2 yr 1: -33.31 (7.88) 2: -33.82 (10.17) 3: -4.74 (6.37) Excess Weight loss at 2 yr, % (SD) 1: 68.08 (12.70)	% Change in Glucose (from baseline), 2 yr 1: -37.81 (33.75) 2: -56.23 (10.01) 3: -14.37 (11.93) % Change in Total Cholesterol (from baseline), 2 yr 1: -6.83 (27.03) 2: -49.25 (11.52)	Intervention *n*'s at 2 yr follow-up: 1: 19 2: 19 3: 18 Duration of follow-up:

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
change, change in CVD risk factors Day Hospital of Metabolic Diseases and Diabetology of the Catholic University Rome Good		confirmed by at least three analyses) an ability to understand and comply with the study protocol Intervention *n*'s (baseline): 1: 20 2: 20 3: 20 Mean Age, yr (SD): 1: 43.90 (7.57) 2: 42.75 (8.06) 3: 43.45 (7.27) Sex, male, *n* (%): 1: 10 (50); 2: 10 (50); 3: 8 (40); Weight, kg (SD): 1: 129.84 (22.58) 2: 137.85 (30.35) 3: 136.40 (21.94) BMI (SD): 1: 44.85 (5.16) 2: 45.14 (7.78) 3: 45.62 (6.24) WC, cm (SD) 1: 125.40 (16.58) 2: 130.35 (19.73) 3: 126.90 (14.68)	2: 69.36 (17.60) 3: 9.29 (12.94) % Change in BMI (from baseline), 2 yr 1: -33.31 (7.88) 2: -33.82 (10.17) 3: -4.73 (6.37) % Change in WC (from baseline), 2 yr 1: -19.91 (8.44) 2: -20.70 (8.34) 3: -7.69 (7.80)	3: -16.82 (11.60) % Change in HDL-C (from baseline), 2 yr 1: 29.66 (18.21) 2: 12.98 (20.66) 3: 6.03 (6.25) % Change in LDL-C (from baseline), 2 yr 1: -17.21 (36.21) 2: -64.63 (15.93) 3: -20.31 (15.24) % Change in Triglycerides (from baseline), 2 yr 1: -21.17 (41.23) 2: -56.79 (16.70) 3: -18.28 (7.84) % Change in DBP (from baseline), 2 yr 1: -7.30 (9.42) 2: -13.06 (8.97) 3: -7.14 (11.51)	1: 2 yr 2: 2 yr 3: 2 yr

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
		Fasting Glucose, mmol/liter (SD) 1: 9.55 (3.35) 2: 9.70 (3.44) 3: 9.94 (3.43) Total Cholesterol (SD) 1: 4.71 (0.91) 2: 5.54 (1.50) 3: 6.12 (1.55) HDL-C (SD) 1: 1.13 (0.23) 2: 0.99 (0.21) 3: 0.99 (0.21) LDL-C (SD) 1: 2.83 (0.84) 2: 3.41 (1.21) 3: 3.99 (1.40) Triglycerides, mmol/liter (SD) 1: 1.66 (0.86) 2: 2.49 (1.21) 3: 2.49 (0.80) SBP mmHg (SD) 1:145.75 (20.54) 2: 154.50 (29.73) 3: 155.20 (34.18) DBP mmHg (SD) 1: 91.50 (14.15) 2: 95.90 (12.87) 3: 96.00 (17.52)			
O'Brien et al, 2006 Randomized Control Trial Weight change	G1. Surgical group (LAGB) G2. Nonsurgical group (very-low calorie diets, pharmacotherapy, and	Inclusion criteria: Between 20–50 yr; BMI of 30–35; identifiable problems; attempts to reduce	Mean excess weight loss at 24 mo, % (95% CI): G1: 87.2 (77.7–96.6) G2: 21.8 (11.9–31.6) *p*-value between groups <0.001	*Change in SBP at 2 yr, % (SD): G1: -10.8 (10.8) G2: -7.2 (9.7) 95% CI = –9.9 to 1.9 *Change in DBP at 2 yr, % (SD): G1: -10.9 (2.5)	*n*'s at 2-yr follow-up: G1: 39 (98) G2: 33 (83) Duration of follow-up: G1: 24 mo

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
University and affiliated private hospital (G1, G2) Australia Good	lifestyle change	weight over at least the previous 5 yr *N*'s at baseline G1: 40 G2: 40 Age, mean (SD): G1: 41.8 (6.4) G2: 40.7 (7.0) Sex, % (men): G1: 25 G2: 22.5 BMI, mean (SD): G1: 33.7 (1.8) G2: 33.5 (1.4) Weight, mean (SD): G1:96.1 (11.2) G2: 93.6 (11.9)	BMI, kg/m2 (95% CI) Baseline: G1: 33.7 (32.9–34.4) G2: 33.5 (32.7–34.2 24 mo G1: 26.4 (25.6–27.2) G2: 31.5 (30.6–32.4) *p*-value between groups <0.001 Weight, kg (95% CI) Baseline G1: 95.0 (94.1–95.9) G2: 94.8 (93.9–95.7) 24 mo G1: 74.5 (72.4–76.7) G2: 89.5 (80.5–83.6) *p*-value between groups <0.001 *Change in weight at 2 yr, % (SD): G1: 20.5 (6.4) G2: 6.1 (8.5) 95% CI = –18.9 to –11.6	G2: -1.58 (11.2) 95% CI = –17.0 to –3.4 *Change in Plasma Glucose at 2 yr, % (SD): G1: -7.3 (15.2) G2: 0.35 (8.3) 95% CI = –13.0 to –0.7 *Change in Plasma Insulin at 2 yr, % (SD): G1: -22.2 (26.8 G2: -8.5 (22.4) 95% CI = –29.3 to 1.00 *Change in Triglyceride at 2 yr, % (SD): G1: -19.1 (35.7) G2: -3.7 (39.4) 95% CI = –33.7 to 2.9 *Change in HDL-C at 2 yr, % (SD): G1: 30.0 (28.9) G2: 6.9 (18.9) 95% CI =10.6–35.4 *Change in LDL-C at 2 yr, % (SD): G1: -6.5 (19.0) G2: -5.2 (21.6) 95% CI = -11.3 to 8.8 *Change in Total Cholesterol at 2 yr, % (SD): G1: -0.4 (18.1) G2: -3.0 (17.0) 95% CI = –5.9 to 11.2 SF-36 Domain Scores for QOL: G1 had statistically significantly greater improvement (in the surgical group) at 2 yr, compared to G2 (the nonsurgical group), on 5 of 8 SF-36 domain scores: Physical Function, Physical Role, General Health, Energy, and Emotional Role.	G2: 24 mo
SOS Trial Karlsson, Sjöström &	G1. Surgical group G2. Control group G1: Subjects underwent	Inclusion Criteria: Age 37–60 yr	BMI, kg/m2 (95% CI) Baseline: G1:	Mean 2-yr changes in HRQOL Outcomes, (95% CI)	*n*'s (%), at 2 yr follow-up: G1: 477 (98)

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
Sullivan, 1998 Sjöström, 2003 Karlsson et al *2007* Controlled, prospective, non-randomized, matched-group trial Weight, BMI, change in weight (%) Surgical departments and health care centers (G1, G2) Sweden Good Related Articles*: Grunstein 2007, Narbro 1999, Naslund 2005, Sjostrom 2000, Sjostrom 2001, Sjostrom 2008, Sjostrom 2009 *Related articles are other included articles from this study that do not provide additional data	either nonadjustable/adjustable banding, vertical banded gastroplasty, or gastric bypass surgery; all surgery patients were given instructions on nutrition (no further details given) G2: Subjects were offered treatment at primary health care centers and the treatment regimen varies according to the local routines G1. Surgical group G2. Conventional group	BMI >34 (men) and 38 (women) *N*'s at baseline G1: 487 (315 vertical banded gastroplasty; 136 gastric banding and 36 gastric bypass cases) G2: 487 Age, mean (95% CI): G1: 46.6 (46.1–47.1) G2: 47.7 (47.2–48.3) Sex, *n*: G1: Females: 327 Males: 160 G2: Females: 327 Males: 160 BMI, mean (95% CI): G1: Men: 40.8 (40.1–41.5) Females: 42.3 (41.9–42.7) G2: Men: 38.7 (38.0–39.5); Females: 40.7 (40.1–41.2) Weight, mean (95% CI): G1: Men: 130.8 (128.1–133.4) Females: 115.1 (113.6–116.5) G2: Men: 124.4 (121.8–127.0); Females:	Men 40.8 (40.1–41.5); Females 42.3 (41.9–42.7) G2: Men 38.7 (38.0–39.5); Females 40.7 (40.1–41.2) 2 yr: G1: Men 31.5 (30.7–32.3); Females 32.5 (32.0–33.0) G2: Men 38.5 (37.6–39.3); Females 40.3 (39.7–40.9) *p*-value between groups <0.0001 Weight, kg (95% CI) Baseline: G1: Men 130.8 (128.1–133.4); Females 115.1 (113.6–116.5) G2: Men 124.4 (121.8–127.0); Females 109.5 (107.8–111.3) 2 yr: G1: Men 100.6 (98.0–103.2); Females 88.4 (86.7–90.1) G2: Men 123.6 (120.7–126.5); Females 108.6 (106.8–110.5) *p*-value between groups <0.0001	**Outcome:** ***Group 1 Baseline:*** : HAD: Anxiety: 2 yr *p*-value between groups = NS: 6.3 (5.9–6.7) : HAD: Depression: 2 yr *p*-value between groups = 0.0001: 5.2 (4.9–5.5) ***Change:*** : Hospital Anxiety and Depression (HAD): Anxiety: 2 yr *p*-value between groups = NS: -1.7 : HAD: Depression: 2 yr *p*-value between groups = 0.0001: -2.2 ***Group 2 Baseline:*** : HAD: Anxiety: 2 yr *p*-value between groups = NS: 5.7 (5.3–6.1) : HAD: Depression: 2 yr *p*-value between groups = 0.0001: 4.5 (4.2–4.8) ***Change:*** : HAD: Anxiety: 2 yr *p*-value between groups = NS: -0.6 : HAD: Depression: 2 yr *p*-value between groups = 0.0001: -0.4 **Outcome:** ***Group 1 Baseline:*** Obesity-related problem scale (OP)-scale: Males: 2 yr *p*-value between groups = 0.0001: 1.60 (1.47–1.73) OP-scale: Females: 2 yr *p*-value between groups = 0.0001: 1.94 (1.85–2.03) ***Change:*** OP-scale: Males: 2 yr *p*-value between groups = -1.01 OP-scale: Females: 2 yr *p*-value between groups = 0.0001: -1.10 ***Group 2 Baseline:***	G2: 407 (84) Duration of follow-up: G1: 2 yr G2: 2 yr Comments on Interventions: Planned follow-up of 10 yr for entire SOS trial

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
for this summary table beyond the data already included in the summary table from the main articles		109.5 (107.8–111.3)		OP-scale: Males: 2 yr *p*-value between groups = 0.99 (0.87–1.12) OP-scale: Females: 2 yr *p*-value between groups = 0.0001: 1.45 (1.36–1.54) ***Change:*** OP-scale: Males: 2 yr *p*-value between groups =-0.07 OP-scale: Females: 2 yr *p*-value between groups = 0.0001: -0.16 **Outcome:** ***Group 1 Baseline:*** Sickness Impact Profile/social interaction (SIP/SI): Males: 2 yr *p*-value between groups = 0.001: 10.4 (8.7–12.0) SIP/SI: Females: 2 yr *p*-value between groups = 0.0001: 11.3 (10.2–12.5) ***Change:*** SIP/SI: Males: 2 yr *p*-value between groups = 0.001: -3.3 SIP/SI: Females: 2 years *p*-value between groups = 0.0001: -5.2 ***Group 2 Baseline:*** SIP/SI: Males: 2 years *p*-value bet. groups = 0.001: 8.2 (6.5-10.0) SIP/SI: Females: 2 yr *p*-value between groups = 0.0001: 7.4 (6.4-8.4) ***Change:*** SIP/SI: Males: 2 yr *p*-value between groups = 0.001: +1.5 SIP/SI: Females: 2 yr *p*-value between groups = 0.0001: +1.2 **Outcome:** ***Group 1 Baseline:***	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
				Mood adjective checklist (MACL): Pleasantness/Unpleasantness: 2 yr *p*-value between groups = 0.0001: 2.96 (2.90–3.02) MACL: Activation/De-activation: 2 years *p*-value between groups = 0.0001: 2.86 (2.81–2.92) ***Change:*** MACL: Pleasantness/Unpleasantness: 2 yr *p*-value between groups = 0.0001: +0.21 MACL: Activation/De-activation: 2 yr *p*-value bet. groups = 0.0001: +0.32 ***Group 2 Baseline:*** MACL: Pleasantness/Unpleasantness: 2 yr *p*-value between groups = 0.0001: 3.04 (2.98–3.10) MACL: Activation/De-activation: 2 yr *p*-value between groups = 0.0001: 3.01 (2.95–3.07) ***Change:*** MACL: Pleasantness/Unpleasantness: 2 yr *p*-value between groups = 0.0001: -0.04 MACL: Activation/De-activation: 2 yr *p*-value between groups = 0.0001: 0.00 **Outcome:** ***Group 1 Baseline:*** MACL: Calmness/Tension: 2 yr *p*-value between groups = 0.0001: 2.90 (2.84–2.96) ***Change:*** MACL: Calmness/Tension: 2 yr *p*-value between groups = 0.0001: 0.20 ***Group 2 Baseline:*** MACL: Calmness/Tension: 2 yr *p*-value between groups = 0.0001: 2.98 (2.92–3.04) ***Change:*** MACL: Calmness/Tension: 2 yr *p*-value between groups = 0.0001: -0.01	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
				Mean 10-yr changes in HRQOL Outcomes, (SD) **Outcome:** ***Group 1 Baseline:*** Current health perceptions: Anxiety: 2 yr *p*-value between groups = NS: 51.8 (24.1) HAD: Depression: 2 yr *p*-value between groups = 0.0001: 5.2 (4.9–5.5) Change: Current health perceptions: Anxiety: 2 yr *p*-value between groups = NS: 0.21 HAD: Depression: 2 yr *p*-value between groups = 0.0001: -2.2 ***Group 2 Baseline:*** Current health perceptions: Anxiety: 2 yr *p*-value between groups = NS: 58.8 (24.8) HAD: Depression: 2 yr *p*-value between groups = 0.0001: 4.5 (4.2–4.8) ***Change:*** Current health perceptions: Anxiety: 2 yr *p*-value between groups = NS: -0.13 HAD: Depression: 2 yr *p*-value between groups = 0.0001: -0.4	
SOS Trial Sjöström CD, Lissner L, Wedel & Sjöström, 1999 Sjöström et al, 2004 Controlled, prospective, non-randomized,	Treatment Groups: G1. Surgical group G4. Control group Intervention: G1: Subjects underwent either Nonadjustable/adjustable banding, vertical banded gastroplasty, or gastric bypass surgery; all surgery patients	Inclusion Criteria: Age 37–60 yr BMI >34 (men) and 38 (women) *N*'s at baseline G1: 845 G2: 845 Sjostrom et al, 2004	Change in weight at 2 yr, kg (SD): G1: -28 (15) G2:-0.5 (8.9) *p*-value between groups ≤ 0.001 Change in weight at 10 yr, %: G1: -16.1 G2: 1.6 *p*-value between groups <0.001 Change in BMI at 2 yr, kg/m^2 (SD): G1: -9.7 (5) G2: 0 (3)	Change in SBP at 2 yr, mm Hg (SD): G1: -7.0 (18) G2: 0 (15) *p*–value between groups <0.001 Change in SBP at 10 yr, %: G1: 0.5 G2: 4.4 p-value between groups NS Change in DBP at 2 yr, mm Hg (SD): G1: -6.0 (11) G2: -1.0 (9)	*n*'s (%), at 2 yr follow-up: G1: 767 (91) G2: 712 (84 *n*'s (%), at 10 yr follow-up: G1: 641 (75) G2: 627 (74) Duration of follow-up: G1: 2 yr

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
matched-group trial Change in CVD risk factors Surgical departments and health care centers (G1, G2) Sweden Fair	were given instructions on nutrition* G2: Subjects were offered treatment at primary health care centers and the treatment regimen varies according to the local routines**	G1: 851 G2: 852 Age, mean (SD) G1: 47.0 (5.8) G2: 48.6 (6.3) Sex, Women, % G1: 69 G2: 68 BMI, mean (SD): G1: 42.1 (4.3) G2: 39.8 (4.6) Weight, mean (SD): G1: 120.5 (16) G2: 114.1 (17)	*p*-value between groups <0.001 Change in BMI at 10 yr, %: G1: -15.7 G2: 2.3 p-value between groups <0.001	*p* –value between groups <0.001 Change in DBP at 10 yr, %: G1: -2.6 G2: -2.0 *p*-value between groups <0.001 Change in Plasma Glucose at 2 yr, mmol/l (SD): G1: -1.1 (1.8) G2: 0.1 (1.4) *p*–value between groups <0.001 Change in Plasma Glucose at 10 yr, %: G1: -2.5 G2: 18.7 *p*-value between groups <0.001 Change in Plasma Insulin at 2 yr, mmol/l (SD): G1: -11.4 (12) G2: -0.7 (10) *p* –value between groups <.001 Change in Plasma Insulin at 10 yr, %: G1: -28.2 G2: 12.3 *p*-value between groups <0.001 Change in Total Cholesterol at 2 yr, mmol/l (SD): G1: -0.25 (1) G2: -0.06 (0.8) *p* –value between groups <0.001 Change in Total Cholesterol at 10 yr, %: G1: -5.4 G2: -6.0 *p*-value between groups <0.05 Change in Triglyceride at 2 yr, mmol/l (SD): G1: -0.7 (1.3) G2: -0.1 (1.2) *p* –value between groups <0.001 Change in Triglyceride at 10 yr, G1: -16.3 G2: 2.2	G2: 2 yr Sjostrom et al, 2004 G1: 10 yr G2: 10 yr Withdrawal, *n* (%): Sjostrom et al, 2004 G1: 210 (24.7) G2: 225 (26.4) Comments on Interventions: Planned follow-up of 10 yr for entire SOS trial Comments: Authors reported the use of ITT analysis 10-yr data reported from Sjostrom et al, 2004; Authors reported the use of BOCF analysis and stated those who dropped out before 10 yr had similar matching values between surgically treated and controls; however, data is reported for those who completed the 10-yr examination

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
				p –value between groups <0.001 Change in HDL-C at 2 yr, mmol/l (SD): G1: 0.18 (0.3) G2: 0.01 (0.2) *p* –value between groups <.001 Change in HDL at 10 yr, %: G1: 24.0 G2: 10.8 *p* –value between groups <.001 Incidence of Diabetes at 2 yr, % G1: 1 G2: 8 *p*-value <0.001 Incidence of Diabetes at 10 yr, % G1: 7 G2: 24 *p*-value <0.001 Incidence of Hypertension at 2 yr, % G1: 24 G2: 29 *p*-value = 0.06 Incidence of Hypertension at 10 yr, % G1: 41 G2: 49 *p*-value = 0.13 Rate of Recovery, Diabetes, at 2 yr, % G1: 72 G2: 21 *p*-value <0.001 Rate of Recovery, Diabetes, at 10 yr, % G1: 35 G2: 13 *p*-value = 0.001 Rate of Recovery, HTN, at 2 yr, % G1: 34 G2: 21	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
				p-value <0.001 Rate of Recovery, HTN, at 10 yr, % G1: 19 G2: 11 *p*-value = 0.02	
SOS Trial Sjöström et al, 2007 Controlled, prospective, non-randomized, matched-group trial Mortality Surgical departments and health care centers (G1, G2) Sweden Fair	Treatment Groups: G1. Surgical group G4. Control group Intervention: G1: Subjects underwent either Nonadjustable/adjustable banding, vertical banded gastroplasty, or gastric bypass surgery; all surgery patients were given instructions on nutrition* G2: Subjects received the customary nonsurgical treatment for obesity at their given center of registration; no attempt was made to standardize the conventional treatment	Inclusion Criteria: Age 37–60 yr BMI >34 (men) and 38 (women) *N*'s at baseline G1: 2010 G2: 2037 Age, mean years (SD): At matching examination: G1: 46.1 (5.8) G2: 47.4 (6.1) *p*-value <0.001 Sex, *n*: At matching examination: G1: Male – 590; Female – 1,420 G2: Male – 590; Female – 1,447 *p*-value = 0.79 BMI, mean kg/m^2 (SD): At matching examination: G1: 41.8 (4.4) G2: 40.9 (4.3) *p*-value <0.001 Weight, mean kg (SD): At matching examination: G1: 119.2 (16.1) G2: 116.9 (15.4)	Change in weight after 1–2 yr, % (SD): G1: Banding: 20 (10); Vertical-banding gastroplasty: 25 (9); Gastric bypass: 32 (8) G2: NR* *p*-value between groups NR** Change in weight after 10 yr, % (SD): G1: Banding: 14 (14); Vertical-banding gastroplasty: 16 (11); Gastric bypass: 25 (11) G2: NR* *p*-value between groups NR** Change in weight after 15 yr, % (SD): G1: Banding: 13 (14); Vertical-banding gastroplasty: 18 (11); Gastric bypass: 27 (12) G2: NR* *p*-value between groups NR** Comments about weight change outcomes: *For weight change in the control group, authors reported findings in graphical form (p. 747); authors state that average weight change in this group remained within +/- 2% during the observation period **While *p*-values were not	Overall Mortality, *n*: G1: 101 G2: 129 HR (95% CI): 0.76 (0.59–0.99) Deaths by Age, *n* G1: ≤47.8: 42 >40.8: 59 G2: ≤47.8: 37 >47.8: 92 Interaction *p*-value = 0.40 Deaths by gender, *n* G1: Males 49 Females 52 G2: Males 59 Females 70 Interaction *p*-value = 0.60 Deaths by CVD Risk Factor - Diabetes, *n* G1: No 79 Yes 22 G2: No 94 Yes 34 Interaction *p*-value = 0.50 Deaths by CVD Risk Factor - BMI, *n* G1: ≤40.8: 40 >40.8: 61 G2: ≤40.8: 75 >40.8: 54 Interaction *p*-value = 0.60 Deaths by CVD Risk Factor – Prior CV event, *n* G1: Without 92 With 9	*n*'s, 2-yr follow-up: G1: 1846 (banding: 357; vertical-banding gastroplasty: 1244; gastric bypass: 245) G2: 1660 *n*'s, 10-yr follow-up: G1: 1,041 (banding: 237; vertical-banding gastroplasty: 746; gastric bypass: 58) G2: 886 *n*'s, 15-yr follow-up: G1: 170 (Banding: 52; Vertical-banding gastroplasty: 108; gastric bypass: 10) G2: 190 Duration of follow-up: G1: 15 yr G2: 15 yr Participation Rates, %: Vital Status (overall) 99.9 Weight Change Data At 2 yr G1: 94

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups, Component Details	Sample Characteristics, Baseline Population Characteristics	Weight Reduction Outcomes	CVD Risk Factor, Morbidity, HRQOL & Mortality Outcomes	Duration, Attrition
		p-value <0.001	reported, graph shows that CIs between the control and the surgery groups did not overlap (indicating significant differences)	G2: Without 117 With 12 Interaction *p*-value = 1.00	G2: 83 At 10 yr G1: 84 G2: 75 At 15 yr G1: 66 G2: 87

Summary Table 5.2. Component 2: Predictors—Patient Characteristics

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
Marinari 2006 Prospective cohort study with one or more comparison groups Fair Inpatient medical setting/Hospital Italy	Treatment Groups: 1. Diabetics 2. Nondiabetics Intervention: 1. BPD 2. BPD Total Group Size at baseline, *n*: 1: 268 2: 268 Interventions *n*'s before BPD 1: 268 2: 266 Interventions *n*'s at 1 yr 1: 260 2: 261 Interventions *n*'s at 2 yr 1: 259 2: 255	Inclusion Criteria: Obese patients undergoing BPD Exclusion Criteria: NR Primary Outcome: Weight before and after surgery Secondary Outcome: Serum glucose concentration	Mean Age, yr (range): 1. 42.1 (18–59) 2. NR* Weight, range, kg 1. 98.3 – 209.7 2. NR* BMI, range, kg/m2 1. 36.3 – 74.5 2. NR* Comments on baseline data: * Diabetic patients were carefully matched for gender, age, and preoperative BMI values. Preoperative fasting serum glucose concentration requirement for group 1 was >126 mg/dl; this group was matched with obese patients undergoing BPD whose preoperative fasting serum	Mean weight before BPD, kg (SE): G1: 134.8 (1.49) G2: 135.6 (1.58) Mean weight at 1 yr, kg (SE): G1: 87.4 (1.05) G2: 88.8 (1.12) Mean weight at 2 yr, kg (SE): G1: 87.4 (1.05) G2: 86.8 (1.12) Mean weight at 3 yr, kg (SE): G1: 84.9 (1.09) G2: 83.1 (1.24) BMI before BPD, kg/m2 (SE): G1: 49.6 (0.48) G2: 49.6 (0.50) BMI at 1 yr, kg/m2 (SE): G1: 32.2 (0.33) G2: 31.7 (0.36) BMI at 2 yr, kg/m2 (SE): G1: 30.9 (0.34)

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
	Interventions *n*'s at 3 yr 1: 261 2: 259 Interventions *n*'s at 5 yr 1: 190 2: 185 Follow-up Rate at 5 yr, %: 1. 71 2. 69		glucose concentration was <110 mg/dl.	G2: 29.8 (0.35) BMI at 3 yr, kg/m2 (SE): G1: 31.3 (0.36) G2: 30.4 (0.40) Glucose Concentration before BPD, mg% (SE) 1. 178 (3.44) 2. 95 (0.82) Glucose Concentration at 1 yr, mg% (SE) 1. 84 (0.93) 2. 80 (0.73) Glucose Concentration at 2 yr, mg% (SE) 1. 85 (1.16) 2. 80 (0.58) Glucose Concentration at 3 yr, mg% (SE) 1. 84 (0.96) 2. 81 (0.65) Comments on Outcomes: 5-yr data not reported here due to high attrition

Summary Table 5.2. Component 2: Predictors—Types of Surgery

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
Angrisani, 2007 RCT Fair Hospital Italy	Treatment Groups: 1. LAGB group 2. LRYGB group Total Group Size: 1: 27 2: 24 Interventions 1: LAGB	Inclusion Criteria: BMI >35 to BMI <50 kg/m2 Ages 17–49 yr Absence of hiatal hernia No previous abdominal operations Had to accept	Mean Age, yr (SD) 1: 33.8 (9.1) 2: 34.1 (8.9) Sex, *n* 1: Male 5 Female 22 2: Male 4 Female 20 Weight, kg (SD)	Mean weight at 12 mo, kg: G1: 102.4 G2: 92.8 Mean weight at 36 mo, kg: G1: 98.7 G2: 83.5 Mean weight at 60 mo, kg: G1: 97.9 G2: 84

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
	2: Laparoscopic RYGB	randomization to 1 of 2 surgical groups Exclusion Criteria: - Refusal to undergo the operation to which they had been assigned Primary Outcome: Weight loss, BMI, EWL, Complications	1: 117.1 (12.8) 2: 118.2 (13.2) BMI, kg/m2 (SD) 1: 43.4 (4.2) 2: 43.8 (4.1) EWL, kg (SD) 1: 47.1 (10.9) 2: 48.2 (11.7) EWL, % (SD) 1: 83.1 (9.2) 2: 83.8 (8.9)	*p*-value between groups at 5 yr <.001 BMI at 12 mo, kg/m2: G1: 38.7 G2: 35.4 BMI at 36 mo, kg/m2: G1: 35.6 G2: 29.1 BMI at 60 mo, kg/m2: G1: 34.9 G2: 29.8 *p*-value between groups at 5 yr <.001 EWL at 12 mo, % 1: 34.7 2: 51.3 EWL at 36 mo, % 1: 47.3 2: 67.3 EWL at 60 mo, % 1: 47.5 2: 66.6 *p*-value between groups at 5 yr <.001
Bessler, 2007 RCT Good Inpatient medical setting/Hospital USA	Treatment Groups: 1: Gastric bypass with banding 2: Gastric bypass without banding Intervention: 1: Laparoscopic long-limb gastric bypass with banding 2: Laparoscopic long-limb gastric bypass without banding Interventions *n*'s at baseline G1: 46 G2: 44 Mean Duration of follow-up:	Inclusion Criteria Patients with BMI> 50 kg/m2 underwent surgery by one surgeon from 6/01 to 7/05 Exclusion Criteria Patients who had undergone previous gastric surgery Minors were excluded Primary Outcome: Excess weight loss Secondary Outcome: Resolution of comorbidities	Mean Age, yr (SD) 1: 40.6 (7.4) 2: 42.6 (7.2) *Actual *p*-value NR; authors states difference between groups is NS Sex, % women 1: 56.5 2: 73.8 **p*-value between groups = .09 BMI, kg/m^2 (SD) 1. 59.4 (7.3) 2. 59.7 (7.1) *Actual *p*-value NR; authors states difference between groups is NS	Excess Weight Loss at 6 mo, % 1: 43.1 2: 24.7 Excess Weight Loss at 12 mo, % 1: 64 2: 57.4 Excess Weight Loss at 24 mo, % 1: 64.2 2: 57.2 Excess Weight Loss at 36 mo*, % 1: 73.4 2: 57.7 *p*-value between groups <0.05 Patients attaining BMI <35 kg/m^2 at 12 mo, % 1: 47.8

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
	G1: 36 mo G2: 36 mo		Hypertension, % 1: 50 2: 46 *Actual *p*-value NR; authors states difference between groups is NS DM, % 1: 26 2: 26 *Actual *p*-value NR; authors states difference between groups is NS Hyperlipidemia, % 1: 31 2: 30 *Actual *p*-value NR; authors states difference between groups is NS	2: 41.0 Patients attaining BMI <35 kg/m^2 at 24 mo, % 1: 52.9 2: 37.5 Resolution of HTN, % 1: 79 2: 90 *Actual *p*-value NR; authors states difference between groups is NS Diabetes Mellitus, % 1: 92 2: 98 *Actual *p*-value NR; authors states difference between groups is NS Hyperlipidemia, % 1: 50 2: 62 *Actual *p*-value NR; authors states difference between groups is NS Comments on Outcomes: * Authors state that "at 36 mo, the banded patients had lost significantly more weight than had the non-banded patients (*p*<.05). However, this was calculated from the small number of patients reaching the 36-mo follow-up period; actual *n* at 36 mo not reported
Dixon et al, 2008 RCT Glycemic control University Obesity Research Center, G1 and G2 Australia Fair	G1: Subjects underwent placement of a LAGB via the pars flaccid technique by 1 of 2 experienced surgeons within 1 mo of randomization; plus all aspects of the conventional-therapy program for G2 (below) G2: Lifestyle modification programs were individually structured to reduce energy intake to reduce intake of	Inclusion criteria: Between 20–60 yr; BMI of 30–40; had been diagnosed with clearly documented type 2 diabetes within the previous 2 yr *N*'s at baseline G1: 30 G2: 30 Age, mean (SD): G1: 46.6 (7.4)	Mean weight loss at 2 yr, % (SD): G1: 20.0 (9.4) G2: 1.4 (4.9) p-value between groups <.001 Mean weight change at 2 yr, kg (SD): G1: -21.1 (10.5) G2: -1.5 (5.4) *p*-value between groups <0.001	Change in SBP at 2 yr, mm Hg (SD): G1: -6.0 (17.9) G2: -1.7 (14.2) *p*–value between groups = .37 Change in DBP at 2 yr, mm Hg (SD): G1: -0.7 (11.1) G2: -0.9 (11.1) *p*–value between groups = .92 Change in Plasma Glucose at 2 yr, mg/dL (SD): G1: -51.2 (37.6) G2: -18.4 (41.2) *p*–value between groups = .002

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
	fat (<30%) and saturated fats, and to encourage intake of low- glycemic index and high-fiber foods. Physical activity advice encouraged 10,000 steps per day and 200 min/wk of structured activity, including moderate intensity aerobic activity and resistance exercise	G2: 47.1 (8.7) Sex, *n* (% male): G1: 15 (50) G2: 13 (43) BMI, mean (SD): G1: 37.0 (2.7) G2: 37.2 (2.5)		Change in Plasma Insulin at 2 yr, µIU/mL (SD): G1: -12.4 (8.4) G2: -1.0 (14.8) *p* –value between groups <.001 Change in Total Cholesterol at 2 yr, mg/dL(SD): G1: 3.6 (51.6) G2: -0.4 (31.4) *p*–value between groups = .72 Change in Triglyceride at 2 years, mg/dL (SD): G1: -71.7 (92.9) G2: -2.1 (120.6) *p*–value between groups = .02 Change in HDL-C at 2 yr, mg/dL (SD): G1: 12.6 (9.8) G2: 2.6 (6.1) *p*–value between groups <.001
Ikonomidis et al, 2007 Prospective cohort study aortic elastic properties and cardiac function Outpatient medical setting – hospital (G1, G2, G3) Greece Fair	Treatment Groups: G1. Surgical group G2. Nonsurgical Group Intervention: G1: Subjects underwent BPD with RYGB G2: Morbidly obese individuals who refused any surgical or medical intervention; maintained their weight over the course of the study	Inclusion Criteria: Not reported in detail *N*'s at baseline G1: 60 G2: 20 Age, mean (SD): G1: 35 (11) G2: 37 (12) Sex, Women, n (%) G1: 45 (75) G2: 16 (80) BMI, mean (SD): G1: 48.68 (7.8) G2: 48.57 (5.9)	BMI, mean kg/m^2 (SD): 3 yr G1: 32 (6) G2: 49.8 (5.8) *p*-value between groups <0.001 Weight, mean kg (SD): 3 yr G1: 87 (17) G2: 134 (23) *p*-value between groups <0.001	Plasma glucose level, mg/dl: 3 yr G1: 87 (13) G2: 106.5 (24) *p*-value between groups <0.001 Total Cholesterol, mg/dl: 3 yr G1: 147 (34) G2: 234 (29) *p*-value between groups <0.001 Triglycerides, mg/dl: 3 yr G1: 74 (24) G2: 148 (53) *p*-value between groups <0.001
Kehagias, 2011 RCT	Treatment groups: 1: Laparoscopic RYGB	Inclusion Criteria: Patients were recruited from waiting list pool for	Age, Mean, yr (SD) 1: 36 (8.4) 2: 33.7 (9.9)	Mean BMI, at 3 yr, kg/m2 (SD) 1: 31.3 (3.9) 2: 29.6 (4.1)

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
Good Academic medical hospital Greece	2: Laparoscopic SG) Intervention *n*, at baseline: 1: 30 2: 30 Intervention *n*, at 1 yr 1: 30 2: 30 Intervention *n*, at 2 yr 1: 30 2: 30 Intervention *n*, at 3 yr 1: 29 2: 28 Follow-up rate at 1 yr, %: 1:100 2:100 Follow-up rate at 2 yr, %: 1:100 2:100 Follow-up rate at 3 yr, %: 1:97 2:93	bariatric surgery; consisted only from the Greek population Exclusion Criteria: Chronic medical or psychiatric illness: substance abuse; previous gastrointestinal surgery Primary endpoint: Weight loss Secondary endpoints: Perioperative and late morbidity and mortality, improvement of comorbidities and nutritional deficiencies	Male to Female Ratio: 1: 8:22 2: 8:22 Baseline mean weight, kg (SD): 1: 123.1 (13.9) 2: 126.9 (18) Baseline mean BMI, kg/m^2 (SD): 1: 45.8 (3.7) 2: 44.9 (3.4) Preoperative hypertension (SBP ≥140 and/or DBP ≥90 mmHg or antihypertensive drug therapy), *n* 1: 5 2: 4 Preoperative Type 2 diabetes, *n* 1: 5 2: 5 Impaired Glucose Tolerance, *n*: 1: 5 2: 5 HDL <40 mg/dl for men, <50 mg/dl for women, *n* 1: 4 2: 3 LDL >100 mg/dl, *n* 1: 10 2: 8 Triglycerides >150, *n* 1: 5 2: 3 Obstructive Sleep Apnea, *n* 1: 3 2: 6 Gastroesophageal reflux disease (GERD), *n* 1: 5	*p*-value between groups = 0.11 % Excess BMI loss, 3 yr 1: 61.4 2: 68.2 *p*-value between groups = 0.12 %Excess weight loss (EWL), at 1 yr 1: 65.6 2: 72.9 *p*-value between groups = 0.05 %EWL, at 2 yr 1: 65.3 2: 73.2 *p*-value between groups = 0.05 %EWL, at 3 yr 1: 62.1 2: 68.5 *p*-value between groups = 0.05 Percentile of patients with %EWL >50 after surgery, at 1 yr 1: 83 2:93 *p*-value between groups = 0.42 Percentile of patients with %EWL >50 after surgery, at 2 yr 1: 83 2:87 *p*-value between groups = 0.9 Percentile of patients with %EWL >50 after surgery, at 3 yr 1: 77 2:83 *p*-value between groups = 0.74 <u>Resolution of Comorbidities</u> Hypertension (SBP ≥140 and/or DBP ≥90 mmHg or antihypertensive drug therapy), *n* (%) 1: 3 (60) 2: 3 (75) Preoperative type 2 diabetes, *n* (%) 1: 4 (80)

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
			2: 2 Degenerative Arthritis, *n* 1: 6 2: 5 Menstrual Irregularities, *n* 1: 7 2: 7	2: 4 (80) Impaired Glucose Tolerance, *n* (%): 1: 5 (100) 2: 5 (100) HDL <40 mg/dl for men, <50 mg/dl for women, *n* (%) 1: 4 (100) 2: 2 (67) LDL >100 mg/dl, *n* (%) 1: 9 (90) 2: 6 (75) Triglycerides >150, *n* (%) 1: 5 (100) 2: 2 (67) Obstructive Sleep Apnea, *n* (%) 1: 2 (67) 2: 4 (67) GERD, *n* (%) 1: 5 (100) 2: 2 (100) Degenerative Arthritis, *n* (%) 1: 5 (83) 2: 4 (80) Menstrual Irregularities, *n* (%) 1: 7 (100) 2: 7 (100)
Mingrone, 2012 Single-center, non-blinded, randomized, controlled trial Day Hospital of Metabolic Diseases and Diabetology of the Catholic University Rome Good	Treatment Groups: 1. Gastric bypass 2. BPD 3. Medical therapy Total Group Size: 1: 20 2: 20 3: 20 Intervention *n*'s (baseline):	Inclusion Criteria: Age of 30–60 yr BMI ≥35 A history of type 2 diabetes of at least 5 yr A glycated hemoglobin level of ≥7.0% (as confirmed by at least three analyses) An ability to understand	Mean Age, yr (SD): 1: 43.90 (7.57) 2: 42.75 (8.06) 3: 43.45 (7.27) Sex, male, *n* (%): 1: 10 (50); 2: 10 (50); 3: 8 (40); Weight, kg (SD): 1: 129.84 (22.58) 2: 137.85 (30.35)	% Change in Weight loss (from baseline), 2 yr 1: -33.31 (7.88) 2: -33.82 (10.17) 3: -4.74 (6.37) Excess Weight loss at 2 yr, % (SD) 1: 68.08 (12.70) 2: 69.36 (17.60) 3: 9.29 (12.94) % Change in BMI (from baseline), 2 yr 1: -33.31 (7.88)

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
	1: 20 2: 20 3: 20 Intervention *n*'s at 2 yr follow-up: 1: 19 2: 19 3: 18 Duration of follow-up: 1: 2 yr 2: 2 yr 3: 2 yr	and comply with the study protocol Exclusion Criteria: History of type 1 diabetes; diabetes secondary to a specific disease or glucocorticoid therapy Previous bariatric surgery Pregnancy Other medical conditions requiring short-term hospitalization Severe diabetes complications Other severe medical conditions Geographic inaccessibility Primary Outcomes: Weight change, change in CVD risk factors	3: 136.40 (21.94) BMI (SD): 1: 44.85 (5.16) 2: 45.14 (7.78) 3: 45.62 (6.24) WC, cm (SD) 1: 125.40 (16.58) 2: 130.35 (19.73) 3: 126.90 (14.68) Fasting Glucose, mmol/liter (SD) 1: 9.55 (3.35) 2: 9.70 (3.44) 3: 9.94 (3.43) Total Cholesterol (SD) 1: 4.71 (0.91) 2: 5.54 (1.50) 3: 6.12 (1.55) HDL-C (SD) 1: 1.13 (0.23) 2: 0.99 (0.21) 3: 0.99 (0.21) LDL-C (SD) 1: 2.83 (0.84) 2: 3.41 (1.21) 3: 3.99 (1.40) Triglycerides, mmol/liter (SD) 1: 1.66 (0.86) 2: 2.49 (1.21) 3: 2.49 (0.80) SBP mmHg (SD) 1:145.75 (20.54) 2: 154.50 (29.73) 3: 155.20 (34.18) DBP mmHg (SD) 1: 91.50 (14.15) 2: 95.90 (12.87) 3: 96.00 (17.52)	2: -33.82 (10.17) 3: -4.73 (6.37) % Change in WC (from baseline), 2 yr 1: -19.91 (8.44) 2: -20.70 (8.34) 3: -7.69 (7.80) % Change in Glucose (from baseline), 2 yr 1: -37.81 (33.75) 2: -56.23 (10.01) 3: -14.37 (11.93) % Change in Total Cholesterol (from baseline), 2 yr 1: -6.83 (27.03) 2: -49.25 (11.52) 3: -16.82 (11.60) % Change in HDL-C (from baseline), 2 yr 1: 29.66 (18.21) 2: 12.98 (20.66) 3: 6.03 (6.25) % Change in LDL-C (from baseline), 2 yr 1: -17.21 (36.21) 2: -64.63 (15.93) 3: -20.31 (15.24) % Change in Triglycerides (from baseline), 2 yr 1: -21.17 (41.23) 2: -56.79 (16.70) 3: -18.28 (7.84) % Change in DBP (from baseline), 2 yrs 1: -7.30 (9.42) 2: -13.06 (8.97) 3: -7.14 (11.51)

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
O'Brien et al, 2006 Randomized Control Trial Weight change University and affiliated private hospital (G1, G2) Australia Good	G1. Surgical group (LAGB) G2. Nonsurgical group (very-low calorie diets, pharmacotherapy, and lifestyle change	Inclusion criteria: Between 0–50 yr BMI of 30–35 Identifiable problems Attempts to reduce weight over at least the previous 5 yr; *N*'s at baseline G1: 40 G2:40 Age, mean (SD): G1: 41.8 (6.4) G2: 40.7 (7.0) Sex, % (men): G1: 25 G2: 22.5 BMI, mean (SD): G1: 33.7 (1.8) G2: 33.5 (1.4) Weight, mean (SD): G1:96.1 (11.2) G2: 93.6 (11.9)	Mean excess weight loss at 24 mo, % (95% CI): G1: 87.2 (77.7–96.6) G2: 21.8 (11.9–31.6) *P*-value between groups <0.001 BMI, kg/m2 (95% CI) Baseline G1: 33.7 (32.9–34.4) G2: 33.5 (32.7–34.2) 24 mo: G1: 26.4 (25.6–27.2) G2: 31.5 (30.6–32.4) *p*-value between groups <0.001 Weight, kg (95% CI) Baseline G1: 95.0 (94.1–95.9) G2: 94.8 (93.9–95.7) 24 mo G1: 74.5 (72.4–76.7) G2: 89.5 (80.5–83.6) *p*-value between groups <0.001 *Change in weight at 2 yr, % (SD): G1: 20.5 (6.4) G2: 6.1 (8.5) 95% CI = –18.9 to –11.6	*Change in SBP at 2 yr, % (SD): G1: -10.8 (10.8) G2: -7.2 (9.7) 95% CI = –9.9 to 1.9 *Change in DBP at 2 yr, % (SD): G1: -10.9 (2.5) G2: -1.58 (11.2) 95% CI = –17.0 to –3.4 *Change in Plasma Glucose at 2 yr, % (SD): G1: -7.3 (15.2) G2: 0.35 (8.3) 95% CI = –13.0 to –0.7 *Change in Plasma Insulin at 2 yr, % (SD): G1: -22.2 (26.8 G2: -8.5 (22.4) 95% CI = –29.3 to 1.00 *Change in Triglyceride at 2 yr, % (SD): G1: -19.1 (35.7) G2: -3.7 (39.4) 95% CI = –33.7 to 2.9 *Change in HDL-C at 2 yr, % (SD): G1: 30.0 (28.9) G2: 6.9 (18.9) 95% CI = 10.6–35.4 *Change in LDL-C at 2 yr, % (SD): G1: -6.5 (19.0) G2: -5.2 (21.6) 95% CI = -11.3 to 8.8 *Change in Total Cholesterol at 2 yr, % (SD): G1: -0.4 (18.1) G2: -3.0 (17.0) 95% CI = –5.9 to 11.2
Sekhar, 2007 Retrospective Cohort Fair Medical Setting, Hospital	Treatment Groups: 1. LYGB surgery group 2. Open RYGB surgery group Total Group Size:	Inclusion Criteria: BMI >60 (men) and >70 (women) Patient had undergone significant or multiple	Mean Age, years (both groups) 42.9 Gender, % Female 1: 86 2: 76	30-day Mortality Rate, % 1: 0.50 2: 0.17 *p*-value between groups = 0.37 EWL at 1 yr, % (SD) 1: 66.9 (16)

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
USA	1: 568 2: 399	previous abdominal surgeries, especially Nissen fundoplication Exclusion Criteria: - Not reported Primary Outcome: EWL, readmission and reoperation rates, mortality Follow-up Response Rate at 2 yr, %: 1: 79 2: 84 *p*-value between groups = 0.26) Withdrawals by group, % 1: 16 2: 21	*p*-value between groups = 0.001 Preoperative BMI, kg/m2 (SD) 1: 58.9 (10.6) 2: 49.1 (7.6)	2: 57 (13.5) *p*-value between groups = 0.01 EWL at 2 yr, % (SD) 1: 71.3 (18.4) 2: 67.3 (15.3) *p*-value between groups = 0.03
Sjöström, 2004 Controlled, prospective, nonrandomized, matched-group trial Fair Surgical departments and health care centers Sweden	Treatment Groups: 1. Surgical group 2. Control group Intervention: G1: Subjects underwent either nonadjustable/ adjustable banding, vertical banded gastroplasty, or gastric bypass surgery; all surgery patients were given instructions on nutrition* G2: Subjects were offered treatment at primary health care centers and the treatment regimen varies according to the local routines** Interventions *n*'s at baseline G1: 851	Inclusion Criteria: Age 37–60 yr BMI >34 (men) and 38 (women) Exclusion Criteria: Minimal exclusion criteria with the aim of obtaining an operable surgery group Severe illness Alcohol or drug abuse Previous bariatric surgery Primary Outcome: Change in CVD risk factors Secondary Outcome: Weight, BMI, change in weight (%)	Baseline data only presented for surgical group overall, not broken down by types of surgical procedures	Mean weight change after 10 yr, % (SD): G1: Banding: -13.2 (13); Vertical banding gastroplasty: -16.5 (11); Gastric bypass: -25 (11) G2: +1.6 (12) *p*-value between groups NR. Graphical depiction of 95% CIs indicates that the weight loss for gastric bypass was statistically superior to weight loss for the other types of surgical procedures at 10 yr and at all earlier time periods

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
	G2: 852 *n*'s (%), at 10-yr follow-up: G1: 641 (91) G2: 712 (84 Duration of follow-up: G1: 10 yr G2: 10 yr Withdrawal, *n* (%): G1: 210 (24.7) G2: 225 (26.4)			
Sjöström, 2007 Controlled, prospective, nonrandomized, matched-group trial Fair Surgical departments and health care centers Sweden	Treatment Groups: 1. Surgical group 4. Control group Intervention: G1: Subjects underwent either nonadjustable/ adjustable banding, vertical banded gastroplasty, or gastric bypass surgery G2: Subjects received the customary nonsurgical treatment for obesity at their given center of registration; No attempt was made to standardize the conventional treatment, which ranged from sophisticated lifestyle intervention and behavior modification to no treatment whatsoever Interventions *n*'s at baseline G1: 2010 G2: 2037 *n*'s, at 2 yr follow-up: G1: 1846 (banding: 357; vertical banding gastroplasty: 1244; gastric	Inclusion Criteria: Age 37–60 yr BMI >34 (men) and 38 (women) Exclusion Criteria: Minimal exclusion criteria with the aim of obtaining an operable surgery group Severe illness Alcohol or drug abuse Previous bariatric surgery Primary Outcome: Mortality Secondary Outcome: Interaction between mortality and weight, BMI, and CVD risk factors	Baseline data only presented for surgical group overall, not broken down by types of surgical procedures	Change in weight after 1–2 yr, % (SD): G1: Banding: -20 (10); Vertical banding gastroplasty: -25 (9); Gastric bypass: -32 (8) G2: NR* *p*-value between groups NR** Change in weight after 10 yr, % (SD): G1: Banding: -14 (14); Vertical banding gastroplasty: -16 (11); Gastric bypass: -25 (11) G2: NR* *p*-value between groups NR** Change in weight after 15 yr, % (SD): G1: Banding: -13 (14); Vertical banding gastroplasty: -18 (11); Gastric bypass: -27 (12) G2: NR* *p*-value between groups NR** *Control group weight loss remained within ±2% of baseline throughout the 15-yr observation period **Graphical depiction of 95% CIs indicates that the weight loss for gastric bypass was statistically superior to weight loss for the other types of surgical procedures at 10 yr and at all earlier time periods. At 15 yr, the 95% CIs between gastric bypass and vertical banded gastroplasty were overlapping

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
	bypass: 245) G2: 1660 *n*'s, at 10-yr follow-up: G1: 1041 (banding: 237; vertical banding gastroplasty: 746; gastric bypass: 58) G2: 886 *n*'s, at 15-yr follow-up: G1: 170 (banding: 52; vertical banding gastroplasty: 108; gastric bypass: 10) G2: 190 Duration of follow-up: G1: 15 yr G2: 15 yr Participation Rates, %: Vital Status (overall) 99.9 Weight Change Data At 2 yr G1: 94 G2: 83 At 10 yr G1: 84 G2: 75 At 15 yr G1: 66 G2: 87			
Weber, 2004 Prospective cohort study with one or more comparison groups Fair Inpatient medical setting –	Treatment Groups: 1. LAGB 2. LGB Intervention: 1: Laparascopic RYGB 2: LAGB	Inclusion Criteria: BMI >40 or BMI >35 with comorbidities History of obesity >5 yr Failed conservative treatment of >2 yr.	Mean Age, years (SD): 1: 40.1 (9.9) 2: 39.6 (10.1) Sex, female/male 1: 84/19 2: 84/19	Mean BMI, at 6 mo, kg/m2 (SD) 1: 36 (2) 2: 42 (0) Mean BMI, at 12 mo, kg/m2 (SD) 1: 33 (1) 2: 39 (0)

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
hospital Switzerland	Total Group Size: 1: 103 2: 103	Age 18–60. Exclusion Criteria: - The first 50 patients in the surgical series were excluded Primary Outcome: BMI	BMI, kg/m^2 (SD) 1: 47.8 (6.1) 2:48.0 (6.3) Mean Body Weight, kg (SD) 1: 131.5 (20.9) 2: 132.5 (20.9) Fat mass, kg (SD) 1: 58.0 (12.9) 2: 59.2 (13.5) Excessive Weight, kg (SD) 1: 72.3 kg (17.6) 2: 73.9 kg (17.9) CHD, *n* (%) 1: 5 (5) 2: 3 (3) Hypertension, *n* (%) 1: 54 (52) 2: 62 (60) Dyslipidemia, % 1: 75 (74) 2: 64 (62) Type 2 diabetes, *n* (%) 1: 38 (37) 2:45 (44) Sleep Apnea, % 1: 47 2: 37 Comments on Comorbidities:	Mean BMI, at 24 mo, kg/m2 (SD) 1: 31 (9) 2: 36 (8) EWL, at 6 mo, % (SD) 1: 44 (0) 2: 24 (9) EWL, at 12 mo, % (SD) 1: 54 (8) 2: 35 (1) EWL, at 24 mo, % (SD) 1: 54 (0) 2: 42 (1) HTN, *n* (%) at 24 mo 1: 12 (13) 2: 18 (18) *p*-value between groups = .18 Diabetes mellitus at 24 mo, *n* (%) 1: 6 (6) 2: 18 (18) *p*-value between groups = .007 Dyslipidemia at 24 mo, *n* (%) 1: 35 (37) 2: 64 (65) *p*-value between groups = .001

Study Characteristics, Design, Duration, and Research Objective	Study Design Details	Criteria for Study Inclusion/Exclusion Interventions and Composite Endpoints	Baseline Population Characteristics	Outcomes of Interest for Obesity Panel CQ4 (weight, body fat measures, weight loss maintenance, percent reduction of excess weight)
			Metabolic syndrome with hypertension and type 2 diabetes occurred with the same frequency in the 2 groups	

Summary Table 5.3. Component 3: Complications

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
Adami, 2005 Prospective cohort study with one or more comparison groups Inpatient Medical Setting, hospital, Italy Good	BPD (before and after surgery)	Inclusion Criteria: Severely obese Hypertensive before surgery (defined as either the chronic use of antihypertensive drugs (97 patients) or by SBP ≥140 mm Hg and/or DBP ≥90 mmHg) *N*, at baseline: 461 Sample Mean Age, yr (range): 41.5 (18–57) Sex, *n*: Males: 189 Females: 269 Weight, kg (SD): 134.4 (125.6) BMI, kg/m2 (SD) 49.0 (9.1) Waist-Hip Ratio, cm/cm (SD) 1.034 (0.121) SBP, mmHg (SD) 161 (23) DBP, mmHg (SD)	Mean weight at 1 yr, kg (SD): 87.0 (16.8) *p*-value vs. preoperative weight <0.001 Mean weight at 2 yr, kg (SD): 82.3 (16.7) *p*-value vs. preoperative weight <0.001 Mean weight at 3 yr, kg (SD): 84.4 (16.8) *p*-value vs. preoperative weight <0.001 BMI at 1 yr, kg/m2 (SD): 31.4 (7.7) *p*-value vs. preoperative BMI <0.001 BMI at 2 yr, kg/m2 (SD): 30.0 (5.4) *p*-value vs. preoperative BMI <0.001 BMI at 3 yr, kg/m2 (SD): 30.6 (5.4) *p*-value vs. preoperative BMI <0.001 Waist-to-hip ratio at 1 yr, cm/cm (SD) 0.963 (0.107) *p*-value vs. preoperative waist-to-hip ratio <0.001	Complications within 1 yr after BPD, *n* (%) Surgical 10 (2.2) Anastomotic leak, *n* 1 Pulmonary embolism, *n* 3 Wound disruption, *n* 2 Bleeding, *n* 4 Anemia 114 (24.9) Stomal ulcer 9 (2) Protein malnutrition 8 (1.8) Complications 1–3 yr after BPD, *n* (%) Anemia 92 (20.1) Stomal ulcer 7 (1.5) Protein malnutrition 12 (2.5) Peripheral neuropathy 2 (0.4)	Duration of follow-up: 3 yr Follow-up rate: Over 3 yr of follow-up, the follow-up rate ranged from 90% to 95%.

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
		99 (16) Comments on baseline/outcome measurements: The WC was measured at level of the umbilicus and the hip circumference at the level of the anterior iliac spine with the subject in a supine position, and the waist-to-hip ratio (cm/cm) was used as an index of body fat distribution Blood pressure was taken as the average of two measurements made using a wide cuff sphygmomanometer with the patient lying down	Waist-to-hip ratio at 2 yr, cm/cm (SD) 0.953 (0.099) *p*-value vs. preoperative waist-to-hip ratio <0.001 Waist-to-hip ratio at 3 yr, cm/cm (SD) 0.950 (0.108) *p*-value vs. preoperative waist-to-to-hip ratio <0.001 SBP at 1 yr, mmHg (SD) 136 (20) *p*-value vs. preoperative SBP <0.001 SBP at 2 yr, mmHg (SD) 133 (22) *p*-value vs. preoperative SBP <0.001 SBP at 3 yr, mmHg (SD) 132 (20) *p*-value vs. preoperative SBP <0.001 DBP at 1 yr, mmHg (SD) 85 (11) *p*-value vs. preoperative DBP <0.001 DBP at 2 years, mmHg (SD) 82 (12) *p*-value vs. preoperative DBP <0.001 DBP at 3 yr, mmHg (SD) 81 (9) *p*-value vs. preoperative DBP <0.001 Hypertension Resolution at 1 yr, cases (%) 221/435 (51) Hypertension Resolution at 2 yr, cases (%) 236/421 (56) Hypertension Resolution at 3 yr, cases (%) 243/412 (59) *Results for subject with arterial hypertension normalization over		

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
			3-yr follow-up Mean Age at 1 yr, yr (SD): 40 (10.9) *p*-value vs. BPD subjects that are still hypertensive <0.001 Mean Age at 2 yr, years (SD): 38.2 (10.7) *p*-value vs. BPD subjects that are still hypertensive <0.001 Mean Age at 3 yr, yr (SD): 39.4 (10.3) *p*-value vs. BPD subjects that are still hypertensive <0.001 Mean weight at 1 yr, kg (SD): 83.0 (18.3) *p*-value vs. BPD subjects that are still hypertensive <0.001 Mean weight at 2 yr, kg (SD): 81.0 (16.3) *p*-value vs. BPD subjects that are still hypertensive <0.01 Mean weight at 3 yr, kg (SD): 80.6 (18.5) *p*-value vs. BPD subjects that are still hypertensive <0.001 BMI at 1 yr, kg/m2 (SD): 30.0 (7.2) *p*-value vs. BPD subjects that are still hypertensive <0.001 BMI at 2 yr, kg/m2 (SD): 29.5 (5.3) *p*-value vs. BPD subjects that are still hypertensive <0.02 BMI at 3 yr, kg/m2 (SD): 29.6 (5.3) *p*-value vs. BPD subjects that are still hypertensive <0.01 Waist-Hip Ratio at 1 yr, cm/cm (SD)		

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
			0.942 (0.103) *p*-value vs. BPD subjects that are still hypertensive NS Waist-Hip Ratio at 2 yr, cm/cm (SD) 0.947 (0.103) *p*-value vs. BPD subjects that are still hypertensive NS Waist-to-hip ratio at 3 yr, cm/cm (SD) 0.944 (0.109) *p*-value vs. BPD subjects that are still hypertensive NS Weight loss at 1 yr, kg (SD) 47.6 (16.7) *p*-value vs. BPD subjects that are still hypertensive NS Weight loss at 2 yr, kg (SD) 54.7 (20.7) *p*-value vs. BPD subjects that are still hypertensive NS Weight loss at 3 yr, kg (SD) 52.5 (20.7) *p*-value vs. BPD subjects that are still hypertensive NS Preoperative SBP at 1 yr, mmHg (SD) 153 (18) *p*-value vs. BPD subjects that are still hypertensive <0.001 Preoperative SBP at 2 yr, mmHg (SD) 156 (22) *p*-value vs. BPD subjects that are still hypertensive <0.001 Preoperative SBP at 3 yr, mmHg (SD) 158 (24) *p*-value vs. BPD subjects that are still hypertensive <0.01 Preoperative DBP at 1 yr, mmHg (SD) 94 (17)		

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
			p-value vs. BPD subjects that are still hypertensive <0.001 Preoperative DBP at 2 yr, mmHg (SD) 96 (16) *p*-value vs. BPD subjects that are still hypertensive < 0.001 Preoperative DBP at 3 yr, mmHg (SD) 97 (18) *p*-value vs. BPD subjects that are still hypertensive <0.02 *Results for subjects who did not reach BP normalization over the 3-yr follow-up Mean weight at 1 yr, kg (SD): 91.4 (19.0) Mean weight at 2 yr, kg (SD): 84.7 (16.7) Mean weight at 3 yr, kg (SD): 88.1 (17.0) BMI at 1 yr, kg/m2 (SD): 33.1 (6.2) BMI at 2 yr, kg/m2 (SD): 30.8 (5.8) BMI at 3 yr, kg/m2 (SD): 32.0 (5.6) Waist-to-hip ratio at 1 yr, cm/cm (SD) 0.975 (0.127) Waist-to-hip ratio at 2 yr, cm/cm (SD) 0.961 (0.086) Waist-to-hip ratio at 3 yr, cm/cm (SD) 0.971 (0.105) Weight loss at 1 yr, kg (SD) 48.2 (17.3) Weight loss at 2 yr, kg (SD)		

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
			49.7 (20.3) Weight loss at 3 yr, kg (SD) 48.6 (18.7) Preoperative SBP at 1 yr, mmHg (SD) 168 (25) Preoperative SBP at 2 yr, mmHg (SD) 167 (24) Preoperative SBP at 3 yr, mmHg (SD) 166 (23) Preoperative DBP at 1 yr, mmHg (SD) 103 (15) Preoperative DBP at 2 yr, mmHg (SD) 102 (16) Preoperative DBP at 3 yr, mmHg (SD) 101 (17)		
Angrisani, 2007 RCT of individuals Hospital, Italy Fair	1: LAGB 2: Laparascopic RYGB	Inclusion Criteria BMI >35 to BMI <50 kg/m2 Ages 17–49 yr Absence of hiatal hernia No previous abdominal operations Had to accept randomization to 1 of 2 surgical groups Total Group Size: 1: 27 2: 24 Mean Age, years (SD) 1: 33.8 (9.1) 2: 34.1 (8.9) Sex, *n* 1: Male 5 Female 22	Mean weight at 12 mo, kg: G1: 102.4 G2: 92.8 Mean weight at 36 mo, kg: G1: 98.7 G2: 83.5 Mean weight at 60 mo, kg: G1: 97.9 G2: 84 *p*-value between groups at 5 yr <.001 BMI at 12 mo, kg/m2: G1: 38.7 G2: 35.4 BMI at 36 mo, kg/m2: G1: 35.6 G2: 29.1 BMI at 60 mo, kg/m2:	Complications, *n* Gastric Pouch Dilation 1: 2 2: 0 *One case occurred at 24 mo, and the other occurred at 36 mo; both were treated with band removal Jejunal Perforation 1: 0 2: 1 *Occurred 3 days after operation and was treated with perforation suture/intestinal resection Internal hernia 1: 0 2: 1 *Occurred 15 mo after surgery and was treated with intestinal resection	Duration: 5 yr Lost to follow-up: 1: 1 2: 0

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
		2: Male 4 Female 20 Weight, kg (SD) 1: 117.1 (12.8) 2: 118.2 (13.2) BMI, kg/m2 (SD) 1: 43.4 (4.2) 2: 43.8 (4.1) EWL, kg (SD) 1: 47.1 (10.9) 2: 48.2 (11.7) EWL, % (SD) 1: 83.1 (9.2) 2: 83.8 (8.9)	G1: 34.9 G2: 29.8 *p*-value between groups at 5 yr <.001 EWL at 12 mo, % 1: 34.7 2: 51.3 EWL at 36 mo, % 1: 47.3 2: 67.3 EWL at 60 mo, % 1: 47.5 2: 66.6 *p*-value between groups at 5 yr <.001	Posterior Pouch Leak 1: 0 2: 1 *Occurred during surgery, which was converted to laparotomy and suture closure	
Bessler, 2007 RCT of individuals Inpatient medical setting/Hospital, USA Good	Intervention: 1: LAGB long limb gastric bypass with banding 2: LAGB long limb gastric bypass without banding	Inclusion Criteria Patients with a BMI > 50 kg/m2 underwent surgery by one surgeon from June 2001 to July 2005 Interventions *n*'s at baseline G1: 46 G2: 44 Mean Age, yr (SD) 1: 40.6 (7.4) 2: 42.6 (7.2) *Actual *p*-value NR; authors states difference between groups is NS Sex, % women 1: 56.5 2: 73.8 *p-value between groups = .09 BMI, kg/m^2 (SD) 1. 59.4 (7.3) 2. 59.7 (7.1) *Actual *p*-value NR; authors states difference between groups	Excess Weight Loss at 6 mo, % 1: 43.1 2: 24.7 Excess Weight Loss at 12 mo, % 1: 64 2: 57.4 Excess Weight Loss at 24 mo, % 1: 64.2 2: 57.2 Excess Weight Loss at 36 mo*, % 1: 73.4 2: 57.7 *p*-value between groups <0.05 Patients attaining BMI <35 kg/m^2 at 12 mo, % 1: 47.8 2: 41.0 Patients attaining BMI <35 kg/m^2 at 24 mo, % 1: 52.9 2: 37.5 Resolution of Hypertension, % 1: 79	Complications, *n* (%) Wound infection 1: 7 (15.2) 2: 5 (11) Anastomatic leak 1: 0 2: 2 (4.8) Pnuemonia 1: 1 (2.1) 2: 1 (2.2) Pulmonary Embolsm 1: 0 2: 0 Small Bowel Obstruction 1: 1 (2.1) 2: 1 (2.2) Band Erosion/slippage/removal 1: 0 2: N/A Other 1: 3 (6.5) 2: 4 (9.0)	Mean Duration of follow-up: G1: 36 mo G2: 36 mo

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
		is NS Hypertension, % 1: 50 2: 46 *Actual *p*-value NR; authors states difference between groups is NS DM, % 1: 26 2: 26 *Actual *p*-value NR; authors states difference between groups is NS Hyperlipidemia, % 1: 31 2: 30 *Actual *p*-value NR; authors states difference between groups is NS	2: 90 *Actual *p*-value NR; authors states difference between groups is NS DM, % 1: 92 2: 98 *Actual *p*-value NR; authors states difference between groups is NS Hyperlipidemia, % 1: 50 2: 62 *Actual *p*-value NR; authors states difference between groups is NS Comments on Outcomes: * Authors state that "at 36 mo, the banded patients had lost significantly more weight than had the non-banded patients ($p<.05$). However, this was calculated from the small number of patients reaching the 36-mo follow-up period"; actual *n* at 36 mo not reported	Mortality 1: 0 2: 0 Total Complications 1: 12 (26) 2: 13 (29.5)	
Biertho, 2005 Case Series Inpatient medical setting Bern and Zurich, Switzerland Good	Swedish Adjustable Gastric Band Comments on bariatric surgery: The aim of band filling was to reduce the quantity of food consumed by more than one third of preoperative meal volumes while avoiding food intolerance. Follow-up at 1 yr, %: 97	Inclusion Criteria: At least one obesity-related comorbidity (i.e., dyslipidemia, type 2 diabetes, hypertension, obesity-related infertility, sleep apnea syndrome, degenerative joint disease of the lower extremities related to obesity, CVD, left-sided heart failure related to obesity). BMI >40 or BMI >35 with at least one obesity-related comorbidity, compassionate use of banding in BMI 30–35 kg/m2 for more than 5 yr duration, or previous failure of at least 2 yr of conservative treatment (3.4% of patients).	Excess Weight Loss, % (SE) Year 1: 30.1 (.5) Year 2: 41.5 (.6) Year 3: 47.6 (.8) Year 4: 52.0 (1.1) Year 5: 54.8 (1.7) Insufficient Weight loss, *n* 143* Comments on outcomes: * 20% of patients who exhibited insufficient weight loss ($n = 28$) were managed surgically by the addition of BPD an average of 1.9 ± .2 years after banding (at 32% ± 4% EWL). This intervention achieved ongoing weight loss in all patients by study end (60% ± 5% EWL). A further	Complications: All, %** Year 1: 2.9 Year 2: 6.7 Year 3: 6.6 Year 4: 5.8 Year 5: 3.2 Band leakage, %** Year 1: 1.3 Year 2: 1.1 Year 3: 1.5 Year 4: 2.9 Year 5: 1.6 Band migration, %** Year 1: .5 Year 2: .5 Year 3: .3	Duration: 5 yr Total sample at 2 yr, *N*: 744 Total sample at 3 yr, *N*: 593 Total sample at 4 yr, *N*: 380 Total sample at 5 yr, *N*: 184 **High attrition at 3 (28%), 4 (54%) and 5 (78%) years; these rates correspond to the number of subjects at that time point only (3 yr: *n*=593; 4 yr: *n*=380;

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
		Total sample at 1 yr, *N*: 821 Age, mean (SE): 43 (1) Sex, *N*: 1: Male: 188 Female: 636 Race/Ethnicity: Swiss BMI, kg/m2 (SE): 42.4 (1) Weight, kg (SE): 118 (1) Excess Body Weight, % (SE) 90 (1)	60% of these patients (*n* = 86) were treated medically with the addition of either orlistat (*n* = 59) or sibutramine (*n* = 27) on average 1.7 ± .1 years after banding (at 23.3% ± 1.3% EWL); of these, 66% achieved ongoing weight loss (32.2% ± 1.9% EWL by study end). Some 20% of patients with insufficient weight loss (*n* = 29) refused additional therapy during the study period and failed to lose further weight, achieving 14% ± 7% EWL by the study end.	Year 4: .3 Year 5: 0 Band slipping, %** Year 1: 0 Year 2: 1.5 Year 3: 1.3 Year 4: 1.3 Year 5: .5 Band infection, %** Year 1: .1 Year 2: .1 Year 3: 0 Year 4: 0 Year 5: 0 Band intolerance, %** Year 1: 1.0 Year 2: 3.5 Year 3: 3.5 Year 4: 1.3 Year 5: 1.1	5 yr: *n*=184)
Favretti, 2007 Case series Inpatient Medical Setting, Italy Good *Related Article*:* Favretti, 2002 *Related article is another included article from this study that does not provide additional data for this summary table beyond the data already included in the summary table from the main article.	Intervention: 125 patients (7%) underwent preoperative application of a Bioenterics Intragastric Balloon; 1393 (77.8%) patients underwent perigastric dissection; 384 (21.5%) patients had the pars flaccida technique; 14 (0.8%) patients had a combination of the perigastric dissection and the pars flaccida technique	Inclusion Criteria: - Consecutive patients presenting to the Obesity Centers of Vicenza Regional Hospital and Padova University between September 1993 and December 2005 Age, mean (SD): 38.7 (10.9) Sex, *n* (%): Male: 446 (24.9) Female: 1345 (75.1) Race/Ethnicity: Italian *N* at baseline: 1791 Mean Baseline Weight, kg (SD) 127.7 (24.3) Mean BMI, kg/m^2 (SD)	At yr 1: Mean Weight, kg (SD) 103.7 (21.6) Mean BMI, kg/m^2 (SD) 37.7 (7.1) %EWL, (SD) 40.3 (19.7) At yr 2: Mean Weight, kg (SD) 101.5 (23.3) Mean BMI, kg/m^2 (SD) 36.8 (7.6) %EWL, (SD) 43.7 (21.7) At yr 3: Mean Weight, kg (SD) 102.5 (22.5)	Complications, *n* (%) Stomach Slippage + Pouch Dilation 70 (3.9) Erosion 16 (0.9) Psychological Intolerance 14 (0.7) Miscellaneous (HIV, infections, microperforations) 5 (0.27) Gastric Necrosis 1 (0.05) Total 106 (5.9)	Duration: 12 yr

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
	Mean follow-up at 12 yr, %: 91	46.2 (7.7) Comorbidities, % Osteoarthritis 57.8 Hypertension 35.6 Obstructive Sleep Apnea Syndrome 31.4 Dyslipidemia 27.1 T2D 22 Depression 21.2 Heart failure 1.4	Mean BMI, kg/m^2 (SD) 37.2 (7.2) %EWL, (SD) 41.2 (23.2) At yr 4: Mean Weight, kg (SD) 104.1 (23.5) Mean BMI, kg/m^2 (SD) 37.8 (7.5) %EWL, (SD) 38.6 (24.4) At yr 5: Mean Weight, kg (SD) 105.0 (23.6) Mean BMI, kg/m^2 (SD) 38,1 (7.6) %EWL, (SD) 37.3 (25.3) At yr 6: Mean Weight, kg (SD) 105.3 (24.6) Mean BMI, kg/m^2 (SD) 38.1 (8.1) %EWL, (SD) 37.4 (28.2) At yr 7: Mean Weight, kg (SD) 106.8 (24.3) Mean BMI, kg/m^2 (SD) 38.5 (7.9) %EWL, (SD) 35.9 (26.7) At yr 8: Mean Weight, kg (SD) 105.0 (24.0)		

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
			Mean BMI, kg/m^2 (SD) 37.8 (7.9) %EWL, (SD) 37.7 (26.7) At yr 9: Mean Weight, kg (SD) 103.3 (26.2) Mean BMI, kg/m^2 (SD) 37.5 (8,5) %EWL, (SD) 38.5 (27.9) At yr 10: Mean Weight, kg (SD) 101.4 (27.1) Mean BMI, kg/m^2 (SD) 37.7 (9.1) %EWL, (SD) 35.4 (29.6) At yr 11: Mean Weight, kg (SD) 101.2 (31.9) Mean BMI, kg/m^2 (SD) 38.1 (11.5) %EWL, (SD) 38.4 (32.8) At yr 12: Mean Weight, kg (SD) 84.0 (27.5) Mean BMI, kg/m^2 (SD) 31.6 (8.5) %EWL, (SD) 49.2 (49.5)		
Longitudinal Assessment of Bariatric Surgery	Intervention: 1. Laparoscopic	Inclusion criteria: ≥18 years	Total Mortality at 30 days, *n* (%): 15 (0.3) Mortality at 30 days, *n* (%):	Complications, *n* (%) Tracheal Reintubation G1: 2 (0.2)	Duration of follow-up: G1: 30 Days G2: 30 Days

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
Consortium (LABS), 2009 University Hospital setting, USA Prospective, multicenter, observational cohort Good	RYGB 2. Laparoscopic RYGB 3. Open Roux-en-Y Gastric Bypass Comments: *Procedures that comprised –3% of all procedures (BPD) with or without a duodenal switch, SG,vertical banded gastroplasty, and open adjustable gastric banding) were excluded from the outcome analyses; total *N* included in analysis = 4,610	Underwent bariatric surgical procedures from March 11, 2005 through December 31, 2007, performed by 33 LABS-certified surgeons Interventions *n*'s at baseline* G1: 1,198 G2: 2,975 G3: 437 Age, mean years (SD): G1: 46.0 (12.5) G2: 43.6 (11.0) G3: 45.9 (10.7) Gender, Male Sex, *n* (%): G1: 277 (23.1) G2: 534 (17.9) G3: 140 (32.0) BMI, median kg/m^2: G1: 44.1 G2: 46.9 G3: 50.9 Race, *n*/ total *n* (%) G1: 130/1184 (11.0) G2: 338/2943 (11.5) G3: 31/437 (7.1) Hypertension, % 55.1 Obstructive Sleep Apnea, % 48.9 Diabetes, % 33.2 Asthma, % 23.1 Ischemic Heart Disease, % 4.4 Congestive Heart Failure, % 2.2	G1: 0 G2: 6 (0.2) G3: 9 (2.1) *p*-value between groups <0.001	G2: 12 (0.4) G3: 6 (1.4) *p*-value between groups = 0.004 Deep vein thrombosis G1: 3 (0.3) G2: 12 (0.4) G3: 5 (1.1) *p*-value between groups = 0.05 Endoscopy G1: 1 (0.1) G2: 45 (1.5) G3: 5 (1.1) *p*-value between groups <0.001 Tracheostomy G1: 0 G2: 6 (0.2) G3: 5 (1.1) *p*-value between groups = 0.001 Placement of Percutaneous Drain G1: 0 G2: 13 (0.4) G3: 3 (0.7) p-value between groups = 0.48 Abdominal Operation G1: 9 (0.8) G2: 94 (3.2) G3: 15 (3.4) *p*-value between groups <0.001 Failure to be discharged by day 30: G1: 0 G2: 13 (0.4) G3: 4 (0.9) *p*-value between groups = 0.02 Composite endpoint G1: 12 (1.0) G2: 143 (4.8) G3: 34 (7.8) *p*-value between groups <0.0001	G3: 30 Days Total *N* at 30 days: 4776

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
Larrad-Jimenez, 2007 Case Series Inpatient Medical Setting, Spain Fair	Biliopancreatic Diversion 1: - 343 patients underwent BPD surgery. Of them, 325, 194 and 65 were evaluated at 2, 5, and 10 yrs.	Inclusion Criteria: - Patients were selected for surgery according to the criteria of Van Italie. Mean Age, *n* (SD): 41.2 (10.5) Sex, *n* (%): Male: 70 (20) Female: 273 (80) Race/Ethnicity: Spanish Weight, kg (SD) 151.2 (28.7) BMI, kg/m^2 (SD) 52.2 (11.1)	Percentage Excess Weight Loss (%EWL), (SD) At 24 mo Morbid Obese patients (*n*=146) 81.6 (16.1) Super Obese patients (*n*=179) 70.2 (16.7) At 60 mo* Morbid Obese patients (*n*=87) 79.3 (13.8) Super Obese patients (*n*=107) 64.3 (10.8) At 120 mo** Morbid Obese patients (*n*=29) 77.8 (11.2) Super Obese patients (*n*=36) 63.2 (11.8)	Early Complications (30 days), *n* (%) Pneumonia 3 (0.88) Atelectasis 2 (0.58) Intra-abdominal hemorrhage 2 (0.58) Gastric hemorrhage 1 (0.29) Urinary Infection 6 (1.76) Thrombophlebitis 1 (0.29) Acute gastric dilation 1 (0.29) Wound Infection 5 (1.47) Noninfected seroma 3 (0.88) Bile Leak 2 (0.58) Late Complications (5 yr), *n* (%)* Clinical Hernia 85 (43.8) Subclinical Hernia 55 (28.3) Digestive Complication Rates (5 yr), *n* (%)* Marginal Ulcer 1 (0.51) Hemorrhagic Gastritis 1 (0.51) Intestinal Obstruction due to adhesions 7 (3.6) Perforated Intestine	Duration: 10 yr Follow-up at 2 yr, *n* (%): 325 (95) Follow-up at 5 yr, *n* (%): 194 (75) Follow-up at 10 yr, *n* (%): 65 (67.7) Comments: High attrition at yr 5 and 10 *Retention at 5 yr was 75%; these rates correspond to the 194 subjects who fulfilled the follow-up requirements at 5 yr only **Retention at 10 yr was 67.7%; these rates correspond to the 65 subjects who fulfilled the follow-up requirements at 10 yr only

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
				1 (0.51) Anal Pathology 15 (7.7) Severe Diarrhea 6 (2.5) Mild Diarrhea 21 (10.8) Constipation 18 (9.2) Flatulence 16 (8.2) Occasional Vomiting 3 (1.5) Abdominal Pain due to Kidney Stones 3 (1.5) Choleithiasis 38 (19.5) Acute Cholecystitis 16 (8.2) Metabolic Sequelae, 2 yr post-surgery (%) Anemia (hemoglobin <12 g/dl) 13 Iron Deficiency (ferritin <30 ug/l in men; < 10ug/l in women) 17 Hypoproteinemia (albumin <3.5 mg/dl) 0.29 Zinc Deficiency 6 Asymptomatic Mg Deficiency 0.29	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
				Asymptomatic Vit A and E Deficiency 5/6.5 Vit B_{12} Deficiency 5 Vit K Deficiency 0.29 Folate Deficiency 0 Hypoglycemia 0.58 Calcium-dependent increased parathyroid hormone Pre-op 28 Post-op 45 Post Treatment 15 Vit D Deficiency Pre-op 30 Post-op 43 Post Treatment 12	
Lopez-Jimenez, 2005 Case Series Inpatient Medical Setting, USA Good	Treatment Groups: 1. RYGB - with Coronary Artery Disease. 2. RYGB - without Coronary Artery Disease.	Inclusion Criteria: Presence of coronary artery disease defined by having one or more of the following criteria: 1) History of coronary revascularization 2) Coronary artery stenosis (>30%) on angiography in at least one major coronary branch 3) Inducible ischemia on stress sestamibi testing or stress echocardiography 4) Clinical history of myocardial infarction Mean Age, yr (SD): 1: 51.2 (8.8) 2: 44.3 (0.4) Sex, *n* (%): Male: 30 (58)	Postoperative CVD factor Values BMI (kg/m2) 36 (9) *p*- value <.01 **n*=48 % Excess weight 56 (35) *p*- value <.01 **n*=48 Total cholesterol (mg/dL) 142 (37) *p*- value<.01 **n*=36 LDL-C (mg/dL) 75 (26) *p*- value <.01 **n*=6 Triglycerides (mg/dL)	Cardiovascular complications, *n* (%) Non-ST segment myocardial infarction 1: 2 (3.8) 2: 0 Unstable angina 1:1 (1.9) 2:0 Pulmonary edema 1:0 (0) 2:5 (1) Pulmonary embolism 1:0 (0) 2:1 (0.2) Stroke 1:0 (0) 2:1 (0.2)	Among patients with coronary artery disease, followup BMI outcome was complete on 48 patients. Follow-up was complete on 36, 43, 45, and 50 patients for the blood lipid, blood pressure, glucose, and HbA1c outcomes, respectively. Dropouts are not reported among those without coronary artery disease.

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
		*Coronary artery disease only Race/Ethnicity: USA CVD Risk Factors, *n* (%): *Coronary artery disease only Hyperlipidemia: 36 (69) Hypertension: 46 (88) Diabetes mellitus: 33 (63) Current smoker: 6 (12) Family history: 33 (63) BMI, kg/m^2 (SD): 50 (11) Excess weight, % (SD): 121 (46) Lipids, mg/Dl (SD): Total cholesterol 198 (41) LDL-C 115 (33) Triglycerides 197 (106) HDL-C 44 (14) Blood pressure, mm Hg (SD): Systolic 142 (19) Diastolic 82 (12) Fasting glucose, mg/Dl (SD): 149 (49)	119 (52) *p*- value <.01 **n*=36 HDL-C (mg/dL) 43 (11) *p*- value = NS **n*=36 Blood pressure (mm Hg) Systolic 132 (17) *p*- value <.01 **n*=43 Diastolic 73±11 *p*- value <.01 **n*=43 Fasting glucose (mg/dL) 113±31 *p*- value <01 **n*=45	Ventricular arrhythmias 1:0 (0) 2:0 (0) Total, % (95% CI) 1: 3 (5.8; 0-12.2) 2: 7 (1.4; 0.4-2.4) *p*-value: .06 Noncardiovascular complications, *n* Fever, infection 1: 2 2:14 Small bowel obstruction/ileus 1: 0 2: 5 Wound dehiscence 1: 0 2: 4 Anastomotic leak 1: 0 2: 2 Bile/pancreatic leak 1: 0 2: 2 Tube-related complications 1: 0 2: 1 Total, (%) 1: 2 (3.8) 2: 28 (5.5) *p*-value: .90	
Schauer, 2012 RCT Medical Setting, USA Good	Intervention: 1: Lifestyle counseling, weight management, frequent home glucose monitoring, and the use of	Inclusion Criteria; Age of 20–60 yr; a diagnosis of T2D (glycated hemoglobin level, >7.0%), and a BMI of 27–43 *n*'s at baseline: 1: 50 2: 50	Body Weight at 12 mo (SD) 1: 77.3 (13.0) 2: 75.5 (12.9) 3: 99.0 (16.4) **p*- value between groups G1 and G3 ≤0.001 **p*- value between groups G2 and G3	Complications: Requiring Hospitalization, *n* (%) 1: 11 (22) 2: 4 (8) 3: 4 (9) Intravenous Treatment for	Duration: 12 mo Follow-up rate: 93%

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
	newer drug therapies (e.g., incretin analogues) approved by the FDA (FDA); All patients were treated with lipid -lowering and antihypertensive medications, according to ADA guidelines; gastric bypass consisted of the creation of a 15 to 20 ml gastric pouch, a 150-cm Roux limb, and a 50-cm biliopancreatic limb; vitamin and nutrient supplementation after gastric bypass included a multivitamin, iron, vitamin B12, and calcium citrate with vitamin D 2: Lifestyle counseling, weight management, frequent home glucose monitoring, and the use of newer drug therapies (e.g., incretin analogues) approved by the FDA (FDA); All patients were treated with lipid -lowering and antihypertensive	3: 50 Mean Age, yr (SD) 1: 48.3 (8.4) 2: 47.9 (8.0) 3: 49.7 (7.4) Sex, female, *n* (%) 1: 29 (58) 2: 39 (78) 3: 31 (62) Weight, kg (SD) 1; 106.7 (14.8) 2: 100.8 (16.4) 3: 106.5 (14.7) Mean BMI (SD) 1: 37.0 (3.3) 2: 36.2 (3.9) 3: 36.8 (3.0) WC, cm (SD) 1: 116.4 (9.2) 2: 114.0 (10.4) 3: 114.5 (9.4) Waist-to-Hip Ratio (SD) 1: 0.95 (0.07) 2: 0.96 (0.09) 3: 0.95 (0.09) White Race, *n* (%) 1: 37 (74) 2: 36 (72) 3: 37 (74) Fasting Glucose, mg/dl 1: 193 2: 164 3: 155 Metabolic Syndrome, *n* (%) 1: 45 (90) 2: 47 (94) 3: 46 (92)	≤0.001 *p- value between groups G1 and G = 0.50 % Change in Body Weight (from baseline), 12 mo 1: -29.4 (8.9) 2: -25.1 (8.5) 3: -5.4 (8.0) Excess Weight loss at 12 mo, % (SD) 1: 88 2: 81 3: 13 *p- value between groups G1 and G3 ≤0.001 *p- value between groups G2 and G3 ≤0.001 *p- value between groups G1 and G2 ≤0.001 % Change in HDL-C (from baseline), 12 mo 1: 28.5 (22.7) 2: 28.4 (21.9) 3: 11.3 (25.7) *p- value between groups G1 and G3 =0.001 *p- value between groups G2 and G3 =0.001 *p- value between groups G1 and G2 = 0.98 Median % Change in Triglycerides (from baseline), 12 mo (interquartile range) 1: -44 (-65- (-16)) 2: -42 (-56- 0) 3: -14 (-40-3) *p- value between groups G1 and G3 =0.002 *p- value between groups G2 and G3 =0.08	dehydration, *n* (%) 1: 4 (8) 2: 2 (4) 3: 0 Reoperation, *n* (%) 1: 3 (6) 2: 1 (2) 3: 0 Transfusion, *n* (%) 1: 1 (2) 2: 1 (2) 2: 0 Hemoglobin decrease ≥5 g/dl, *n* (%) 1: 1 (2) 2: 0 3: 0 Gastrointestinal Leak, *n* (%) 1: 0 2: 1 (2) 3: 0 Transient Renal Insufficiency, *n* (%) 1: 1 (2) 2: 0 3: 0 Cholelthiasis, *n* (%) 1: 1 (2) 2: 0 3: 0 Arrhythmia/palpitations, *n* (%) 1: 0 2: 1 (2) 3: 2 (5) Pleural Effusion, *n* (%) 1: 0 2: 0 3: 1 (2) Ketoacidosis, *n* (%) 1: 1 (2) 2: 0	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
	medications, according to ADA guidelines; SG involved a gastric-volume reduction of 75–80% by resecting the stomach alongside a 30-French endoscope beginning 3 cm from the pylorus and ending at the angle of His; after SG,, such supplementation included a multivitamin and vitamin B12 3: Lifestyle counseling, weight management, frequent home glucose monitoring, and the use of newer drug therapies (e.g., incretin analogues) approved by the FDA (FDA); All patients were treated with lipid -lowering and antihypertensive medications, according to ADA guidelines	History of Dyslipidemia, *n*/total *n* (%) 1: 44/50 (88) 2: 40/50 (80) 3: 36/43 (84) History of Hypertension, *n*/total *n* (%) 1: 35/50 (70) 2: 30/50 (60) 3: 26/43 (60) j Number of Diabetes Medications: 1: 2.6 2: 2.4 3: 2.8	**p*- value between groups G1 and G2 = 0.17 BMI at 3 mo 1: 31.8 2: 31.3 3: 35.4 BMI at 6 mo 1: 28.2 2: 28.3 3: 34.8 BMI at 9 mo 1: 26.9 2: 28.3 3: 34.8 BMI at 12 mo 1: 26.8 2: 27.2 3: 34.4 Fasting Glucose, mg/dl, 3 mo 1: 109 2: 118 3: 122 Fasting Glucose, mg/dl, 6 mo 1: 96 2: 104 3: 113 Fasting Glucose, mg/dl, 9 mo 1: 96 2: 102 3: 120 Fasting Glucose, mg/dl, 12 mo 1: 99 2: 97 3: 120 Number of Diabetes Medications, 3 mo: 1: 1.1 2: 1.1	3: 0 Wound Infection, *n* (%) 1: 1 (2) 2: 0 3: 0 Cellulitis, *n* (%) 1: 0 2: 0 3: 1 (2) Pneumonia, *n* (%) 1: 2 (4) 2: 0 3: 0 Kidney Stone, *n* (%) 1: 0 2: 0 3: 1 (2) Hernia, *n* (%) 1: 1 (2) 2: 0 3: 0 Hypoglycemic episode (self-reported), *n* (%) 1: 28 (56) 2: 39 (80) 3: 35 (81) Anemia, *n* (%) 1: 6 (12) 2: 6 (12) 3: 3 (7) Hypokalemia, *n* (%) 1: 2 (4) 2: 2 (4) 3: 1 (2) Anastomotic Ulcer, *n* (%) 1: 4 (8) 2: 0 3: 0	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
			3: 3.1 Number of Diabetes Medications, 6 mo: 1: 0.6 2: 0.9 3: 3.1 Number of Diabetes Medications, 9 mo: 1: 0.4 2: 0.8 3: 3.0 Number of Diabetes Medications, 12 mo: 1: 0.3 2: 0.9 3: 3.0	Excessive weight gain (>5% over baseline), *n* (%) 1: 0 2:0 3: 3 (7)	
Steffen, 2003 Case series Good	Treatment Group: Swedish Adjustable Gastric Banding Intervention: LAGB	Inclusion Criteria: Passed a careful interdisciplinary evaluation (Patients with a BMI >50 kg/m2 and severe obesity-related metabolic syndrome were offered a malabsorptive operation including SAGB with distal gastric bypass or SAGB with BPD and duodenal switch); Mean Age, yr (SD) 43 (2) Gender, n Male 188 Female 636 Height, cm (SD) 167 (1) Weight, kg (SD) 118 (1) BMI, kg/m2 (SD) 42.4 (1) Excess Body Weight, % (SD)	Mean EWL, % (SD) *calculated using Metropolitan Life Insurance tables At Yr 1: 29.5 (0.5) At Yr 2: 41.1 (0.7) At Yr 3: 48.7 (0.9) At Yr 4: 54.5 (1.2) At Yr 5: 57.1 (1.9) Mean Postoperative BMI, kg/m^2 (SD) At Yr 1: 35.8 (0.2) At Yr 2: 33.2 (0.1) At Yr 3: 31.5 (0.2) At Yr 4: 30.0 (0.3) At Yr 5: 29.2 (0.4) Insufficient weight loss, *n* (%) *defined as <50% EWL and no weight loss in the previous 3 mo before 50% EWL was obtained, or weight regain >10% of weight loss 141 (17.1) Mortality rates: First 30 postoperative days: 0%	Intraoperative Complications, *n* (%): Liver hematoma 5 (0.6) Splenic hemorrhage 3 (0.4) Hemorrhage from gastroepiploic veins 2 (0.2) CO_2 embolism 1 (0.1) Esophageal Perforation 1 (0.1) Traumatic Intubation 12 (1.5) Postoperative TECHNICAL complications related to the band, *n* (%) Band leakage 14 (1.8) Band Infection	Follow-up duration: 5 years Follow-up rate at 5 years, % 97

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
		90 (1)	Beyond 30 days: 0.4% (*N*=3)	2 (0.0) Band Slippage 22 (2.7) Band Penetration 13 (1.6) Total (*N*=824), *n* (%) 51 (6.3) Postoperative complications related to the access-port or tube, *n* (%) Port infection 8 (1.0) Port hematoma 2 (0.2) Port discomfort/prominence 19 (2.3) Port Dislocation 8 (1.0) Tube Leak 10 (1.2) Tube disconnection/kinking 9 (1.1) Total (*N* = 824), % 6.8 Postoperative FUNCTIONAL complications related to the band, *n* (%) Band intolerance (primary) 8 (1.0) Band intolerance (secondary) 50 (6.1) Total (*N* = 824), *n* (%) 58 (7.0) Insufficient Weight Loss at 5 yr, *n* (%)	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
				141 (17.1) Major Reoperative Rate (either laparoscopy or laparotomy), % 16.5 (3.3/yr) Minor Reoperations due to access-port complications, % 6.8 Total reoperations Major reoperation rate: 16.5% Minor reoperation rate (due to access-port complications): 6.8% Comments on Adverse Events: - Not included in the list above: 26 out of the 81 (32%) first-generation SAGBs had to be replaced because of a leak at the seam The 8 cases of primary band intolerance required band removal; 7 of the 8 patients converted to a standard RYGB, and one refused further operations The 50 cases of secondary band intolerance resulted in total band deflation; Patients converted to standard RYGB or an open or laparoscopic BPD was added to the band	
Wolnerhanssen 2008 Prospective cohort study with one or more comparison groups Fair Inpatient medical setting – hospital, Switzerland	Treatment group: Patients undergoing LAGB surgery Intervention: LAGB	Inclusion Criteria: Morbidly obese patients with a BMI >40 kg/m2 or >35 kg/ m2 with severe, obesity-related comorbidities who were treated with LAGB Total *N* at baseline: 380 Median age, yr (range): 40 (17–66) *adult population in criteria	EWL, % (range) Band in situ 40 (10–100) Band removed 26 (-38-110) Proportion of patients who still had their band at 5 yr with EWL >50%, % 25	Number of patients who had band removed, *n* (%) 128 (33.7) Number of patients who still had their band at 5 yr, *n* (%) 252 (66.3) Predictors of poor outcome after LAGB, HR (95% CI) Predictor HR (95% CI) P-value Older age*	Duration of follow-up; 5 years (median)

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
		Median weight, kg (range): 122 (87–250) Median BMI, kg/m2 (range): 43.4 (35–75) Sex, % female: 78		1.3 (1.00–1.67) .05 Initial BMI* .94 (.79–1.12) 5 Gender** 1.25 (.99–1.58) 3 Hypertension*** 1.17 (.86–1.6) .3 Coronary Heart Disease*** 1.16 (.7–1.91) .56 Diabetes*** .85 (.58–1.25) .4 Sleep Apnea Syndrome*** 1.31 (.73–2.33) 38 Hyperlipidemia*** 1.28 (.94–1.74) .12 Depression*** 1.23 (.91–1.65) .18 Comments on Outcomes: * Relative risk comparison first to third quartile **0 = female, 1 = male (i.e., men at increased risk of poor outcome with factor 1.25) *** Adjusted for age, sex, and initial BMI	
Weiner, 2007 Prospective Cohort Medical Setting, hospital, Poland Fair	Intervention: Laparoscopic SG performed without a calibration tube; Laparoscopic SG performed with a calibration tube of 44 Fr; Laparoscopic SG performed with a	Inclusion Criteria: Super-super-obese patients (BMI >60) *n*'s at baseline: 1: 25 2: 32 3: 63 Mean Age, yr 1: 38.1 2: 38.9	Comorbidities: Before and after LSG: *BEFORE* Hypertension, *n* (%): Preop: 67 (55.8%) Unchanged: 2 (3%) Improved: 37 (55%) Solved: 28 (42%) Worsened: 0 (0%) Diabetes, *n* (%):	Complications: Gastrointestinal Side Effects (before, 1 mo after, and 2 yr after LSG: *BEFORE* Reflux Symptoms, n: Total Preop (All 3 Groups): 42 Severe Esophagitis, *n*: Total Preop: 27	Duration: 2 yr

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
	calibration tube of 32 Fr	3: 41.9 Sex, female 1: 16 2: 20 3: 50 Sex, male 1: 9 2: 12 3: 13 Weight, kg 1: 185.1 2: 185.7 3: 174.7 Mean BMI (kg/m^2) 1: 61.6 2: 60.8 3: 60.3 Height, m 1: 1.73 2: 1.75 3: 170.8 Excess Weight, kg 1: 121.4 2: 120.3 3: 113.8 Note: There seems to be an error with the height data (Group 3). However, this is how the data is presented in the article.	Preop: 14* (11.7%) Unchanged: 0 (0%) Improved: 12 (86%) Solved: 2 (14%) Worsened: 0 (0%) Sleep Apnea, *n* (%): Preop: 28 (23.3%) Unchanged: 0 (0%) Improved: 17 (61%) Solved: 11 (39%) Worsened: 0 (0%) Hyperlipidemia, *n* (%): Preop: 34 (28.3%) Unchanged: 6 (18%) Improved: 26 (77%) Solved: 2 (5%) Worsened: 0 (0%) Hyperuricemia, *n* (%): Preop: 19 (15.8%) Unchanged: 0 (0%) Improved: 14 (74%) Solved: 5 (26%) Worsened: 0 (0%) Arthritis, *n* (%): Preop: 72 (60%) Unchanged: 42 (58%) Improved: 26 (36%) Solved: 0 (0%) Worsened: 6 (8%) Asthma, *n* (%): Preop: 14 (11.7%) Unchanged: 2 (14%) Improved: 11 (79%) Solved: 1 (7% Worsened: 0 (0%) Incontinence, *n* (%): Preop: 10 (8.3%) Unchanged: 3 (30%) Improved: 6 (60%) Solved: 0 (0%)	Permanent use of proton pump inhibitor medications, *n:* Total Preop: 27 Diarrhea (3 patients with colitis), *n*: Total Preop: 3 Constipation, *n*: Total Preop: 0 Gastric Pain, *n*: Total Preop: 6 Vomiting, *n*: Total Preop: 0 *1 MONTH* Reflux Symptoms, *n*: 1: 18 2: 23 3: 39 Total: 80 Severe Esophagitis, *n*: 1: 1(5)* 2: 0(1))* 3: 1(8)* Total: 2(14)* Permanent use of proton pump inhibitor medications, *n*: 1: 25 2: 32 3: 63 Total: 120** Diarrhea (3 patients with colitis), *n*: 1: 0 2: 1 3: 1 Total: 2 Constipation, *n*: 1: 6 2: 7 3: 14 Total: 27	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
			Worsened: 1 (10%) Gastroesophageal reflux disease, *n* (%): Preop: 42 (35%) Unchanged: 0 (0%) Improved: 18 (43%) Solved: 24 (57%) Worsened: 0 (0%) Polycystic ovarian disease, *n* (%): Preop: 3 (2.5%) Unchanged: 0 (0%) Improved: 0 (0%) Solved: 3 (100%) Worsened: 0 (0%) *Patients with type 2 diabetes in most cases were selected for single-stage RYGBP	Gastric Pain, *n*: 1: 5 2: 6 3: 5 Total: 16 Vomiting, *n*: 1: 0 2: 2 3: 5 Total: 7 *2 YEARS* Reflux Symptoms, *n*: 1: 1 2: 3 3: 2 Total: 6 Severe Esophagitis, *n*: 1: 1(4)* 2: 2 (14)* 3: 5 (9)* Total: 8 (27)* Permanent use of PPI-medications, *n*: 1: 3 2: 5 3: 2 Total: 10 Diarrhea (3 patients with colitis), *n*: 1: 0 2: 0 3: 0 Total: 1 Constipation, *n*: 1: 1 2: 2 3: 3 Total: 5 Gastric Pain 1: 1 2: 2	

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
				3: 3 Total: 5 Vomiting 1: 0 2: 1 3: 0 Total: 1 *Endoscopic signs of severe esophagitis (no. of investigations) **All patients were on regular PPI medications for 6 wk after surgery Note: There seems to be an error in the total counts for the Diarrhea, Constipation, and Gastric Pain sections. However, this is how the data is presented in the article.	
Mingrone, 2012 Single-center, non-blinded, randomized, controlled trial Weight change, change in CVD risk factors Day Hospital of Metabolic Diseases and Diabetology of the Catholic University Rome Good	1. Gastric bypass 2. Biliopancreatic diversion 3. Medical therapy	Inclusion Criteria: Age of 30–60 yr; BMI of ≥35; a history of T2D of at least 5 yrs; a glycated hemoglobin level of ≥7.0% (as confirmed by at least three analyses); an ability to understand and comply with the study protocol Intervention *n*'s (baseline): 1: 20 2: 20 3: 20 Mean Age, yr (SD): 1: 43.90 (7.57) 2: 42.75 (8.06) 3: 43.45 (7.27) Sex, male, *n* (%): 1: 10 (50); 2: 10 (50); 3: 8 (40); Weight, kg (SD): 1: 129.84 (22.58)	% Change in Weight loss (from baseline), 2 yr 1: -33.31 (7.88) 2: -33.82 (10.17) 3: -4.74 (6.37) Excess Weight loss at 2 yr, % (SD) 1: 68.08 (12.70) 2: 69.36 (17.60) 3: 9.29 (12.94) % Change in BMI (from baseline), 2 yr 1: -33.31 (7.88) 2: -33.82 (10.17) 3: -4.73 (6.37) % Change in WC (from baseline), 2 yr 1: -19.91 (8.44) 2: -20.70 (8.34) 3: -7.69 (7.80) % Change in Glucose (from baseline), 2 yr 1: -37.81 (33.75) 2: -56.23 (10.01)	Complications*: Incisional Hernia (9 mo): 1: 0 2: 1 Male patient (5%) Intestinal Occlusion (6 mo): 1: 1 Male patient (5%) 2: 0 Iron-Deficiency Anemia: 1: 2 Female patients (11%) 2: 2 Female patients (11%)** Hypoalbuminemia (Albumin, <3.5 g/dl): 1: 0 2: 1 Female and 1 male patient (11%)** Osteopenia (BMD T score, -2): 1: 0 2: 1 Female patient (5%) Osteoporosis (BMD T score, -2.7): 1: 0 2: 1 Female patient (5%)** *These complications developed	Intervention *n*'s at 2 yr follow-up: 1: 19 2: 19 3: 18 Duration of follow-up: 1: 2 yr 2: 2 yr 3: 2 yr

Study Cited, Study Design, Primary Outcomes, Setting, Quality Rating	Intervention Groups. Component Details	Sample Characteristics, Baseline population characteristics	Weight Reduction, CVD Risk Factor, Morbidity, HRQOL and Mortality Outcomes	Complications Outcomes	Duration, Attrition
		2: 137.85 (30.35) 3: 136.40 (21.94) BMI (SD): 1: 44.85 (5.16) 2: 45.14 (7.78) 3: 45.62 (6.24) WC, cm (SD) 1: 125.40 (16.58) 2: 130.35 (19.73) 3: 126.90 (14.68) Fasting Glucose, mmol/liter (SD) 1: 9.55 (3.35) 2: 9.70 (3.44) 3: 9.94 (3.43) Total Cholesterol (SD) 1: 4.71 (0.91) 2: 5.54 (1.50) 3: 6.12 (1.55) HDL-C (SD) 1: 1.13 (0.23) 2: 0.99 (0.21) 3: 0.99 (0.21) LDL-C (SD) 1: 2.83 (0.84) 2: 3.41 (1.21) 3: 3.99 (1.40) Triglycerides, mmol/liter (SD) 1: 1.66 (0.86) 2: 2.49 (1.21) 3: 2.49 (0.80) SBP mmHg (SD) 1:145.75 (20.54) 2: 154.50 (29.73) 3: 155.20 (34.18) DBP mmHg (SD) 1: 91.50 (14.15) 2: 95.90 (12.87) 3: 96.00 (17.52)	3: -14.37 (11.93) % Change in Total Cholesterol (from baseline), 2 yr 1: -6.83 (27.03) 2: -49.25 (11.52) 3: -16.82 (11.60) % Change in HDL-C (from baseline), 2 yr 1: 29.66 (18.21) 2: 12.98 (20.66) 3: 6.03 (6.25) % Change in LDL-C (from baseline), 2 yr 1: -17.21 (36.21) 2: -64.63 (15.93) 3: -20.31 (15.24) % Change in Triglycerides (from baseline), 2 yr 1: -21.17 (41.23) 2: -56.79 (16.70) 3: -18.28 (7.84) % Change in DBP (from baseline), 2 yr 1: -7.30 (9.42) 2: -13.06 (8.97) 3: -7.14 (11.51)	9–18 mo after the operation. BMD= Bone mineral density at the femoral neck ** One female patient had multiple complications.	

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