2013 Report on Lifestyle Management to Reduce Cardiovascular Risk:

Full Work Group Report Supplement

Based on a Systematic Review From the National Heart, Lung, and Blood Institute

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1. 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

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; should not be performed/ administered/ other; is not useful/ beneficial/ effective COR III: Harm: potentially harmful; causes harm; associated with excess morbidity/mortality; should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

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 G.

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 B and C for an explanation of the NHLBI recommendation grading methodology.

Table B. 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 Workgroup 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 Workgroup 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 Workgroup 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 Workgroup.
†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 C. 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. 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.	Moderate
• 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 Workgroup 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.

Organization of Panel

The Work Group was composed of 12 members and 4 ex-officio members which includes physicians and experts in BP, blood cholesterol, obesity, and lifestyle management. The authors came from primary care, nursing, pharmacology, nutrient, exercise, behavioral science, and epidemiology disciplines and also included senior scientific staff from NHLBI and the National Institute of Health.

Document Review

A formal peer review process was initially completed under the auspices of the NHLBI which included 6 expert reviewers and representatives of Federal agencies. This document was also reviewed by 4 expert reviewers nominated by the ACC and the AHA when the management of the guideline transitioned to the ACC/AHA.

2. Executive Summary

A. Introduction

A healthy lifestyle is important in the prevention of cardiovascular disease (CVD), the leading cause of morbidity and mortality in Americans. The intent of the Lifestyle Workgroup was to evaluate evidence that particular dietary patterns, nutrient intake, and levels and types of physical activity can play a major role in CVD prevention and treatment through effects on modifiable CVD risk factors (i.e., blood pressure (BP) and lipids). These evidence statements (ESs) and recommendations may be used as appropriate in the management of hypercholesterolemia and hypertension. The target audience of the report is primary care providers.

LIFESTYLE WORKGROUP CRITICAL QUESTIONS:	
CQ1.	Among adults[1], what is the effect of dietary patterns and/or macronutrient composition on CVD risk factors, when compared with no treatment or with other types of interventions?
CQ2.	Among adults, what is the effect of dietary intake of sodium and potassium on CVD risk factors and outcomes, when compared with no treatment or with other types of interventions?
CQ3.	Among adults, what is the effect of physical activity on blood pressure and lipids when compared with no treatment or with other types of interventions?

[1]Those ≥18 years and <80 years.

To formulate the nutrition recommendations, the Workgroup used randomized controlled trials (RCTs), observational studies, meta-analyses, and systematic reviews of studies carried out in adults (≥18 years) with or without established coronary heart disease (CHD)/CVD, with or without CHD/CVD risk factors, and who were of normal weight, overweight, or obese. The evidence review date range was 1998 to 2009. In order to capture historic data or more recent evidence, there were instances in which date ranges were changed for sub-questions. The evidence date ranges are clearly described in each critical question (CQ) section. We assessed the impact of both dietary patterns and macronutrient composition on plasma LDL-C, HDL-C, and TG, and on systolic blood pressure (SBP) and diastolic blood pressure (DBP) over a minimum RCT intervention period of 1 month, in studies performed in any geographic location and research setting.

Overall, we emphasized dietary patterns rather than individual dietary components. Patterns were characterized by habitual or prescribed combinations of daily food intake. Dietary patterns offer the opportunity to characterize the overall composition and quality of the eating behaviors of a population (e.g., Mediterranean-style dietary pattern). Eating patterns consist of various combinations of foods that may differ in macronutrient, vitamin, and mineral compositions. The macronutrients saturated, *trans*, monounsaturated, and polyunsaturated fatty acids are particularly relevant for their effects on plasma lipids and lipoproteins. Dietary sodium and potassium are particularly relevant for their effects on BP. Epidemiological research has examined the dietary patterns of populations and identified associations between various patterns and CVD risk factors and outcomes. Intervention studies have tested *a priori* hypotheses involving prescribed dietary patterns specifically formulated on the basis of these data (e.g., Dietary Approaches to Stop Hypertension or DASH or Mediterranean-style dietary patterns, etc.). Population-based prospective cohort studies and randomized clinical trials suggest that there are *healthier* overall dietary patterns (foods and/or their constituent macronutrient, vitamin, and mineral combinations) that are associated with lower chronic disease risk, including CVD and its risk factors, such as type 2 diabetes and hypertension (HTN). We reviewed data exclusively on dietary intake, rather than nutritional supplements provided in pharmaceutical preparations (e.g., potassium pills), which may not have similar effects and are not considered “lifestyle” interventions.

The Workgroup focused on CVD risk factors to provide a free-standing lifestyle document and to inform the Blood Cholesterol guideline and the hypertension panel It also recognized that RCTs examining the effects on hard outcomes (myocardial infarction, stroke, HF, and CVD related death) are difficult if not impossible for a number of reasons (e.g., long-term adherence to dietary changes). However, the Workgroup also supplemented this evidence on risk factors with observational data on hard outcomes for sodium because there has been much attention to this topic and reviewing this evidence would benefit clinicians. The Workgroup prioritized topics for the evidence review and was unable to review the evidence on hard outcomes for dietary patterns or physical activity.

For physical activity, substantial epidemiologic evidence links higher levels of aerobic physical activity to lower rates of CVD and other chronic diseases such as type 2 diabetes. Evidence indicates there is a dose-dependent inverse relationship between levels of physical activity and rates of CVD. The proposed mechanisms mediating the relationship between physical activity and decreased CVD rates include beneficial effects on lipids and lipoproteins, BP, and type 2 diabetes. The search for evidence related to physical activity and CVD health included only systematic reviews and meta-analyses of RCTs or individual controlled clinical trials in adults (≥18 years) that were published from 2001–2011. For this critical question, the intervention was defined as physical activity interventions of any type.

Weight loss and maintenance are critical for prevention and control of CVD risk factors. The Overweight and Obesity Expert Panel is simultaneously performing a systematic review of the evidence for weight management and CVD risk factors and outcomes. The primary intent of the Lifestyle Workgroup’s systematic review was to

focus on the effects of diet and physical activity on CVD risk factors **independent of** effects on weight. Therefore, studies in which the primary outcome was weight loss or in which treatment was associated with more than 3 percent change in weight were excluded from the review. However, the Workgroup expects that recommendations from both evidence reviews will apply to many patients.

Because of limited resources and time, the Workgroup had to make some choices and could not review every study pertaining to lifestyle and CVD risk factors and outcomes. Priority was given to strong study design and a contemporaneous timeframe (1998–2009). There were instances when the evidence review was extended beyond this timeframe. Landmark evidence on the effect of fatty acids on lipids was included back to 1990. The sodium evidence review included evidence through April 2012 and the physical activity meta-analysis review was extended to May 2011. Given the expertise of Workgroup members and their familiarity with the literature in this field, the Workgroup is confident that a broader review would not substantially change our conclusions or recommendations.

The results of the Lifestyle Workgroup systematic review are the 10 lifestyle recommendations (8 dietary and 2 physical activity recommendations). Because the Lifestyle Workgroup was convened to inform the development of ***clinical*** guidelines, and because most data meeting our criteria for review are derived from studies of high-risk populations, these recommendations are directed at patients with CVD risk factors (i.e., abnormal lipids and/or prehypertension and hypertension). The majority of adults in the United States either currently have one of these risk factors (33.5 percent with elevated LDL-C; 27.3 percent with hypertension and 31 percent prehypertension; 11.3 percent with diabetes), with risk factors increasing with age.(4) The Workgroup encourages heart healthy nutrition and physical activity behaviors for all adult Americans heart healthy nutrition and physical activity behaviors (see Exhibit 1).

For both BP and lipids, most studies of diet and/or physical activity exclude people taking antihypertensive or lipid-lowering medications. Although there is no direct evidence, it is reasonable to expect that the beneficial effects of these lifestyle recommendations apply to those taking these medications, and that following these recommendations can potentially lead to better BP and lipid control in those taking medications and/or reduced medication needs. The recommendations apply to adults <80 years old with and without CVD.

3. Lifestyle Workgroup Members

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4. Process and Methods Overview

A. 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 National Heart, Lung, and Blood Institute (NHLBI) has sponsored the development of clinical practice guidelines since the 1970s. Recognizing the need to update the most recent cardiovascular guideline reports, beginning in 2005, the NHLBI convened stakeholder groups to provide input on the next-generation guidelines development process.

The resulting recommendations were used to design the process for the next versions of the guidelines. The recommendations emphasized the need to:

- 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 guideline development and implementation.
- Give more attention to dissemination and implementation issues and work closely with stakeholders in health care and community systems for translation and dissemination of the evidence base.
- Develop an integrated 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 three Expert Panels to develop updates of the guidelines for high blood cholesterol, high BP, and overweight/obesity. Three crosscutting Workgroups on risk assessment, lifestyle, and implementation were formed to develop their own recommendations or to provide crosscutting input to the Expert Panels. A Guidelines Executive Committee composed of all Panel and Workgroup co-chairs and NHLBI staff provided coordination for the work of the Panels and Workgroups. This report summarizes the findings and recommendations of the Lifestyle Workgroup.

The five topics (blood cholesterol, blood pressure, overweight/obesity, lifestyle, and risk assessment) are seen as integral and complementary. An Integrated CVD Risk Reduction Guideline was defined as a next step and will follow.

B. Evidence-Based Approach

i. Overview of Evidence-Based Methodology

To continually improve the quality and impact of the guidelines sponsored by the NHLBI, the guideline development process was updated to assure rigor and minimize bias. This new effort involves the use of rigorous evidence-based methodology and the development of evidence statements and recommendations based on a systematic review of the biomedical literature for specific periods of time.

The process followed most of the standards from the Institute of Medicine (IOM) 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 from key affected group
- 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

All of the Panels and Workgroups followed the same methods, with variations as needed to reflect the evidence in the field. The methodology implemented for this project involved numerous components and followed a prespecified development process. Expert Panels and Workgroups consisting of cardiologists, primary care clinicians, nutritionists, and other clinical and nonclinical experts were convened to develop the guidelines. Directed by the NHLBI, with support from a methodology contractor and a systematic review and general support contractor, the Expert Panels and Workgroups:

- Constructed critical questions (CQs) most relevant to clinical practice. Critical questions followed the "PICOTS" (population, intervention/exposure, comparison group, outcome, timing, and setting) format.
- Identified (*a priori*) inclusion/exclusion (I/E) criteria for each CQ.

Directed by the NHLBI, with input from the Panels and Workgroups, 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.
- Screened, by two independent, masters/Ph.D.-level reviewers, thousands of abstracts/full-text articles returned from the search to identify relevant original articles, systematic reviews, and/or meta-analyses. Rigorous validation procedures were applied to ensure that the selected articles met the preestablished detailed I/E criteria before being included in the final review results.
- Determined the quality of each included study through the use of two independent raters. For the most part, these were the same reviewers who had screened the literature previously. However, due to limited resources, this was not always possible. The methodology staff, with input from the NHLBI, adapted study-rating instruments and trained study raters on the use of these instruments.
- Abstracted relevant information from the included studies into an electronic 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, which organized 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 Workgroups:

- 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.

- Used the graded evidence statements to write clinical recommendations and graded the strength of each recommendation.
- Performed Guideline Implementability Appraisals (GLIA), planned and coordinated by the NHLBI Implementation Workgroup, to identify and address barriers to guideline implementation. GLIA is a tool for the appraisal of the implementability of clinical guidelines.
- Drafted a report that underwent external review by Federal agencies and a group of experts selected by the NHLBI.

ii. System for Grading the Body of Evidence and Strength of Recommendation

The NHLBI adapted a system developed by the U.S. Preventive Services Task Force (USPSTF) to grade the body of the evidence and the strength of the recommendations.

- Evidence statements were graded as high, moderate, or low quality.
- Recommendations were graded 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).

The grades provide guidance to primary care physicians, clinicians, and other stakeholders on how much support the evidence provided for the evidence statement. 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. The Appendix, section xiii, describes how four domains of the body of evidence—risk of bias, consistency, directness, and precision—were used to grade the strength of evidence. The procedure for grading the recommendations is also described.

C. Critical Question (CQ)-Based Approach

The Lifestyle Workgroup developed an initial set of questions based on their expertise and a brief literature review to identify topics of the greatest relevance and impact for the target audience of the guideline, primary care providers. Due to time and resource limitations, the Workgroup prioritized the final three critical questions below.

LIFESTYLE WORKGROUP CRITICAL QUESTIONS	
CQ1.	Among adults[2], what is the effect of dietary patterns and/or macronutrient composition on CVD risk factors, when compared with no treatment or with other types of interventions?
CQ2.	Among adults, what is the effect of dietary intake of sodium and potassium on CVD risk factors and outcomes, when compared with no treatment or with other types of interventions?
CQ3.	Among adults, what is the effect of physical activity on blood pressure and lipids when compared with no treatment or with other types of interventions?

Diet and physical activity interventions of interest to the Workgroup that were not included in this report due to time and resource limitations were: calcium, magnesium, alcohol, cardiorespiratory fitness, single behavioral intervention or multicomponent lifestyle interventions, the addition of lifestyle intervention to pharmacotherapy, and smoking. Additionally, outcomes of interest that were not covered in this evidence review were the

[2] Those ≥18 years and <80 years.

following risk factors: diabetes- and obesity-related measurements, incident diabetes, metabolic syndrome, high-sensitivity C-reactive protein (hs-CRP), and other inflammatory markers. The Workgroup was interested in reviewing the evidence for CVD outcomes in all of the critical questions; however, the evidence for mortality and CVD outcomes was only reviewed in CQ2.

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

- The rationale for its selection is provided and methods are described.
- The body of evidence is summarized, and evidence statements are presented which include a rating for quality. A rationale also supports each evidence statement.
- Recommendations and recommendation strength are provided, accompanied by a summary of how the recommendation derives from the evidence and a discussion of issues taken into consideration by the Workgroup in formulating the recommendation.

A detailed description of methods is provided in the Appendix. The Appendix presents documentation for search strategies and results from the search of the published literature.

The evidence statements and recommendations are presented by CQ and grouped by topic:

CQ1 presents evidence on dietary patterns and macronutrients and their effect on BP and lipids. The dietary recommendations for LDL-C lowering are described at the end of CQ1. CQ2 presents the evidence on the effect of dietary sodium and potassium intake on BP and CVD outcomes. The dietary recommendations for BP lowering are located at the end of CQ2. Finally, CQ3 presents evidence on the effect of physical activity on lipids and BP and physical activity recommendations for BP and lipid lowering. The physical activity recommendations for BP and lipid lowering are located at the end of CQ3.

5. CQ1—Dietary Patterns and Macronutrients: Blood Pressure and Lipids

CQ1:
Among adults, what is the effect of dietary patterns and/or macronutrient composition on CVD risk factors, when compared with no treatment or with other types of interventions?

A. Introduction/Rationale

The importance of nutrition in modifying the risk of cardiovascular disease (CVD) has been repeatedly emphasized.(5-9) Historically, the role of dietary components has been the predominant focus; however, foods are typically consumed in combinations rather than individually. Over the last few years, increasing attention has been given to dietary patterns and their relationship to health outcomes, including CVD.(10-18)

In intervention studies, specific dietary patterns of defined macronutrient composition are identified based upon expert evidence and *a priori* hypotheses (such as the DASH or Mediterranean-style dietary patterns) and then evaluated in RCTs. In observational studies, associations between intake and risk factors are assessed. Due to resource limitations, CVD morbidity and mortality outcomes were not included in the evidence review of this question. The charge of the Workgroup was to inform the treatment of lipids and BP; therefore, those risk factors were the outcomes of focus.

B. Selection of Inclusion/Exclusion (I/E) Criteria

Workgroup members developed eligibility criteria, based on a Population, Intervention, Comparator, Outcomes, Timing, and Setting (PICOTS) approach for screening potential studies for inclusion in this evidence review. Table 1 presents the details of the PICOTS approach for CQ1.

CQ1 examined studies that assessed either the impact on or the association between dietary patterns or changes in macronutrient composition with regard to CVD risk factors (plasma LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), and triglycerides, and on systolic blood pressure and diastolic blood pressure). Studies were included that assessed effects after a minimum period of 1 month of exposure in any geographic location and clinical or research settings. Studies that were evaluated included adults (≥18 years) with or without established CVD, with or without CVD risk factors, with or without tobacco use, and who were of normal weight, overweight, or obese. Excluded were studies using dietary supplements, non-oral routes of nutrient delivery, and where the primary outcome of the nutritional intervention was weight change or when the weight change was >3 percent (so that the effects would be independent of weight change).

Dietary patterns included in the search terms are listed in Table 1. Studies examined by the Workgroup assessed macronutrients (types and amount) and included the effects of saturated fatty acids (SFAs), polyunsaturated fatty acids (PUFAs), monounsaturated fatty acids (MUFAs), *trans* fatty acids, dietary cholesterol, and the effects of the glycemic index (GI).

Table 1. PICOTS (Population, Intervention, Comparator, Outcomes, Timing, and Setting) for CQ1

PICOTS Category	Inclusion/Exclusion (I/E) Criteria
Population	Adults, ≥18 years of age

Intervention (RCTs, meta-analyses, observational studies)	1. Dietary pattern interventions or different dietary patterns Studies that identify dietary pattern interventions prospectively or retrospectively defined as (these categories are not exhaustive): • Isocaloric diets • DASH (Dietary Approaches to Stop Hypertension) • Optimal Macronutrient Intake Strategies Against Heart Disease (OMNI) • Mediterranean Diets (defined broadly) • Therapeutic Lifestyle Changes (TLC) • Vegetarian • Vegan • Ornish diet • Pritikin diet • American Diabetes Association (ADA) Diet for patients with diabetes or metabolic syndrome • Low-fat • High-protein • High-carbohydrate (High-CHO) • Low-carbohydrate (Low-CHO) • High-fiber • Low-glycemic index • Glycemic load • Atkins • Portfolio • Ketogenic • National Cholesterol Education Program (NCEP) Diet • American Heart Association (AHA) diet • Step I diet and Step 2 diet • Meal replacement • Seventh Day Adventist Diet • Raw food diet 2. Macronutrient composition interventions Studies that identify controlled diets with the isocaloric substitution of a macronutrient (types and amount) and compare their effect on reducing plasma lipids: • Dietary fats: The effects of saturated fatty acids, unsaturated fatty acids, omega–6 polyunsaturated fatty acids, omega–3 polyunsaturated fatty acids, monounsaturated fatty acids, *trans* fatty acids, alpha-linolenic acid, and dietary cholesterol.

Table 1. PICOTS (Population, Intervention, Comparator, Outcomes, Timing, and Setting) for CQ1 (continued)

PICOTS Category	Inclusion/Exclusion (I/E) Criteria

Comparator	• There may be no predetermined comparison group for observational studies • Placebo • Usual care • No treatment • Other dietary pattern/macronutrient interventions • Drugs • Nondietary lifestyle interventions (e.g., physical activity or smoking)
Outcomes	• Risk factors and other outcomes • Cholesterol/lipid-related measurements: LDL-C, HDL-C, triglycerides, non-HDL-C, ApoB, Lp (a), particle number (LDL-P), Apo A–1, % at lipid goal • Blood pressure-related measurements: systolic blood pressure, diastolic blood pressure, or hypertensive/nonhypertensive, % at blood pressure goal • Incident hypertension
Timing	Intervention/exposure time period: Risk factors and other outcomes ≥4 weeks (of treatment in RCTs and of exposure in observational studies) Followup time period: Risk factors and other outcomes ≥4 weeks
Setting	• Any geographic location • Any clinical or research setting

C. Literature Search Yield

i. Dietary Pattern Evidence

In all, 17 studies (28 articles) satisfied the final inclusion criteria and were rated good or fair quality.(19-46)

The Dietary Pattern Summary Tables (tables B–1 through B–8) present summary data on the included studies organized by dietary pattern/macronutrient composition or subpopulations of interest, defined by age, sex, race, or comorbid condition. Some studies appear in more than one summary table because they address more than one corresponding macronutrient composition or dietary pattern comparison.

D. CQ1 Evidence Statements

i. Dietary Patterns

a. Mediterranean-style dietary pattern

Three RCTs conducted in free-living populations and one prospective cohort study that met criteria for inclusion on strategies for CVD risk factor reduction focused on the Mediterranean-style dietary (MED) pattern.(23,24,35,37) Summary Table B–1 summarizes the design, characteristics, and results of these studies.

Mediterranean-style dietary pattern description: There is no uniform definition of the Mediterranean-style dietary pattern (MED) diet in the randomized trials and cohort studies examined. The most common features in

these studies were diets that were: higher in fruits (particularly fresh), vegetables (emphasizing root and green varieties), whole grains (cereals, breads, rice, or pasta), and fatty fish (rich in omega–3 fatty acids); lower in red meat (and emphasizing lean meats); substituted lower-fat or fat-free dairy products for higher-fat dairy foods; and used oils (olive or canola), nuts (walnuts, almonds, or hazelnuts) or margarines blended with rapeseed or flaxseed oils in lieu of butter and other fats. The MED dietary patterns examined tended to be moderate in total fat (32–35 percent of total calories), relatively low in saturated fat (9–10 percent of total calories), high in fiber (27–37g/day), and high in polyunsaturated fatty acids (PUFA), particularly omega–3s.

Blood pressure

ES1. Counseling to eat a Mediterranean-style dietary pattern, as compared with minimal advice to consume a low-fat dietary pattern, in free-living middle-aged or older adults (with type 2 diabetes or at least 3 CVD risk factors), reduced BP by 6–7/2–3 mm Hg. In an observational study of healthy younger adults, adherence to a Mediterranean-style dietary pattern was associated with lower blood pressure (2–3/1–2 mmHg).

Strength of evidence: low

Lipids

ES2. Counseling to eat a Mediterranean-style dietary pattern compared with minimal or no dietary advice, in free-living middle aged or older adults (with or without CVD or at high risk for CVD) resulted in no consistent effect on plasma LDL-C, HDL-C, and triglycerides, in part due to substantial differences and limitations in the studies.

Strength of evidence: low

Rationale for ES1 and ES2: Four studies examined a MED dietary pattern in relation to BP and lipid outcomes under weight-stable conditions. Although none were randomized feeding studies in which exact nutrient intake could be determined, these three behavioral intervention trials and one observational study, all in free-living populations, provide some evidence of the effects of MED on BP and lipids, although as noted above, the strength of this evidence was low. One large, good-quality RCT with 762 high-risk free-living adults in Spain compared counseling on one of two MED diets (differing on the provision of olive oil or tree nuts) with a low-fat diet on 3-month changes in BP and lipids.(35) A fair-quality prospective cohort study(37) in 9,408 Spanish adults evaluated adherence to a MED diet in relationship to BP outcomes at 6 years. Two other fair-quality trials(23,24) examined the MED diet in relationship to lipid outcomes. One was a crossover trial that was conducted with 120 male Finnish workers(23) who had previously untreated hypercholesterolemia; it examined the 3-month impact of counseling on a MED diet (in combination with simvastatin or placebo) in comparison with maintenance of habitual eating behavior. The other(24) was carried out with 101 German patients who had received treatment for coronary artery disease (CAD); it compared an intensive outpatient MED dietary and lifestyle intervention with provision of written information only (basic MED diet principles and stress management) on 12-month lipid level changes.

The first of the four studies providing evidence for ES1 and ES2 was a 3-month RCT called PREDIMED.(35) It compared two energy-balanced MED diets with a control group (minimal advice to reduce all types of fat). The MED diets were generally comparable in composition, but differed in the primary fat sources of either virgin olive oil or mixed nuts (walnuts, hazelnuts, almonds). Participants were 762 Spanish men (55–80 years old) and women (60–80 years old) with either type 2 diabetes or three or more CHD risk factors. Those on the MED pattern received weekly supplies of either virgin olive oil or mixed nuts and intensive ongoing dietary counseling; control group participants received minimal instruction and written information. Physical activity was consistent across groups. At 3 months under weight-stable conditions, systolic and diastolic BP fell by 6–7

mmHg and 2–3 mmHg in the olive oil and tree nut MED groups, respectively, compared with the control group. HDL-C differed (+3 and +2 mg/dL, respectively) in the olive oil and tree nut MED groups compared with control. The LDL-C levels did not differ among groups, and TG levels differed (–13 mg/dL, $p<0.022$) between the tree nut MED group and the control group only.

The second source of evidence was a prospective cohort study(37) in Spain of 9,408 professional adult men and women aged 20–90 at a mean of 4 years of followup, in which better compliance with the MED pattern (based on scores derived from validated, self-administered food frequency questionnaires) was associated with lower systolic/diastolic BP levels (–2 to –3 /–1 to –2 mmHg; for moderate and high Mediterranean dietary pattern score groups compared to the low score referent group). Effects on plasma lipids were not reported.

The third source was another RCT,(23) in which 120 free-living weight-stable male industrial plant and government workers, aged 35–64, with previously *untreated* hypercholesterolemia (total cholesterol $\geq$232 mg/dL fasting) (TG <266 mg/dL), body mass index (BMI) (<32 kg/m^2), were randomized and crossed-over on a 12-week modified MED pattern versus no dietary change (i.e., subjects maintain their habitual intakes) with either simvastatin or placebo. The intervention encouraged reduced saturated fat intake (10 percent of energy or less), *trans* fats, and cholesterol (no more than 250 mg), and was enriched in omega–3 fatty acids from plants (alpha-linolenic acid) and marine origin, fruits, vegetables, and soluble fiber. It also encouraged leaner meats, low-fat cheese, fat-free milk, fat-free sour milk, and low-fat yogurt. Participants were supplied with fish; rapeseed margarine and oils (to replace butter and butter-vegetable oil mixtures or sunflower margarine); oat bran and frozen berries. Dietary adherence achieved target levels. Compared to maintenance of habitual dietary patterns (which tended to be higher in total and saturated fat), a 12-week MED dietary intervention lowered LDL-C (–19mg/dL (10.8 percent), $p<0.001$) and HDL-C (–2 mg/dL (4.9 percent), $p<0.01$) but there were no differences in triglyceride level compared to no dietary change, independent of simvastatin. Effects on BP were not reported.

The final source of evidence for ES1 and ES2 was a study(24) in which 105 free-living German patients with treated CAD [79$^+$% on statins] and BMI below 33 kg/m^2 were randomized to either: (1) written advice on an MED diet and stress management, or (2) a comprehensive and intensive diet and stress management lifestyle intervention. Physical activity was encouraged but not prescribed. The intensive intervention group achieved a MED dietary pattern that was higher in fruits and low-fat dairy products, whole grain breads and pastas, fish, walnuts, and margarine; and lower in meat, sausage, and butter. At 12 months, MED pattern compliance was generally good, but changes in nutrient profiles, albeit improved, were relatively modest compared to controls; weight was stable. There were no differences observed between the MED or control groups in LDL-C, HDL-C, or TG levels in these patients with treated CAD. Effects on BP were not reported.

Table 2. Summary of Results: Supporting Evidence for ES1 and ES2

Blood Pressure Change	
Estruch et al. 2006 (PREDIMED)(35)	SBP: –6–7 mmHg ($p< 0.001$) DBP: –2–3 mmHg ($p=0.048$; $p=0.001$) -diet versus control group
Núñez-Cordoba et al. 2009(37)	SBP: –2 to –3 mmHg; p (trend) = 0.01 DBP: –1 to –2 mmHg; p (trend) = 0.05) -moderate and high Mediterranean dietary pattern score groups compared to the low

	score referent group
Change in Lipid Levels (Intervention vs. Control Group)	
Estruch et al. 2006 (PREDIMED)(35)	HDL-C Levels: +3 mg/dL (Olive Oil MED group) +2 mg/ dL (Tree nut MED group) TG Levels: –13 mg/L (*p*<.022) , Tree nut MED group vs. control only
Jula et al. 2002(23)	LDL-C Level: (–19mg/dl (10.8 percent), *p*<0.001) HDL-C Level: (–2 mg/dl (4.9 percent), *p*<0.01)
Michalsen et al. 2006(24)	No differences in lipid levels observed

b. DASH dietary pattern

Two RCTs (6 citations) evaluating the Dietary Approaches to Stop Hypertension (DASH) pattern met eligibility criteria.(26-31) Summary Table B–2 summarizes the design, characteristics, and results of these studies.

DASH dietary pattern description: The DASH dietary pattern is high in vegetables, fruits, and low-fat dairy products, whole grains, poultry, fish and nuts; and low in sweets, sugar-sweetened beverages, and red meats. The DASH dietary pattern is low in saturated fat, total fat, and cholesterol. It is rich in potassium, magnesium, and calcium, as well as protein and fiber.

Blood pressure

ES3. When all food was supplied to adults with blood pressure 120–159/80–95 mm Hg and both body weight and sodium intake were kept stable, the DASH dietary pattern, compared to a typical American diet of the 1990s, lowered blood pressure by 5–6/3 mm Hg.

Strength of evidence: high

Rationale: The DASH trial tested the hypothesis that the specific dietary pattern described above lowers BP. The DASH study was a multicenter randomized trial with 459 participants with unmedicated Stage 1 hypertension or prehypertension. Participants were assigned at random to the DASH diet, a control diet similar to the usual dietary pattern in the United States in the 1990s, or to a diet high in fruits and vegetables, but otherwise the same as the control diet. There were 151–154 participants per group. The study population was 50 percent women, 60 percent African American, 29 percent hypertensive, with average age 45 years, BMI 28 kg/m^2, and baseline BP 132/85 mmHg.

Participants were provided with complete diets for 8 weeks. Body weight at baseline was maintained throughout the trial by adjusting amounts of food given daily. All three diets contained the same amount of sodium, 3,000 mg per day. The DASH diet and its effects did not involve weight loss or sodium reduction. A DASH dietary pattern was provided, including both foods and beverages, for 8 weeks. The daily amounts (standard portions) of foods in the DASH diet compared to the control diet are shown in Table 3.

The DASH diet lowered BP in the entire study population by an average of 5.5/3.0 mmHg, with significant effects in both men and women, African Americans, and non-Hispanic whites, and in those with and without hypertension. The effects on BP of the fruits and vegetables diet were approximately half of the effects of the DASH diet. The effects of the diets on BP were evident after 2 weeks and persisted as long as the diet was provided. A subsequent trial, DASH-Sodium, confirmed the BP-lowering effect of the DASH diet at various levels of dietary sodium intake (see description in CQ2).

Table 3. DASH Diet Composition vs. Control

Number of Servings/Day		
	DASH Diet*	Control
Fruits	5.2	1.6
Vegetables	4.4	2.0
Low-Fat Dairy	2.0	0.1
Regular-Fat Dairy	0.7	0.4
Nuts and Beans	0.7	0.0
Red Meat	0.5	1.5
Fish	0.5	0.2
Snacks and Sweets	0.7	4.1
Macronutrient Content (Percent of Energy) Comparison		
Total Fat (%)	26	36**
Saturated Fat (%)	7	14**
Monounsaturated Fatty Acids (MUFAs) (%)	10	12**
Polyunsaturated Fatty Acids (PUFAs) (%)	7	6**
Carbohydrate (%)	57	51**
Protein (%)	18	14**

* A DASH dietary pattern was provided, as food or beverage, for 8 weeks to adults
**The macronutrient content of the control diet was based on the typical American diet of the early 1990s

Lipids

ES4. When food was supplied to adults with a total cholesterol level <260 mg/dL, LDL-C <160 mg/dL and body weight was kept stable, the DASH dietary pattern, compared with a typical American diet of the 1990s, lowered LDL-C by 11 mg/dL, lowered HDL-C by 4 mg/dL, and had no effect on triglycerides.

Strength of evidence: high

Rationale: The rationale and study design of the DASH trial was described in the ES3 rationale. Blood lipids were measured at baseline and at the end of the 8-week dietary intervention in 436 participants (all randomized participants who provided fasting blood both at baseline and at end-of-intervention [95 percent of total]), with 145–146 participants per diet group. For eligibility, total cholesterol level was <260 mg/dL, and LDL-C was <160 mg/dL. Baseline LDL-C was 119 mg/dL, HDL-C was 49 mg/dL, and TG was 93 mg/dL. Cholesterol-lowering medication was taken by <1 percent. When compared to a typical American diet of the 1990s, the DASH dietary pattern lowered LDL-C by 11 mg/dL, but also lowered HDL-C by 4 mg/dL. It had no effect on TG. The fruits and vegetables diet did not affect blood lipids, reflecting the similar content of saturated and unsaturated fat and cholesterol compared to the control diet. The reduction in LDL-C by DASH is consistent with its lower content of saturated fat and cholesterol, and the reduction in HDL-C is consistent with its higher content of carbohydrate.

These DASH trial effects were confirmed and extended to three dietary sodium levels in the DASH-Sodium trial, described in CQ2. In that trial, the DASH diet lowered LDL-C by 13 mg/dL, lowered HDL-C by 4 mg/dL, and did not affect TG.(30) The OmniHeart trial, described below, tested macronutrient variations of the DASH dietary pattern. When carbohydrates were replaced with MUFAs, there were similar effects (as the original DASH) on BP and LDL-C, but improved HDL-C. HDL-C was increased with the MUFA substitution.

c. DASH Dietary pattern subpopulations

Two studies (8 citations) evaluating the dietary patterns in subgroups met eligibility criteria and were rated good or fair.(26-28,41-45) Tables B–3 (sex), B–4 (race ethnicity), and B–5 (hypertension status) and B–6 (age) summarize the design, characteristics, and results of these studies on subgroups.

Subpopulations and blood pressure

ES5. When all food was supplied to adults with BP 120–159/80–95 mm Hg and body weight was kept stable, the DASH dietary pattern, compared with the typical American diet of the 1990s, lowered BP in women and men; African-American and non-African American adults; older and younger adults; and hypertensive and nonhypertensive adults.

Strength of evidence: high

Rationale—Women and men: The rationale and study design of the DASH trial and details of the diets tested are described in the DASH Dietary Pattern background. The DASH dietary pattern, as compared to a typical American diet of the 1990s, lowered BP by a similar amount in men (5/3 mmHg) and women (6/3 mmHg).(26,28,41) A subsequent trial, DASH-Sodium, confirmed the similar BP-lowering effect among men and women. At the higher sodium intake level (mean urinary sodium 3,300 mg per day), the DASH dietary pattern, as compared with a typical American diet of the 1990s, lowered BP by 5/3 mmHg in men and 7/3 mmHg in women, with no difference by sex.(45)

Rationale—African American and non-African American: In the DASH trial, the DASH dietary pattern, as compared to a typical American diet of the 1990s, lowered BP more in African Americans (7/4 mmHg)

compared to non-African Americans (3/2 mmHg).(26-28,41) In contrast, the subsequent DASH-Sodium trial found a similar BP-lowering effect by race-ethnicity. At the higher sodium intake level (mean urinary sodium of 3,300 mg per day), the DASH dietary pattern, as compared to a typical American diet of the 1990s, lowered BP by 6/3 mmHg in African Americans and 6/2 mmHg in non-African Americans, with no differences by race.(45) Thus, there is no consistent difference in the BP effect of DASH in African American versus non-African American adults.

Rationale—Older and younger adults: In the DASH trial, the DASH dietary pattern, as compared with a typical American diet of the 1990s, lowered BP 5/4 mmHg and 7/3 mmHg in participants aged $\leq$45 and > 45, respectively.(26,28,41) The subsequent DASH-Sodium trial found BP lowering by age similar to the DASH trial results. At the higher sodium intake level (mean urinary sodium of 3,300 mg per day), the DASH dietary pattern, as compared with a typical American diet of the 1990s, lowered BP by 4/2 mmHg and 7/3 mmHg in adults aged $\leq$45 and > 45, respectively.(45)

Rationale—Hypertensive and non-hypertensive adults: In the DASH trial, the DASH dietary pattern, as compared with a typical American diet of the 1990s, lowered BP more in adults with hypertension (11/6 mmHg) compared with those without hypertension (4/2mmHg).(26,27,41) In contrast, the subsequent DASH-Sodium Trial found a similar BP-lowering effect among adults with and without hypertension. At the higher sodium intake level (mean urinary sodium of 3,300 mg per day), the DASH dietary pattern, as compared to a typical American diet of the 1990s, lowered BP by 7/3 mmHg in adults with hypertension and 5/3 mmHg in adults without hypertension, with no differences by hypertension status.(45) Thus, there is no consistent difference in the BP effect of DASH in hypertensive versus pre-hypertensive adults.

Subpopulations and lipids

ES6. When all food was supplied to adults with a total cholesterol level <260 mg/dL and LDL-C <160 mg/dL and body weight was kept stable, the DASH dietary pattern, as compared to a typical American diet of the 1990s, lowered LDL-C similarly in subgroups: African-American and non–African-American adults and hypertensive and nonhypertensive adults.

Strength of evidence: low

ES7. When all food was supplied to adults with a total cholesterol level <260 mg/dL and LDL-C <160 mg/dL and body weight was kept stable, the DASH dietary pattern, compared with a typical American diet of the 1990s, lowered HDL-C similarly in subgroups: African-American and non–African-American adults; hypertensive and non-hypertensive adults; and men and women.

Strength of evidence: low

Rationale: One secondary analysis of the DASH trial(28) was rated fair and met the inclusion criteria for comparing the effects on lipid levels of a typical American diet of the 1990s with a DASH dietary pattern in hypertensive and non-hypertensive adults, men and women, and African Americans and non-African Americans. Participants had a mean BMI of 28 kg/m^2.

Relative to the typical American diet, the DASH diet resulted in lower mean LDL-C and HDL-C in all participants. However, compared with women, men had greater reductions in LDL-C. Changes in total cholesterol, LDL-C, HDL-C, and TG did not differ significantly by race.

d. DASH variations

One randomized trial(36) met eligibility criteria for DASH eating pattern variations. The design, characteristics, and results of the OmniHeart trial are summarized in the main DASH eating pattern summary table, Summary Table B–2.

DASH variations description: In OmniHeart, two variations of the DASH dietary pattern were compared to DASH: one which replaced 10 percent of total daily energy from carbohydrate with protein; the second which replaced the same amount of carbohydrate with unsaturated fat. These patterns were studied in an adequately powered crossover trial of 164 adults in which the participants were given all of their daily food.

Blood pressure

ES8. In adults with BP of 120–159/80–95 mm Hg, modifying the DASH dietary pattern by replacing 10% of calories from carbohydrates with the same amount of either protein or unsaturated fat (8% monounsaturated and 2% polyunsaturated) lowered systolic BP by 1 mm Hg compared with the DASH dietary pattern. Among adults with BP 140–159/90–95 mm Hg, these replacements lowered systolic BP by 3 mm Hg relative to DASH.

Strength of evidence: moderate

Lipids

ES9. In adults with average baseline LDL-C level of 130 mg/dL, HDL-C level of 50 mg/dL, and triglyceride level of 100 mg/dL, modifying the DASH dietary pattern by replacing 10% of calories from carbohydrates with 10% of calories from protein lowered LDL-C by 3 mg/dL, HDL-C by 1 mg/dL, and triglycerides by 16 mg/dL compared with the DASH dietary pattern. Replacing 10% of calories from carbohydrates with 10% of calories from unsaturated fat (8% monounsaturated and 2% polyunsaturated) lowered LDL-C similarly, increased HDL-C by 1 mg/dL, and lowered triglycerides by 10 mg/dL compared with the DASH dietary pattern.

Strength of evidence: moderate

Rationale: DASH had favorable effects on BP and LDL-C, yet it had neutral or slightly adverse effects on TGs and HDL-C. A randomized trial was performed to determine if partial replacement of carbohydrates with either unsaturated fat or protein can improve the effect of DASH on lipid risk factors while maintaining the BP effect. The OmniHeart trial compared the effects of three diets all composed of the same foods used in DASH, but differing in macronutrient composition. Because the effects of the DASH diet were known from two previous controlled feeding trials, the high-carbohydrate DASH diet was used as the control and compared to the lower-carbohydrate DASH variations: the protein diet and the unsaturated fat diet. The macronutrient composition of the carbohydrate diet was 58 percent/27 percent/15 percent of calories from carbohydrates/fat/protein; the "protein diet" was 48 percent/27 percent/25 percent of calories from carbohydrates/fat/protein; and the "unsaturated fat diet" was 48 percent/37 percent/15 percent of calories from carbohydrates/fat/protein. Saturated fat was 8 percent on all diets; MUFA was 13 percent on the carbohydrate and protein diets, compared to 21 percent on the unsaturated fat diet. Polyunsaturated fat was 8 percent on the carbohydrate and protein diets, compared to 10 percent on the unsaturated fat diet. The carbohydrate diet had more fruit and fruit juices, desserts, and other sweets than the other two diets. Meat and plant sources comprised the additional protein in the protein diet. The sodium content was 2,300 mg in all diets. Weight was maintained by adjusting calorie intake as needed.

The OmniHeart trial design was crossover with randomized sequence of the three diets, each provided for 6 weeks. Study design and feeding were otherwise comparable to the DASH and DASH-Sodium trials. Relative to the DASH dietary pattern, both the protein and unsaturated fat diets lowered systolic BP significantly by an average of 1 mmHg compared to the DASH dietary pattern. Among adults with BP 140–159/90–95 mmHg, both these variations lowered systolic blood pressure by 3 mmHg. Compared to baseline measurements taken when the participants were eating their usual diets, the carbohydrate diet (DASH) lowered BP by 8/4mmHg and the protein and unsaturated fat variations lowered BP by 9/5 mmHg. Blood pressure in hypertensives was lowered by 13/6 and 16/8–9 mmHg, respectively; and in prehypertensives by 7/4 and 8/4 mmHg, respectively.

Replacing 10 percent of daily calories from carbohydrate with 10 percent of calories from protein lowered LDL-C by 3 mg/dL, HDL-C by 1 mg/dL, and triglycerides by 16 mg/dL compared to the DASH dietary pattern. Replacing 10 percent of calories from carbohydrate with 10 percent of calories from unsaturated fat (8 percent MUFA and 2 percent PUFA) lowered LDL-C similarly, increased HDL-C by 1 mg/dL, and lowered triglycerides by 10 mg/dL compared to the DASH dietary pattern. Compared to the baseline period, the controlled diets lowered LDL-C by 12–14 mg/dL and reduced HDL-C by 3 mg/dL (with DASH) and did not reduce HDL-C with the unsaturated fat substitution.

In sum, the OmniHeart trial found that the beneficial effects on BP and LDL-C of the DASH dietary pattern are modestly enhanced by replacing some carbohydrates with either protein or unsaturated fat while maintaining the healthy foods that are hallmarks of the DASH approach. The combined findings from the DASH and OmniHeart studies provide a range of macronutrient intakes and foods that substantially improve BP and LDL-C.

e. Glycemic index/load dietary approaches

Three randomized trials evaluating glycemic index met eligibility criteria and were rated good or fair.(25,34,40) Summary Table B–7 summarizes the design, characteristics, and results of these studies.

ES10. There is insufficient evidence to determine whether low-glycemic diets versus high-glycemic diets affect lipids or BP for adults without diabetes. The evidence for this relationship in adults with diabetes was not reviewed.

Strength of evidence: insufficient

Rationale: Carbohydrate content is an important determinant of glycemic control in people with diabetes. The glycemic index is a system of ranking dietary carbohydrates to indicate the degree to which, in equal amounts, they raise blood glucose. However, the glycemic load defines the glycemic effect of a regular serving size of the food with the amount of carbohydrate in a single serving. Carbohydrate foods that result in a lower postprandial blood glucose tend to be those with higher fiber and more complex carbohydrates such as non-starchy vegetables and legumes. The popularity of low-glycemic diets arose from a concern that the increase in type 2 diabetes in tandem with the rise in obesity was due, at least in part, to an increase in large portions of foods that were low in fiber and high in simple sugars.

No studies of low-glycemic diets as compared to high-glycemic diets in people without diabetes satisfied the inclusion criteria for CQ1. Therefore, the available data are insufficient to recommend a diet based on glycemic index as better or worse for improvement in cardiovascular health for people without diabetes mellitus. Diabetes mellitus-related outcomes were not reviewed at this stage of the evidence review due to limited resources. Therefore, the Workgroup did not review the evidence on glycemic index on the effect of cardiovascular risk factors in people with diabetes mellitus.

ii. Dietary Fat and Cholesterol

Five trials evaluating saturated and *trans* fat and dietary cholesterol (26,29,32,33,38,39) were identified in the search. Summary Table B-8 summarizes the design, characteristics, and results of the studies. In addition a search was conducted for meta-analyses and systematic reviews from 1990 to 2009. Four systematic reviews and meta-analyses met inclusion criteria and were rated good or fair.(19-22)

a. Saturated fat

ES11. When food was supplied to adults in a dietary pattern that achieved a macronutrient composition of 5–6% saturated fat, 26–27% total fat, 15–18% protein, and 55–59% carbohydrate compared with the control diet (14–15% saturated fat, 34–38% total fat, 13–15% protein, and 48–51% carbohydrate) LDL-C was lowered 11–13 mg/dL in two studies, and 11% in another study.

Strength of evidence: high

Three feeding trials (DASH, DASH-Sodium, and DELTA [Dietary Effects on Lipoproteins and Thrombogenic Activity]) with dietary patterns of varying saturated fat levels examined the effect on LDL-C.(26,29,32) The DASH dietary pattern utilized in the DASH and DASH-Sodium trials was previously described. The patterns in the 3 studies were compared to a typical American diet control in participants with baseline LDL-C less than 160 mg/dL or described as "healthy." The achieved saturated fat level in the DASH groups was 6 percent of total calories compared to 14–15 percent of total calories in the controls. LDL-C decreased 11mg/dL (p<0.0001) and 13 mg/dL (p<0.0001) in the DASH and DASH-Sodium trials, respectively. The DELTA trial tested three dietary patterns: Low saturated fat; Step 1; and a control containing 5 percent, 9 percent, and 15 percent of calories from saturated fat, respectively. Compared to the control, the LDL-C of the Step 1 group decreased by 7 percent (p<0.1) and an additional 4 percent (p<.01) in the low saturated fat group totaling an 11 percent reduction. Of note, in the DASH trials, the effect of saturated fat on LDL-C could not be isolated because macronutrients and other nutrients such as dietary cholesterol were not held constant. In the DELTA trial, the dietary cholesterol and protein were held constant but other nutrients, including total fat and carbohydrates, differed in the comparison groups as shown in Table 4. The LDL-C lowering is consistent in the DASH trials with the lower saturated fat dietary pattern resulting in lower LDL-C. In DELTA, the greater reduction in saturated fat led to greater LDL-C lowering.

Table 4. Macronutrient Composition and Lipid Effects in DASH, DASH-Sodium, and DELTA-1

	Percentage of Calories From Nutrients						
	Total Fat	SFA	CHO	Protein	LDL Effect Compared to Control	Other Lipid Effects Compared to Control	Participants Baseline LDL
DASH*	27	6	55	18	–11mg/dL	HDL-C: –4 mg/dl	<160 mg/dL
Control	36	14	51	14			
DASH Na†	27	6	58	15	–13 mg/dL	HDL-C: –4 mg/dl TGs: +5 mg/dl	<160 mg/dL
Control	38	15	49	13			

Table 4. Macronutrient Composition and Lipid Effects in DASH, DASH-Sodium, and DELTA-1 (continued)

	Percentage of Calories From Nutrients						
	Total Fat	SFA	CHO	Protein	LDL Effect Compared to Control	Other Lipid Effects Compared to Control	Participants Baseline LDL
DELTA‡ Low SF	26	5	59	15	–11%	HDL-C: –11% TGs: No change	"healthy"
Step 1	29	9	55	15	–7%	HDL-C: –7% TGs: +9%	
Control	34	15	48	15			

* DASH: Dietary Approaches to Stop Hypertension
† DASH-Sodium: Dietary Approaches to Stop Hypertension-Sodium
‡ DELTA: Dietary Effects on Lipoproteins and Thrombogenic Activity

ES12. In controlled feeding trials among adults, for every 1% of energy from saturated fatty acid (SFA) that is replaced by 1% of energy from carbohydrate, MUFA, or PUFA:

- LDL-C is lowered by an estimated 1.2, 1.3, and 1.8 mg/dL, respectively.
- HDL-C is lowered by an estimated 0.4, 1.2, and 0.2 mg/dL, respectively.

For every 1% of energy from SFA that is replaced by 1% of energy from:

- Carbohydrate and MUFA, TG are raised by an estimated 1.9 and 0.2 mg/dL, respectively.
- PUFA, TG are lowered by an estimated 0.4 mg/dL.

Strength of evidence: moderate

ES13. In controlled feeding trials among adults, for every 1% of energy from carbohydrate that is replaced by 1% of energy from:

- MUFA, LDL-C is lowered by 0.3 mg/dL, HDL-C is raised by 0.3 mg/dL, and TG are lowered by 1.7 mg/dL.
- PUFA, LDL-C is lowered by 0.7 mg/dL, HDL-C is raised by 0.2 mg/dL, and TG are lowered by 2.3 mg/dL.

Strength of evidence: moderate

Rationale: When restricting saturated fat, it is helpful to understand the effects of replacing it with other macronutrients. We used two meta-analyses from the same authors published 11 years apart in which they used the same inclusion/exclusion criteria and generated predictive equations to estimate changes in plasma lipids when substituting dietary fat types with carbohydrates or other fat types. The data were insufficient to determine whether type of dietary carbohydrate (refined/unrefined) or amount of dietary fiber could have confounded the study outcomes. The first meta-analysis included 27 RCTs (682 volunteers) and covered the period between January 1970 and December 1991.(19) The updated meta-analysis included 60 trials (1,672 participants) and covered the period between January 1970 and December 1998.(20) In both meta-analyses, inclusion criteria were controlled intervention studies in which the sole variable was macronutrient content; dietary cholesterol was held constant. Eligible study designs included parallel, crossover, or Latin-square under

metabolic ward conditions, with a feeding period >13 days. All participants were aged 21–72 and did not have disturbances of lipid metabolism or diabetes. Studies were excluded if their focus was on omega–3 fatty acids or medium-chain fatty acids. A third review was identified in the search that addressed dietary advice to reduce total fat intake or change PUFA to SFA ratio, but was not used to develop this evidence statement given that it was not possible to isolate the effect of changing SFA intake.(22)

The authors found that replacing 1 percent of SFA with an equal amount of carbohydrate, MUFA, or PUFA led to comparable LDL-C reductions: 1.2, 1.3, and 1.8 mg/dL, respectively. Replacing 1 percent of SFA with carbohydrate, MUFA, or PUFA lowered HDL-C by 0.4, 1.2, and 0.2 mg/dL, respectively. Triglycerides were raised by an estimated 1.9 and 0.2 mg/dL when replacing SFA with carbohydrate or MUFA, respectively, but lowered when SFA was replaced by PUFA. Replacing 1 percent of carbohydrate by an equal amount of MUFA or PUFA raised LDL-C by 0.3 and 0.7 mg/dL, raised HDL-C by 0.3 and 0.2 mg/dL, and lowered TG by 1.7 and 2.3 mg/dL, respectively. Although there were 30 studies in this methodologically strong meta-analysis, this statement was rated moderate because of the relatively small number of participants (*n*=1,672).

b. Trans fat

ES14. In controlled feeding trials among adults, for every 1% of energy from *trans* monounsaturated fatty acids replaced with 1% of energy from:

- MUFA or PUFA, LDL-C is lowered by 1.5 mg/dL and 2.0 mg/dL, respectively.
- SFA, MUFA, or PUFA, HDL-C is increased by an estimated 0.5, 0.4 and 0.5 mg/dL, respectively.
- MUFA or PUFA, TG is decreased by an estimated 1.2 and 1.3 mg/dL.

Strength of evidence: moderate

ES15. In controlled feeding trials among adults, the replacement of 1% of energy as *trans* monounsaturated fatty acids with carbohydrate decreased LDL-C levels by 1.5 mg/dL and had no effect on HDL-C cholesterol and triglyceride levels.

Strength of evidence: moderate

Rationale: During the past two decades, increasing evidence has accumulated that the intake of *trans* fat causes unfavorable modifications of plasma lipids, lipoproteins, and CVD risk. The *trans* fat evidence statements were based on two meta-analyses. The first meta-analysis(21) included 13 trials published through January 2008. Inclusion criteria were controlled dietary trials reporting data on plasma lipid and lipoprotein response at the end of each dietary phase, with each phase lasting at least 2 weeks. In this meta-analysis, replacement of 1 percent of energy as *trans* fatty acids with 1 percent of energy from MUFA lowered LDL-C levels by 1.5 mg/dL ($p<0.05$), increased HDL-C levels by 0.4 ($p<0.05$), and lowered TG levels by 1.2 mg/dL ($p<0.05$). Replacement of 1 percent of energy from *trans* fatty acids with 1 percent energy from PUFA lowered LDL-C levels by 2.0 mg/dL ($p<0.05$), increased HDL-C levels by 0.5 mg/dL ($p<0.05$), and lowered TG levels by 1.3 mg/dL ($p<0.05$).Replacement of 1 percent of energy from *trans* fatty acids with 1 percent energy from SFA increased HDL cholesterol levels by 0.5mg/dL ($p<0.05$).

The second meta-analysis included eight studies(20) and covered the period between January 1970 and December 1998. Inclusion criteria were controlled intervention studies in which the sole variable was the dietary fatty acid prolife and dietary cholesterol was held constant. Study designs included were parallel, crossover, or Latin-square in which the feeding period was at least 13 days. All subjects were aged 21–72 and had no lipid metabolism disturbances or diabetes mellitus. Studies were excluded if their focus was on dietary omega–3 fatty acids or medium-chain fatty acids. In this meta-analysis, replacing 1 percent of energy as *trans*

MUFA with carbohydrate decreased LDL-C levels by an estimated 1.5 mg/dL (p=0.02), with no effect on HDL-C or TG levels.

c. Dietary cholesterol

ES16. There is insufficient evidence to determine whether lowering dietary cholesterol reduces LDL-C.

Strength of evidence: insufficient

Rationale: Dietary cholesterol has been a controversial topic for years. Reasons include the variable effect of increases in dietary cholesterol on LDL-C levels, and the inconsistent relationship between dietary cholesterol intake and CVD. There were no systematic reviews or meta-analyses that met inclusion criteria and were rated good or fair. In the absence of other evidence, two poorly rated meta-analyses were reviewed: Hopkins 1992;(47) and Clarke et al. 1997.(48) In both reports, most of the published studies that were included examined the independent effect of dietary cholesterol on plasma total cholesterol concentrations, not lipoprotein cholesterol or TG. In 6 of these studies, LDL-C data were reported in 128 participants. The dietary cholesterol ranged from 130–200 mg daily on the low end to 700–1,700 mg daily on the high end over intervals that ranged from 10 days to 8 weeks. Because these studies predate our search and the impact of more moderate intakes of dietary cholesterol on lipoprotein cholesterol over a broad range of individuals with normocholesterolemia and hypercholesterolemia has not been addressed adequately, the Work group concluded that there are insufficient data to make a statement.

E. Diet Recommendations for LDL-C Lowering

The following diet recommendations for LDL-C-lowering are based on the evidence statements from CQ1 on dietary patterns and fatty acids. Diet recommendations for BP lowering are based on CQ1 and CQ2 and located after the CQ2 evidence statements. A listing of all of the Lifestyle Workgroup diet and physical activity recommendations are in the Lifestyle guideline. The physical activity and lipids evidence review and recommendations are located in CQ3.

Advise adults who would benefit from LDL-C lowering:[3]

1. Consume a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils and nuts; and limits intake of sweets, sugar- sweetened beverages and red meats.
   - Adapt this dietary pattern to appropriate calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical conditions (including diabetes).
   - Achieve this pattern by following plans such as the DASH dietary pattern, the USDA Food Pattern, or the American Heart Association Diet.

Strength: A (strong)

Rationale: This recommendation is based largely on studies of the DASH dietary pattern (DASH and DASH-Sodium), which provided the highest quality evidence for a dietary pattern causing improvements in BP and lipid profiles(see ES3-ES9). The LDL-C lowering effect has been demonstrated in men and women, African Americans and non-African Americans, and in adults of all ages (ES6). The evidence suggests that the effects of the recommended dietary pattern persist as long as the pattern is consumed.

[3] Refer to 2013 Blood Cholesterol Guideline for guidance on who would benefit from LDL-C lowering.

The caloric (energy) intake should be appropriate for the individual – e.g., restricted for those attempting weight loss. Patients also should be encouraged to adapt the recommended dietary pattern to their personal and cultural preferences. Materials are available to assist patients in achieving the recommended dietary pattern at different calorie levels (see below). The 2010 U.S. Department of Health and Human Services Dietary Guidelines for American recommend the USDA food pattern and the DASH eating plan (49). Overall, the recommended dietary pattern is consistent with the American Heart Association diet(50) and the USDA Food Pattern. (49) The USDA Food Pattern offers lacto-ovo vegetarian and vegan adaptations. Therefore, this recommendation is consistent with other national guidelines. Clinicians should be familiar with the recommendations, advise their patients to adopt them, and provide easy access to information (see below). Dietary planning and nutritional counseling is often facilitated by referral to a nutrition professional.

Resources:

DASH Eating Plan:
- Your Guide to Lowering Your Blood Pressure With DASH
- Your Guide to Lowering Your Blood Pressure With DASH Brochure

AHA Diet and Lifestyle Recommendations:
- AHA Diet and Lifestyle Recommendations Article
- AHA Diet and Lifestyle Recommendations 2006 Scientific Statement (9)

Dietary Guidelines for Americans
- 2010 Dietary Guidelines for Americans (49)
- 2011 Dietary Guidelines for Americans Brochure
- USDA Food Patterns

2. Aim for a dietary pattern that achieves 5–6% of calories from saturated fat.

Strength: A (strong)

Rationale: As described in ES11 in the saturated fat section, there is strong evidence that the reductions in LDL-C were achieved when consuming dietary patterns in which saturated fat intake was reduced from 14 to 15 percent of calories to 5 to 6 percent. As previously noted, these studies did not isolate the effect of saturated fat on LDL-C lowering. Intakes of saturated fat have decreased in the United States over the last few decades, currently estimated at 11 percent of energy in the U.S. population 2 years of age and older.(51) However, this level of saturated fat is higher than that tested in the DASH and DELTA trials (5-6 percent) and is not consistent with consuming a diet rich in vegetables, fruits, low-fat dairy products, whole grains, poultry, fish, legumes and nuts, and vegetable oils; and limited in sweets, sugar-sweetened beverages, and red meat. Given the current average intake of saturated fat at 11 percent, it would be beneficial for those who would benefit from LDL-C lowering to decrease saturated fat intake to 5–6 percent of calories.

3. Reduce percentage of calories from saturated fat.

Strength: A (strong)

Rationale: Reducing saturated fat intake lowers both LDL-C and HDL-C. Since the absolute effect tends to be greater for LDL-C than HDL-C, reducing saturated fat intake has a beneficial effect on the lipid profile. Given that reducing SFA intake lowers LDL-C regardless of whether the saturated fat is replaced by carbohydrate, MUFAs, or PUFAs, we do not specify which of these three macronutrients should be substituted in place of saturated fat. However, favorable effects on lipid profiles are greater when saturated fat is replaced by PUFAs,

followed by MUFAs, and then carbohydrate. It is important to note that there are various types and degrees of refinement of carbohydrates. Substitution of saturated fat with whole grains is preferable to refined carbohydrates. For American adults who eat more SFA than the current average, some reduction is warranted, and adhering to a "heart healthy" dietary pattern from recommendation #1 will likely result in a reduction of saturated fat.

4. Reduce percentage of calories from *trans* fat.

Strength: A (strong)

Rationale: Reducing intake of *trans* fatty acids lowers LDL-C, with little or no effect on HDL-C or TG levels. The direction of the relationship between *trans* fatty acids and LDL-C is consistent, regardless of whether the *trans* fatty acids replace carbohydrate, MUFAs, or PUFAs. Using 2003–2006 National Health and Nutrition Examination Survey (NHANES) data, intake of *trans* fat from partially hydrogenated oils was estimated at a mean of 1.3 to 1.6 g per day among the U.S. population ages 2 and older.(52) Although the intake level appears low, certain subgroups within the U.S. population may still be consuming relatively high levels of *trans* fatty acids. For this reason, we recommend that emphasis continue to be placed on the reduction of *trans* fat in the diet. Even if intake of *trans* fat from partially hydrogenated oils decreases, naturally occurring *trans* fatty acids in the form of ruminant fat from meat and dairy products may still be present in small amounts in the U.S. diet. Adhering to the recommendation to reduce dietary sources of saturated fat (meat and dairy fat) will result in additional reductions in *trans* fat intake.

6. CQ2—Sodium and Potassium: Blood Pressure and CVD outcomes

CQ2:

Among adults, what is the effect of dietary intake of sodium and potassium on CVD risk factors and outcomes, when compared with no treatment or with other types of interventions?

A. Introduction and Rationale

Vitamins and minerals typically are consumed in foods. However, it is sometimes possible to isolate the effect of individual minerals to determine the effects on health outcomes. Therefore, the Workgroup decided that a systematic review was warranted to determine the individual effects of the minerals sodium and potassium, which have been associated with CVD risk factors and outcomes. Other minerals, such as calcium and magnesium, also were considered, but were not included in the systematic review because their consumption is limited to relatively few specific foods or food groups (e.g., calcium and dairy products), and it was unlikely that a recommendation to increase or decrease consumption of the mineral rather than the food could be implemented.

In contrast, sodium was reviewed as a single nutrient because little sodium is found naturally in food, and it is primarily added to foods in preparation, preservation, and/or at the time of consumption. Therefore, it

theoretically is possible to alter sodium intake without altering intake of specific foods or overall dietary pattern. In addition, potassium was reviewed as a single nutrient because it has been hypothesized that dietary potassium intake may lower BP independent of other nutrients or foods. In addition, the effect of sodium on BP may be modulated by concomitant potassium intake.

Most of the clinical trial evidence pertains to effects of minerals on risk factors (i.e., BP and plasma lipids) that are relevant, intermediate outcomes for CVD. In addition, data primarily from observational studies provide evidence on the effects of dietary sodium and potassium on outcomes that are CVD events.

B. Selection of Inclusion/Exclusion (I/E) Criteria

Workgroup members developed eligibility criteria, based on a PICOTS approach, to use for screening potential studies for inclusion in the evidence review. Table 5 presents the details of the PICOTS approach for CQ2.

CQ2 was established to examine studies that assessed the impact of sodium and potassium on BP and cardiovascular morbidity and mortality. The studies included adults with or without established CVD, with or without CVD risk factors, with or without tobacco use, and who were of normal weight, overweight, or obese. In addition to the criteria in Table 5, an intervention sample size must be at least 50 for biomarker and risk factor studies and 500 for cardiovascular morbidity and mortality. Because there is a separate Obesity Guideline Expert Panel reviewing evidence on the effect of weight loss on CVD risk factors and outcomes, we excluded studies in which weight change was more than 3 percent.

Table 5. PICOTS (Population, Intervention, Comparator, Outcomes, Timing, and Setting) for CQ2

PICOTS Category	Inclusion/Exclusion (I/E) Criteria
Population	Adults, ≥18 years of age
Intervention (RCTs, observational studies)	• Randomized trials—intervention is alteration of nutrient intake • Observational studies—the exposure is two different levels of nutrient intake (for hard outcomes only) • Trials that identify well-defined diets with the substitution of a mineral (types and amount) The Workgroup considered the following list of dietary or oral minerals: • Sodium, sodium chloride (salt) • Potassium • Sodium/potassium ratio
Comparator	• There may be no predetermined comparison group for observational studies • Placebo • Usual care • No treatment • Other dietary interventions • Drugs • Nondietary lifestyle interventions (e.g., physical activity or smoking cessation)

PICOTS Category	Inclusion/Exclusion (I/E) Criteria
Population	Adults, ≥18 years of age
Outcomes	1. Hard Health Outcomes 2. CVD-related morbidity or mortality • Acute coronary syndrome: unstable angina, myocardial infarction (MI) • Fatal or nonfatal stroke • Fatal or nonfatal MI (ST-segment elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI). • Coronary revascularization procedures: angioplasty, coronary stent placement, coronary artery bypass • Other atherosclerotic revascularization procedures (carotid endarterectomy) • Fatal heart failure or hospitalization for heart failure • Hospitalization for any CHD/CVD cause 3. Risk Factors and Other Outcomes • Plasma lipid-related measurements: LDL-C, HDL-C, triglycerides, non-HDL-C, ApoB, Lp (a), particle number (LDL-P), Apo A–1, percent at lipid goal • BP-related measurements: systolic blood pressure, diastolic blood pressure, hypertensive/nonhypertensive, or percent at blood pressure goal • Urinary excretion of albumin sodium (Na) or potassium (K) • Change in medication dose • Incident hypertension
Timing	1. Intervention/exposure time period: • Risk factors and other outcomes ≥2 weeks • Hard health outcomes ≥3 months 2. Followup time period: • Risk factors and other outcomes ≥4 weeks • Hard health outcomes ≥6 months
Setting	• Any geographic location • Any clinical or research setting • Any nontreatment setting

C. Literature Search Yield

In all, 34 studies (47 citations) satisfied the CQ2 inclusion criteria and were rated good or fair quality.(29,30,44,45,53-94)

The CQ2 Summary tables present data on the studies used in the evidence review organized by mineral (sodium or potassium), outcomes (BP or CVD outcomes), sodium sub-questions (overall results, different levels of sodium, sodium and other dietary changes), and subpopulations (sex, Summary Table C–4a; race/ethnicity, Summary Table C–4b; age, Summary Table C–4c; and hypertension-status, Summary Table C–4d). Some studies appear in more than one summary table because they address more than one corresponding mineral or sub-question.

D. CQ2 Evidence Statements

i. Sodium and Blood Pressure

A note about the unit of measure presented for dietary and urinary sodium: Sodium is presented in studies in mmol, grams, and milligrams (mg). The Workgroup chose to convert the sodium results to milligrams for the evidence statements, recommendations, and rationales so that the data from different studies would be displayed in a consistent unit. Also, U.S. dietary recommendations and the Nutrition Facts label display sodium in milligrams, and this unit (mg) will be easier for health care providers to communicate with patients. Urinary and dietary sodium are portrayed in the original units from each published study in the summary tables.

a. Overall results of sodium and the effect on blood pressure

What is the overall effect of dietary intake of sodium on BP?

Summary Table C–1 summarizes the design, characteristics, and results of the studies evaluating the overall effect of sodium on BP.(29,53,55,56,59,64,65)

ES1. In adults aged 25–80 years of age with BP 120–159/80–95 mm Hg, reducing sodium intake lowers BP.

Strength of evidence: high

Rationale: Of the three studies included in this evidence table, two of them—the Trial of Nonpharmacologic Interventions in the Elderly (TONE)(55) and Trials of Hypertension Prevention (TOHP II)(59)—were RCTs of behavioral interventions designed to reduce sodium intake in free-living populations. The third study, the Dietary Approaches to Stop Hypertension (DASH)-Sodium trial, was a randomized controlled feeding study that provided prepared foods to study participants.(29) The two different study designs demonstrate what can be achieved in controlled settings with provision of food and known nutrient intake and what is achievable in a less controlled setting (i.e., real-world) with behavioral counseling to lower sodium intake. The three studies share the common feature that weight was kept stable during these trials in the intervention arms reviewed for this specific evidence statement, thereby allowing for isolation of the effect of sodium reduction on BP independent of changes in body weight.

In all three studies, reductions in sodium intake were associated with reductions in BP. In each study, estimation of dietary intake of sodium was confirmed by 24-hour urinary excretion of sodium. (It should be noted that the observed urinary sodium excretions serve as a marker of dietary sodium intake that represents approximately 90 percent of the ingested sodium.) Even though the achieved sodium intake levels varied by study, the relative reductions in sodium intake led to consistent findings across the studies.

TONE was designed to test the effect of a behavioral intervention for sodium reduction in older adults aged 60–80 years and previously taking one antihypertensive medication that was withdrawn at the beginning of the trial. The intervention achieved a 920 mg reduction in urinary sodium excretion from a baseline of 3,312 mg per day.(55) This reduction in sodium was associated with a 4/2 mmHg decrease in BP at a mean of 3.5 months of followup.

TOHP II included overweight adults aged 30–54 with undedicated baseline BP of <140/83–89 mmHg who were randomized to receive or not receive a behavioral intervention with a target of decreasing sodium intake by 1,840 mg per day.(59) Baseline 24-hour urinary sodium excretion was 4,278 mg. Compared to the control group, the behavioral intervention group achieved 24-hour urinary sodium that was approximately 1,012 mg

lower at 18 months and 874 mg lower at 36 months. These reductions were associated with decreases in BP of 4/5 mmHg at 18 months and 1/3 mmHg at 36 months.

The DASH-Sodium trial tested the effects of sodium reduction while consuming a typical American dietary pattern in participants not on BP medication.(29) Using a controlled feeding design, sodium intake was targeted to be reduced initially from 3,450 mg to 2,300 mg and then further to 1,150 mg per day. Even though all food was provided, achieved sodium intake levels differed somewhat from targeted intake levels; the Workgroup decided to use achieved levels based on 24-hour urinary sodium excretion to indicate reductions in sodium intake levels that effectively lowered BP. With each reduction in sodium intake, BP decreased. Reducing sodium excretion to a mean 2,461 mg lowered BP by an average of 2/1 mmHg. Lowering sodium intake by an additional 966 mg to a urinary excretion of 1,495 mg per day on average led to an additional decrease in BP of 5/2 mmHg.

In summary, adults with BP 120–159/80–95mmHg who reduced their sodium intake had decreases in BP. This result was seen consistently in the three large RCTs reviewed, including one feeding study in which nutrient intake was carefully controlled; the effect was independent of changes in body weight or other dietary manipulations. However, it should be noted that, in all studies discussed above, the study populations were not taking BP medication; the evidence statement, strictly speaking, only applies to similar adult populations. However, it may be reasonable to expect that the BP-lowering effects of reduced sodium intake also apply to those taking BP medications, and reducing sodium intake while taking BP medications can potentially lead to better BP control and/or reduced medication needs.

b. Comparison of different levels of sodium intake

What is the effect of different levels of dietary sodium intake on blood pressure?

One randomized trial and four citations(29,44,45,57) evaluating the overall effect of different levels of dietary sodium on BP met eligibility criteria. Summary Table C–2 summarizes the design, characteristics, and results of this study.

ES2. In adults aged 25–75 years with BP 120–159/80–95 mm Hg, a reduction in sodium intake that achieves a mean 24-hour urinary sodium excretion of approximately 2,400 mg/day, relative to approximately 3,300 mg/day, lowers BP by 2/1 mm Hg. A reduction in sodium intake that achieves a mean 24-hour urinary sodium excretion of approximately 1,500 mg/day lowers BP by 7/3 mm Hg.

Strength of evidence: moderate

Rationale: The DASH-Sodium trial serves as the basis for this evidence statement. This singular study is the only RCT identified that specifically compared various levels of sodium intake to each other with regard to the effect on BP. The DASH-Sodium trial studied the effect of sodium intake at low, medium, and high levels in adults with BP 120–159/80–95 mmHg who were not taking BP medication. The target intakes of low, medium, and high sodium levels, adjusted for caloric intake, led to 24-hour urinary sodium excretion of 1,495 mg, 2,438 mg, and 3,337 mg per day, respectively.(29) To isolate the effects of sodium reduction at each level, participants were fed a typical American diet and body weight was kept stable. The achieved intake levels represented approximately 1,000 mg of separation between adjacent sodium levels and nearly 2,000 mg difference between the highest and lowest levels. When sodium was reduced from the highest intake in the DASH-Sodium participants where baseline BP was 120–159/80–95 mmHg, BP decreased by 2/1 mmHg at the medium sodium level and decreased further by 5/2 mmHg at the lowest sodium level. Reducing sodium intake from the highest intake level to the lowest level led to a decrease in BP of 7/3 mmHg.

ES3. In adults 30–80 years of age with or without hypertension, counseling to reduce sodium intake by an average of 1,150 mg/day reduces BP by 3–4/1–2 mm Hg.

Strength of evidence: high

Rationale: Two randomized trials and three citations(55) (56) (58) provide evidence for a reduction in BP based on counseling to reduce dietary sodium. The trials started at various levels of sodium in the diet, conducted differing interventions directed at lowering sodium, and achieved varying levels of reduction in dietary sodium. Both trials showed a reduction in systolic BP of at least 3 mmHg in those assigned to counseling. TOHP II(58) and TONE(55) showed a reduction in diastolic BP of at least 1 mmHg.

In the TOHP II trial in nine clinical centers across the United States, overweight men and women aged 30–54 were randomly allocated to receive either education and counseling about how to reduce sodium or no counseling(58). The intervention goal was to decrease the group average sodium intake to less than 1,840 mg per 24 hours by 6 months. The intervention included an individual counseling session of 60–90 minutes, 10 weekly group sessions, and four monthly group sessions with additional in-person, telephone, and mail contacts as needed. Content included identifying sodium sources in foods, preparing low-sodium items, modifying recipes, making lower sodium selections at and in-between meals and away from home, and general relapse and behavioral techniques. Registered dietitians or other nutrition counselors delivered the intervention with support from behavioral psychologists. Dietary sodium and 24-hour urinary samples were collected at 6, 18, and 36 months. Systolic BP decreased more in the intervention group at 6, 18, and 36 months compared to usual care: 6 vs. 2 ($p<0.001$), 4 vs. 2 ($p<0.01$), and 0.7 vs. 0.6. The reduction in diastolic BP also was significant at 6 months: 4 vs. 3 ($p<0.001$) and at 18 months: 4 vs. 3 ($p<0.002$). Incident HTN was reduced 18 percent in this population.(58)

In TONE, healthy adults aged 60–80 with BP <145/85 mmHg and on one or more hypertensive medications that were weaned during the screening phase were randomly allocated to one of four groups: weight loss and reduced sodium, reduced sodium alone, weight loss alone, or usual lifestyle. The intervention goal for sodium reduction was to achieve and maintain 24-hour dietary sodium of 1,840 mg as measured by 24-hour urine collection. The intervention for sodium included an individual session with a registered dietitian, 4 months of weekly small group (9–12 participants) meetings (individual sessions each fourth week), a 3-month extended phase of biweekly meetings, and a maintenance phase. Content included learning about sources of sodium, alternative foods, and adaptation of the reduced sodium recommendations to individualized lifestyles. The interventionist typically was a registered dietitian. From baseline to 3 months prior to medication withdrawal, sodium reduction was associated with reductions in systolic/diastolic BPs of 4 mmHg and 2 mmHg net control ($p<0.001$). Mean followup at 30 months was associated with a mean reduction in sodium intake of 1,035 mg per day. In adults taking a single medication, this reduced the need for antihypertensive medication by 32 percent.(55)

c. Sodium and blood pressure in subpopulations

What is the effect of sodium on blood pressure in subgroups defined by sex, race/ethnicity, age, and hypertension status?

Summary tables provide the design, characteristics, and results of the studies evaluating the effect of sodium on BP in the following subpopulations: sex (Summary Table C–4a), race/ethnicity (Summary Table C–4b), age (Summary Table C–4c), and hypertension (HTN) status (Summary Table C–4d).

ES4. In adults with prehypertension or hypertension, reducing sodium intake lowers BP in women and men, African-American and non–African-American adults, and older and younger adults.

Strength of evidence: high

Rationale: Three RCTs and five citations(29,44,45,55,58) of 3–6 months' duration examined the effect of lowering sodium intake in subgroups that included men and women, African Americans and non-African Americans, and older and younger individuals. All three trials, which included adults with prehypertension and hypertension, showed that reductions in sodium levels were associated with reductions in systolic and diastolic BPs. As noted in ES1, the TONE, TOHP II, and DASH-Sodium trials involved differing populations, interventions, and varying levels of achieved reductions in sodium; yet these studies led to consistent findings across trials. All three trials in this analysis included individuals aged 25–80 years.

Table 6. DASH-Sodium Blood Pressure Reduction (mm Hg)

Population	Typical American Diet; Reducing Na from 3,300 mg to 2,400 mg	Typical American Diet; Reducing Na from 2,400 mg to 1,500 mg	DASH Dietary Pattern; Reducing Na from 3,300 mg to 2,400 mg	DASH Dietary Pattern; Reducing Na from 2,400 mg to 1,500 mg
Women	2†/1	6*/3*	2†/1‡	2*/1†
Men	3†/1 †	3*/2*	1/1	1/1
AA	2†/2*	6*/3*	2†/1‡	2*/1†
Non-AA	2†/1	3*/2*	1/0.3	1/1‡
>45 years	3*/2*	5*/2*	1‡/1‡	3*/1*
<45 years	1/0.2	4*/3*	1/1	0.1/1

*p<0.01; †p<0.05; ‡p<0.10

Rationale—Women: In the context of the typical American diet in the DASH-Sodium trial, reductions in urinary sodium from 3,300 mg to 2,400 mg per 2,100 kilocalories on average lowered BP in women on average by 2/1 mmHg. Further reductions in urinary sodium to 1,500 mg reduced BP by an additional 6/3 mmHg. In the context of the DASH dietary pattern, reductions in urinary sodium excretion from an average of 3,300 mg to 2,400 mg per day lowered BP by an average of 1 mmHg systolic blood pressure, and further reducing urinary sodium excretion to 1,500 mg reduced systolic BP by an additional 4 mmHg and diastolic BP by an additional 2 mmHg. Among adults aged 60–80 with hypertension, counseling to reduce sodium intake to less than 1,800 mg/day lowered BP by 3/1 in women compared to usual care (p<0.2) at a mean followup of 28 months.(55) In the TOHP II, counseling to reduce sodium intake to <1,840 mg per day lowered BP by 3-5mmHg/2 mmHg in women at 6 months, 2–5/2–4 mmHg at 18 months, and 2–3 /1–2 mmHg at 36 months.

Rationale—Men: In the context of the typical American diet in the DASH-Sodium trial, reductions in urinary sodium from an average of 3,300 mg to 2,400 mg per day lowered BP in men on average by 3/1 mmHg. Further reductions in urinary sodium to 1,500 mg led to a BP reduction of an additional 3/2 mmHg in men. In the context of the DASH dietary pattern, reductions in urinary sodium excretion from about 3,300 mg to 1,500 mg per day on average lowered systolic and diastolic BP by 2 mmHg, although the systolic BP lowering was not significant. In the TONE study, reducing sodium to <1,800 mg lowered blood pressure by 5/3 mmHg in men

compared to usual care (p<0.01) at a mean followup of 28 months. In TOHP II, counseling to reduce sodium intake to <1,840 mg per day lowered BP by 2–5/1–2 mmHg at 6 months, 2/1 mmHg at 18 months, and 1/1mmHg at 36 months.

Rationale—African Americans: In the context of the typical American diet in the DASH-Sodium trial, reductions in urinary sodium from an average of 3,300 mg to 2,400 mg per day lowered BP by an average of 2/2 mmHg in African Americans. Further reductions of urinary sodium excretion to 1,500 mg reduced BP in African Americans by an additional 6/3 mmHg. In the context of the DASH dietary pattern, reductions in 24-hour urinary sodium excretion from about 3,300 mg to 2,400 per day lowered systolic BP by 2 mmHg and diastolic BP by 1 mmHg (nonsignificant); further reductions in urinary sodium excretion to 1,500 mg per day lowered BP an additional 2/1 mmHg. In the TONE trial, reducing sodium to <1,800 mg lowered BP by 5/3 mmHg in African Americans who received counseling compared to usual care (p<0.05). In TOHP II, counseling to reduce sodium to 1,840 mg/day lowered BP by 5/2–3 mmHg at 6 months, 1–5/1–4mmHg at 18 months, and 1–3/1–2 mmHg at 36 months.

Rationale—Non-African Americans: In the context of the typical American diet in the DASH-Sodium trial, reductions in urinary sodium from 3,300 mg to 2,400 mg per day on average lowered BP by 2/1 mmHg. Further reductions in urinary sodium excretion to 1,500 mg led to a BP reduction by an additional 3/2 mmHg. In the context of the DASH dietary pattern, reductions in urinary sodium excretion from about 3,300 mg to 2,400 per day on average lowered systolic BP by 1 mmHg and diastolic BP by 0.3 mmHg (nonsignificant); further reductions in urinary sodium excretion to 1,500 mg per day lowered BP an additional 2/1mmHg.

In the TONE trial, reducing sodium to <1,800 mg lowered BP by 4/2 mmHg in non-African Americans who received counseling compared to usual care. (p<0.01) In TOHP II, counseling to reduce sodium to 1,840 mg/day lowered BP by 2–3/1–2 mmHg at 6 months, 2/1–2 mmHg at 18 months, and 1–2/1 mmHg at 36 months.

Rationale—Age >45 years: In the context of the typical American diet in the DASH-Sodium trial, reductions in urinary sodium from an average of 3,300 mg to 2,400 mg per day lowered systolic BP by an average of 3/2 mmHg. Further reductions in urinary sodium excretion to 1,500 mg lowered BP in those over 45 years by an additional 5/2 mmHg. In the context of the DASH dietary pattern, reductions in urinary sodium excretion from about 3,300 mg to 1,500 per day lowered BP by 5/2 mmHg. Also the reductions in urinary sodium excretion from about 2,400 mg to 1,500 mg per day lowered BP 3/1 mmHg.

In the TONE trial, reducing sodium to 1,800 mg lowered BP by 5/2mmHg in those aged 60–69, and by 2/1 mmHg in those aged 70–80.

Rationale—Age <45 years: In the context of the typical American diet in the DASH-Sodium trial, reductions in urinary sodium from an average of 2,400 mg per day to 1,500 mg on average lowered systolic BP by an average of 4/3 mmHg (p<0.01).

ES5. Reducing sodium intake lowers BP in adults with either prehypertension or hypertension when eating either the typical American diet or the DASH dietary pattern. The effect is greater in those with hypertension.

Strength of evidence: high

Rationale: Three studies (four citations) examined the effects on BP of reducing dietary sodium intake in adults with either prehypertension or hypertension.(44,55,57,58)

Rationale—Prehypertension: Findings from two studies provide evidence that reducing dietary sodium intake lowers BP in adults with prehypertension.(44,57,58) In the context of a typical American diet in the DASH-Sodium trial, reductions in 24-hour urinary sodium excretion in this group from about 3,300 mg to 2,400 mg per day on average lowered BP on average by 2/1 mmHg. Further reductions in urinary sodium excretion to 1,500 mg per day lowered BP an additional 3/2 mmHg.(44,57)

In the context of the DASH dietary pattern, reductions in urinary sodium excretion from about 3,300 mg to 2,400 mg per day in adults with prehypertension lowered BP by an average of 1/1 mmHg but further reducing urinary sodium excretion to 1,500 mg did not lower BP.(44,57) Among adults with prehypertension in the Trials of Hypertension Phase II (TOHP II), counseling to reduce sodium intake to ≤1,840 mg/day lowered BP by about 3/2, 2/1, and 1/1 mmHg, net of control, after 6, 18, and 36 months, respectively.(58)

Rationale—Hypertension: Findings from two studies provide evidence that reducing dietary sodium intake lowers BP in adults with hypertension.(44,55,57) In the context of a typical American diet in the DASH-Sodium trial, reductions in urinary sodium excretion from an average of 3,300 mg to 2,400 mg per day lowered BP by an average of 2/2 mmHg among adults with BP 140–159/90–95 mmHg; further reductions in urinary sodium excretion to 1,500 mg/day lowered BP an additional 6/3 mmHg.(44,57) In the context of the DASH dietary pattern, reductions in urinary sodium excretion from 3,300 mg to 2,400 mg per day lowered systolic BP by an average of 2 mmHg. Further reducing urinary sodium excretion to 1,500 mg lowered BP an additional 3/2 mmHg.(44,57) Among adults aged 60–80 with hypertension (defined as taking a blood pressure medication with blood pressure <145/85 mmHg) in the Trial Of Nonpharmacologic Interventions in the Elderly (TONE), counseling to reduce sodium intake to <1,800 mg/day lowered BP by 4/2 mmHg net of control (p<.001) after a mean of 3.5 months(55).

One trial—the DASH-Sodium trial—included both adults with prehypertension and hypertension, allowing a direct comparison of effects in both subgroups. The effects of reducing sodium intake on BP lowering were greater among adults with BP 140–159/90–95 mmHg compared to those with BP 120–139/80–90 mmHg on both the typical American diet (p=0.01) and the DASH dietary pattern (p=0.003)(29).

d. Sodium and dietary pattern changes

What is the effect of sodium on blood pressure in the context of dietary pattern changes?

Summary Table C–3 summarizes the design, characteristics, and results of the studies evaluating the effect of dietary sodium on BP in the context of other dietary changes.(29,53,55,56,60-62)

ES6. In adults aged 22–80 with BP 120–159/80–95 mm Hg, the combination of reduced sodium intake plus eating the DASH dietary pattern lowers BP more than reduced sodium intake alone.

Strength of evidence: moderate

Rationale: This statement is based on the DASH-Sodium trial. Although this is a single randomized trial, it involved: a large and diverse study population of prehypertensive or hypertensive adults not on BP medication; was a well-designed RCT with high followup rates; and the intervention consisted of providing all foods and beverages to the study participants. This permitted assessment of actual intake of nutrients and food groups. Sodium intake was estimated from 24-hour urinary excretion, which in steady-state generally represents about 90 percent of actual sodium intake.

In the DASH-Sodium trial, the effect of reducing sodium intake while eating the DASH dietary pattern was compared to eating a typical American dietary pattern AND typical intake of sodium (i.e., a mean 24-hour urinary sodium excretion of approximately 3,300 mg). Relative to this "typical" state, following both the DASH

dietary pattern AND reducing sodium intake to a level that achieves a mean 24-hour urinary sodium excretion of approximately 2,400 mg lowers BP by 7/4 mmHg, and following both the DASH dietary pattern AND reducing sodium intake to a level that achieves a mean 24-hour urinary sodium excretion of approximately 1,500 mg lowers BP by 9/5 mmHg.

e. Sodium in the context of other minerals and blood pressure

What is the effect of sodium on BP in the context of other single minerals?

Summary Table C–3 summarizes the design, characteristics, and results of the studies evaluating the effect of dietary sodium on BP in the context of dietary changes designed to alter minerals.(29,53,55,56,60-62)

ES7. There is insufficient evidence from RCTs to determine whether reducing sodium intake plus changing dietary intake of any other single mineral (for example, increasing potassium, calcium, or magnesium) lowers BP more than reducing sodium intake alone.

Strength of evidence: insufficient

Rationale: There were no randomized trials or meta-analyses identified that examined whether reducing sodium intake plus changing dietary intake of any other single mineral lowers BP more than reducing sodium intake alone. Several studies that included modification of multiple minerals were identified and are described briefly below.

In a study of Black South African adults with mild-to-moderate hypertension, commonly consumed foods were altered to achieve approximately 41 percent reduction in sodium intake, 826 percent increase in potassium intake, 388 percent increase in calcium intake, and 368 percent increase in magnesium intake. Following consumption of these altered foods for 8 weeks, systolic BP was lowered by 6 mmHg ($p<0.05$) (with no significant change in diastolic BP), compared to a group that ate unaltered foods. Urinary sodium excretion was not different between the treatment groups, but urinary potassium and magnesium were higher in the group eating altered foods, which suggested that the BP effect was due to changes in intake of minerals other than sodium. In any case, the effect of changing sodium intake in the context of changing intake of other minerals cannot be determined from this study because the sodium intake (reflected in sodium excretion) was not different between treatment and control groups.(62)

In the China Salt Substitute Study, the household use of a salt substitute that included 25 percent potassium chloride, 10 percent magnesium sulfate, and 65 percent sodium chloride for 1 year reduced systolic BP by 4 mmHg ($p<0.001$) relative to usual salt usage. There were no detectable differences in diastolic BP. There were no significant differences in the first morning urinary sodium concentrations between the control and intervention groups. The first morning urinary potassium concentration was higher at 6 months and 12 months, but no measurements of magnesium were reported. Thus, it was not possible to identify the impact of any single mineral.(61)

A 1-year community-based dietary intervention was conducted in free-living rural Japanese villages. The intervention utilized a tailored dietary education effort delivered to increase carotene and vitamin C intake in association with increased intake of fruits and vegetables, which would increase intake of potassium. At the end of 1 year, systolic BP was lowered by a mean of 3 mmHg ($p<0.01$).

In this Japanese study, when analyses were performed based on hypertensive status, there was a lowering of systolic BP by 6 mmHg in subjects who were hypertensive ($p<0.05$), but there was no significant change in normotensive participants. No significant changes were observed in diastolic BP among any of the groups. The intervention group did achieve a significant reduction in reported dietary intake of sodium ($p<0.05$) and urinary

excretion of sodium ($p<0.001$). The reported dietary intakes of both carotene and vitamin C were significantly higher ($p<0.005$) in the intervention group, suggesting that the educational effort was successful. However, neither the reported dietary intake of potassium nor the urinary excretion of potassium changed during the intervention. Overall, the observed changes in systolic BP could not be ascribed to the change in potassium intake.

A secondary analysis of TONE reported that when using pooled estimates of sodium and potassium intake with hierarchical measurement error models, an independent, graded influence on non-pharmacologic BP control was observed.(56) The TONE study interventions inadvertently led to changes in potassium intake, and higher potassium intake was associated with greater BP reduction. However, the intervention was not designed to specifically influence the level of potassium intake, and the changes that took place were in association with changes to facilitate sodium reduction in the diet. Within the report of this secondary analysis, no urinary excretion data were provided to allow additional estimates of change in sodium and potassium intake. The pooled estimates used to derived the relationships with BP control appeared to include participants in the trial who were assigned to all four interventions in the parent trial (sodium only intervention, combined sodium/weight loss intervention, weight loss only intervention, and usual care). Thus, the panel concluded that the observed results from this analysis had limited implications for generalized recommendations.

ii. Sodium and CHD/CVD Outcomes

a. What is the effect of dietary intake of sodium on CVD outcomes?

To answer this question, the Panel reviewed both randomized trials and observational studies. Observational studies were included for this question and not in others due to the paucity of trials with CVD outcomes and the Workgroup's opinion that, given the implications of changing sodium intake for individuals, institutions, and potentially for public policy, it was critical to address what evidence was available, even if it was only observational. Summary Tables C–5 and table C–6 include trials and observational studies that examined the effect of dietary intake of sodium on CVD outcomes. Three trials(55,66,67) are summarized in Summary Table C–5. Summary Table C–6 includes observational studies(72,76,79) that were not included in the meta-analysis(85) in addition to newer observational citations.(77,78,80-84)

ES8. A reduction in sodium intake of approximately 1,000 mg per day reduces CVD events by about 30%.

Strength of evidence: low

Rationale: Three randomized trials tested the effect of reduction in sodium intake on CVD or mortality. In 1,981 elderly male military veterans in a retirement home in Taiwan, substitution of sodium with potassium-enriched salt that reduced sodium intake from 5,200 to 3,800 mg per day for 31 months lowered death from CVD by 41 percent.(67) In a population of 975 elderly patients in the United States who had hypertension, sodium reduction for 29 months lowered daily sodium intake by about 1,000 mg. There were 36 cardiovascular events in the sodium reduction group compared to 46 in the control group, which was not statistically significant (TONE).(55) In an extended observational followup study of 3,126 pre-hypertensive men and women who participated in either an 18-month or 36–48 month trial to reduce sodium intake, compared to control participants, participants who received interventions had a 30 percent reduction in relative risk of cardiovascular events during the 12–15 years of follow-up.(66) Daily sodium intake was reduced by about 800 mg after the initial intervention.

Features of these trials that limit a conclusive interpretation and therefore qualify the strength of evidence as "low" are: their small sample sizes for a disease or mortality outcome; insufficient duration of sodium reduction

or of followup for sufficient events to accumulate; a small reduction in sodium intake; in one trial, the concomitant increase in potassium intake;(67) and the inclusion of one observational study in the evidence base.

ES9. Higher dietary sodium intake is associated with a greater risk of fatal and nonfatal stroke and CVD.

Strength of evidence: low

Rationale: Fifteen observational studies published from 1998–2009 examined the relationship between dietary sodium intake and stroke and/or CVD. All but two of these studies were included in one good-quality systematic review and meta-analysis that summarized the observational studies from January 1966 to December 2008;(85) hence, the estimated risks from the meta-analysis are summarized along with data from the additional two studies. The meta-analysis included data from 13 studies, with a total of 177,025 participants followed 3.5–19 years from six different countries. Studies using fatal, nonfatal, or combined fatal and nonfatal outcomes were combined to produce incident stroke or CVD outcomes. Based on 5,346 stroke events from 10 studies, each 2,000 mg per day higher sodium intake was associated with a 23 percent greater risk of stroke. Similarly, each 2,000 mg per day higher sodium intake was associated with a 17 percent greater risk of CVD based on 5,044 CVD events from nine studies. These risk reductions are likely to be underestimated because of possible misclassification due to the use of a single baseline sodium assessment with no adjustment for day-to-day variability or changes in sodium intake over time, as well as other limitations of the various sodium assessment methods used in some of these studies, most of which provide inadequate estimates of sodium intake.

One of the two studies not included in the meta-analysis was a small Finnish study (n=755) that found no relationship between sodium intake and stroke mortality.(79) In the second study, which followed participants in the first National Health and Nutrition Examination Survey (NHANES), there was an inverse relation between sodium intake and age- and sex-specific CVD mortality rates.(72) However, in multivariate analyses, sodium intake was not associated with CVD mortality (p=0.09). Several methodological concerns have been raised about the latter study; these include the inclusion of participants with existing CVD and simultaneous inclusion of sodium, energy intake, and sodium-to-energy ratio in the model, which likely led to colinearity. A re-analysis of the same dataset excluding participants with preexisting CVD and the sodium-to-energy ratio had opposite findings and was included in the Strazullo et al. 2009 meta-analysis.(75)

Because of the timeliness and importance of this question, an updated search was conducted to include studies published from 2010 through April 2012, and six additional studies were identified that met the inclusion criteria. In a study following participants from two population-based cohorts without CVD (n=3,681) for an average of 7.9 years, the lowest tertile of sodium excretion (mean of 2,185 mg per day in men; 2,760 mg per day in women) was associated with higher CVD mortality (HR=1.56, CI=1.02–2.36) but not with combined fatal and nonfatal CVD.(84) The study's findings contradict themselves, and the methodology has been criticized. Concerns include a large amount of missing data but no sensitivity analyses using imputation to assess the impact of missing data, and perhaps more importantly, a nonstandard approach in which the reference group is the entire study population instead of the group with the highest or lowest urinary sodium excretion.

In the second study, patients who had CVD or were at high risk and enrolled in two randomized drug trials conducted in 40 countries, were followed for a median of 56 months.(78) Although both sodium excretion >7,000 mg per day and <3,000 mg per day were associated with increased risk of fatal and nonfatal CVD in a J-shaped relationship, this study has been criticized for several reasons. An important limitation was that the authors used a first-morning void instead of a 24-hour urine sample to estimate urinary sodium excretion over a 24-hour period. A partial urine sample is suboptimal because sodium excretion varies greatly throughout the day and can be affected by diurnal variations in sodium intake, the use of loop diuretics, older age, and hypertension status, most of which were characteristic of patients in this study. Furthermore, the equation used

to estimate total sodium excretion was developed for an Asian population. Although the authors validated the equation for their study population, they provide only correlation coefficients, which are not sufficient to assess validity. Finally, many patients were ill and may have been advised to reduce sodium intake before taking part in the study; thus, those with lower sodium intake may have already had CVD.

In a NHANES III analysis of 12,267 randomly selected U.S. adults, the estimated usual intakes of sodium and potassium and their ratio in relation to risk of CVD mortality was examined.(77) The findings suggest that a higher sodium:potassium ratio is associated with CVD mortality. The hazard ratio comparing the highest quartile of sodium to potassium ratio with the lowest quartile was 1.46 (95% CI, 1.11–1.92). In this analysis, it is impossible to determine whether the association is related to higher sodium intake or lower potassium intake.

Another study was a population-based study of 2,657 adults living in Manhattan, NY who were followed for a mean of 10 years. In this study, each 500 mg per day higher sodium intake was associated with a 17 percent increased stroke risk (HR=1.17, CI=1.07–1.27). A dietary sodium intake greater than 4,000 mg per day was associated with an increased risk of stroke (HR=2.59, CI=1.27–5.28) and combined stroke, myocardial infarction (MI), and vascular death (HR=1.68, CI=2.67) compared to an intake ≤1,500 mg per day.(82) Sodium intake between these values was not associated with stroke, but intake of 1,501–2,300 mg per day had an increased risk of combined stroke, MI, and vascular death (HR=1.35, CI=1.00–1.82), compared with an intake of ≤1,500 mg per day. One major limitation of this study was the estimate of sodium intake by food frequency questionnaire (FFQ), a method that does not provide enough detail about each food to be a sensitive method for measuring sodium intake.

Two additional studies were conducted in Asian populations with much higher sodium intake than populations in the United States. A study following 77,500 Japanese adults for 7–9 years found that the highest quintile (median 6,844 mg per day) of sodium intake was associated with a higher risk of CVD (HR=1.19, CI=101–1.40) and stroke (HR=1.21, CI=1.01–1.43) compared to the lowest quintile of intake (median 3,084 mg per day).(80) One major limitation of this study was the use of a FFQ, which does not provide enough detail about each food to be a sensitive method for measuring sodium intake. Even though the authors reported that their FFQ was validated for estimating sodium intake, the correlation with urinary sodium excretion was quite low (r=0.42 in men and r=0.3 in women). A case-control study of inpatients recruited from three Chinese hospitals found no relation between sodium intake and ischemic stroke using 374 cases and 464 age-matched controls.(81) Like the previous study, sodium intake was estimated from a FFQ. Additionally, the results from case-control studies may be biased by measuring sodium intake after the stroke has occurred, and in this case, the controls were not matched for sex even though sodium intake is usually higher in men than women.

Although one additional study examined the association between sodium intake and the risk of dying from CVD among people with type 2 diabetes,(83) the Workgroup considered this study insufficient to assess the association between sodium intake and CVD in this subpopulation.

In sum, most studies reported that higher dietary sodium intake was associated with higher risk of stroke and CVD, but findings were inconsistent across studies. Some of this inconsistency may be due to the observational nature of the studies, and there are several general limitations associated with observational studies as well as weaknesses of specific studies presented above. For example, in the majority of studies, the estimated sodium intake may be misclassified due to the use of a single baseline assessment with no adjustment for day-to-day variability or changes in sodium intake over time, as well as other limitations of the varying assessment methods used (i.e., many were self-reported and are known to provide inadequate estimates of sodium intake). In addition, morbidity and mortality outcomes may be under-ascertained, thereby reducing power. Some studies failed to exclude participants with existing CVD, who may have already reduced their sodium intake because of their disease. Finally, confounding by variables not included in the analyses or for those measured with error

may have influenced findings. On the other hand, observational studies often are population-based samples, allowing the results to be broadly generalized, and usually follow participants for longer than is feasible in randomized trials. After considering the strengths and limitations of each study, the Workgroup concluded that, overall, the observational studies suggest that higher dietary sodium intake is associated with higher risk of stroke and CVD. However, because of the methodological limitations of these observational studies, the strength of the evidence was rated low instead of moderate (the highest level possible using observational studies).

ES10. There is insufficient evidence to determine the association between sodium intake and the development of heart failure.

Strength of evidence: insufficient

Rationale: One observational study(76) that met criteria for Workgroup review examined the relationship between dietary sodium intake and incidence of congestive heart failure (HF). However, the Workgroup considered the evidence insufficient to make a statement on dietary sodium intake in the development of HF.

ES11. There is insufficient evidence to assess the effect of reducing dietary sodium intake on cardiovascular outcomes in patients with existing HF.

Strength of evidence: insufficient

Rationale: Three studies (95-97) examined dietary sodium intake in HF patients; however, two failed to meet inclusion criteria due to inadequate sample size for observational studies (n<500). One trial examined the effect of two levels of sodium on hospital readmissions in HF patients; however, this was not enough evidence to make a graded statement on the topic.(95)

iii. Potassium and BP and CHD/CVD Outcomes

a. What is the effect of dietary intake of potassium on BP and CVD outcomes?

Summary Table C–7 and C-8 include details on studies evaluating the effect of potassium on BP and CVD outcomes.(61,62,87-94)

ES12. There is insufficient evidence to determine whether increasing dietary potassium intake lowers BP.

Strength of evidence: insufficient

Rationale: Overall, the Workgroup concluded that the evidence of a BP-lowering effect of dietary potassium alone was suggestive but not compelling. There are no randomized trials that isolate the effect of dietary potassium on BP. However, there are three trials that suggest a BP-lowering effect of increasing dietary potassium intake, but in each of these trials, changes in potassium intake occurred in the context of other dietary changes:

- In the DASH study, a fruit and vegetable dietary pattern that was high in potassium but otherwise similar to a typical American diet lowered BP compared to the typical American diet, but not as much as the DASH diet.(26) The effect of potassium cannot be isolated because of differences in fiber intake and the possibility that fruits and vegetables lower BP independent of potassium intake.
- In the China Salt Substitute Study, the use of a salt substitute that included 25 percent potassium chloride, 10 percent magnesium sulfate, and 65 percent sodium chloride for 1 year reduced systolic BP by 3.7 mmHg

(p<.001) relative to usual salt usage. Urinary sodium excretion was no different from control, but urinary potassium intake was higher, raising the possibility that the BP effect was due to increased potassium intake. Again, however, changes in magnesium intake may have contributed to the effect, making it impossible to isolate the effect of potassium.

- In a study of Black South African adults, commonly consumed foods were altered to achieve approximately 40 percent reduction in sodium intake, 800 percent increase in potassium intake, 400 percent increase in calcium intake, and 400 percent increase in magnesium intake. These altered foods lowered BP by 6 mmHg systolic (with no significant change in diastolic BP), compared to a group that ate unaltered foods. Urinary sodium excretion was not different between the treatment groups, but urinary potassium and magnesium were higher in the group eating altered foods, raising the possibility that the BP effect was due to changes in intake of potassium and/or other minerals.(62)

In contrast, meta-analyses of potassium supplementation (i.e., in pill form) in doses ranging from 40 to 120 mmol per day result in inconsistent effects on BP (no significant effect in one analysis (98) while other meta-analyses suggest BP-lowering effects of 2–6/1–3 mmHg(99-101)).

ES13. In observational studies with appropriate adjustments (BP, sodium intake, etc.), higher dietary potassium intake is associated with lower stroke risk.

Strength of evidence: low

Rationale: There are several large observational studies with a wide range of potassium intake and a large number of stroke events that fairly consistently demonstrate an inverse association between potassium intake and stroke risk, on the order of 20–50 percent reduction in risk comparing highest to lowest intakes.(71,79,88,90,91) Although several of these studies adjusted for age, sex, race, and BP, overall, the independence of this relationship cannot be firmly established.(68,87,88,90,92,94) In addition, as in all observational studies, causality cannot be assessed.

ES14. There is insufficient evidence to determine whether there is an association between dietary potassium intake and congestive heart disease, HF, or cardiovascular mortality rate.

Strength of evidence: insufficient

Rationale: The association between dietary potassium intake and heart disease or overall cardiovascular morbidity and/or mortality has not been extensively studied, but the little observational data that exist suggest that there is no significant relationship.(89,93)

E. Diet Recommendations for Blood Pressure Lowering

Advise adults who would benefit from blood pressure lowering to:

1. Consume a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils and nuts; and limits intake of sweets, sugar-sweetened beverages and red meats.
   - Adapt this dietary pattern to appropriate calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical conditions (including diabetes).
   - Achieve this pattern by following plans such as the DASH dietary pattern, the USDA Food Pattern, or the American Heart Association Diet.

   Strength: A (strong)

Rationale: This recommendation is based largely on studies of the DASH dietary pattern (DASH and DASH-Sodium), which provided the highest quality evidence for this food-based dietary pattern causing improvements in lipid profiles and blood pressure (CQ1 **ES3**–ES9). This evidence was supplemented by studies of low quality in which various adaptations of the Mediterranean-style dietary pattern were tested and also found to reduce blood pressure (CQ1 **ES1**). The evidence suggests that the effects of the recommended dietary pattern persist as long as the pattern is consumed. The blood pressure lowering effect has been demonstrated in adults with hypertension and pre-hypertension, and it is evident in men and women, African Americans and non-African Americans, and in older and younger adults (ES5). The dietary pattern's effect on blood pressure is independent of changes in weight and sodium intake. The magnitude of effect is sufficient to prevent progression from prehypertension to hypertension, to promote non-pharmacologic blood pressure control in those with hypertension, and to supplement pharmacologic blood pressure lowering.

The caloric (energy) intake should be appropriate for the individual – e.g., restricted for those attempting weight loss. Patients also should be encouraged to adapt the recommended dietary pattern to their personal and cultural preferences. Materials are available to assist patients in achieving the recommended dietary pattern at different calorie levels (see below). The 2010 U.S. Department of Health and Human Services Dietary Guidelins for American recommend the USDA food pattern and the DASH eating plan (49). Overall, the recommended dietary pattern is consistent with the American Heart Association diet(50) and the USDA Food Pattern.(49) The USDA Food Pattern offers lacto-ovo vegetarian and vegan adaptations. Therefore, this recommendation is consistent with other national guidelines. Clinicians should be familiar with the recommendations, advise their patients to adopt them, and provide easy access to information (see resources below). Dietary planning and nutritional counseling is often facilitated by referral to a nutrition professional.

Resources:

DASH Eating Plan:
- Booklet
- Brochure

AHA Diet and Lifestyle Recommendations:
- Website
- Scientific statement(9)

Dietary Guidelines for Americans
- Policy document(49)
- Consumer brochure
- USDA Food Patterns

2. Lower sodium intake.

Strength: A (strong)

Rationale: There is strong and consistent clinical trial evidence that reducing sodium intake lowers BP. This BP-lowering effect has been demonstrated in adults with hypertension and prehypertension, in men and women, in African Americans and non-African Americans, and in older and younger adults. Trials contributing to this evidence include well-controlled feeding studies as well as studies in which participants were counseled to lower sodium. The effect of reducing sodium intake on BP is independent of changes in weight. The magnitude of effect is sufficient to both prevent progression from prehypertension to hypertension, and to promote non-pharmacologic BP control in those with hypertension. Observational data also suggest that lower sodium intake is associated with lower risk of cardiovascular events in people with and without hypertension, which is hypothesized to occur through reductions in blood pressure.

3. a. Consume no more than 2,400 mg of sodium per day;
b. Further reduction of sodium intake to 1,500 mg per day can result in even greater reduction in BP;
c. Even without achieving these goals, reducing sodium intake by at least 1,000 mg per day lowers blood pressure.

Strength: B (moderate)

Rationale: One well-conducted trial demonstrated clinically meaningful lowering of BP when sodium was reduced to 2,400 mg per day with lower BPs achieved when sodium intake was reduced to 1,500 mg per day. Reductions of 1,000 mg per day were shown to be beneficial in trials, and observational studies estimated significant reductions in relative risk associated with changes in sodium intake of about 1,000 mg per day. This recommendation is directed at the two-thirds of the U.S. adults who have prehypertension or hypertension, and for whom reducing sodium intake can prevent or improve control of hypertension and potentially reduce cardiovascular events.

The Workgroup acknowledges that the recommendation to reduce sodium intake to less than 2,400 mg per day differs slightly from other current dietary recommendations, specifically, the 2010 *Dietary Guidelines for Americans* and the Institute of Medicine Dietary Reference Intakes, both of which recommend 2,300 mg per day as the upper limit of intake for adults. Although the impact on behavior of a difference between intakes of 2,400 mg versus 2,300 mg of sodium per day would be minimal, these recommendations are based on the strongest clinical trial evidence available: the achieved level of 2,400 mg/day from the DASH-Sodium trial (estimated from average urinary sodium excretion). See CQ2 ES2.

The strength of this recommendation is graded “moderate” because there are fewer clinical trials used to devise the 2,400 and 1,500 goals compared to the large number of trials that are used to inform the overall recommendation on sodium (recommendation 2) that is graded “strong.”

Reducing sodium intake can be challenging for an individual because of the ubiquitous nature of sodium in the American food supply. Educational materials with strategies to help patients lower sodium intake are provided by several Federal and private sources. (49,102-105) Ultimately, however, significant changes in sodium intake among U.S. adults may require changes in both individual behavior and in food manufacturing and processing.

4. Combine the DASH dietary pattern with lower sodium intake.

Strength of evidence: A (strong)

Rationale: Both a healthy dietary pattern as exemplified by DASH and reduced sodium intake independently reduces BP. However, the BP-lowering effect is even greater when these dietary changes are combined. In the 60 percent of U.S. adults with prehypertension or hypertension, simultaneously implementing recommendations 1 and 2 can prevent and control hypertension more than either intervention alone.

7. CQ3—Physical Activity: Lipids and Blood Pressure

CQ3:

Among adults, what is the effect of physical activity on BP and lipids when compared with no treatment or with other types of interventions?

A. Introduction/Rationale

Large bodies of observational data show an association between higher levels of physical activity and lower rates of many chronic diseases, including CVD, and enhanced longevity.(106-108) Further, an inverse dose-response relation exists, with increasing higher levels of activity associated with commensurately lower rates of CVD in a curvilinear fashion.(109,110) A recent analysis has estimated that by eliminating physical inactivity, 6 percent of CHD worldwide may be eliminated, and life expectancy of the world may be increased by 0.68 years.(111)

Among the mechanisms proposed to mediate the relationship between physical activity and decreased CVD rates are beneficial effects of exercise on lipid profile and BP.(112) One study estimated that the effects of physical activity on blood pressure and development of hypertension reduction explained some 27 percent of the activity-related reduction in CVD rates observed, while 19 percent of the reduction in CVD rates could be explained by the beneficial effects of physical activity on traditional lipids, and 16 percent on novel lipids.

Below, we elaborate on findings from meta-analyses of physical activity on changes in lipid profile and BP.

B. Selection of Inclusion/Exclusion (I/E) Criteria

Due to resource limitations, we included only systematic reviews and meta-analyses of RCTs or controlled clinical trials published from 2001–11. Workgroup members identified I/E criteria in eight categories for CQ3, as indicated in Table 7. The criteria included the Population, Intervention, Comparator, Outcomes, Timing, and Setting (PICOTS) criteria as the first four and then also several others related to study design, type of publication, and timeframe for publication.

For each of these I/E criteria, the Workgroup members developed detailed specifications related to each component. The population of interest was defined as all adults, age 18 or higher. For this critical question, the intervention was defined as physical activity interventions of any type. However, studies where the primary outcome was weight change were excluded, to focus on the independent effect of physical activity on the CVD risk factors BP and blood cholesterol. A separate Obesity Guideline Panel is reviewing evidence of the effect of weight loss on CVD risk factors and outcomes.

Table 7. PICOTS (Population, Intervention, Comparator, Outcomes, and Setting) for CQ3

PICOS Category	Inclusion/Exclusion Criteria
Intervention (Meta-analysis/ Systematic review of RCTs)	• For RCTs, include physical activity interventions of any type except for those with a primary outcome of weight change
Population	Adults, ≥18 years of age
Comparator	• There may be no predetermined comparison group for observational studies • For RCTs, the comparison is a group (or groups) of people with varying levels of physical activity or people receiving pharmacotherapy. • For an RCT, the comparison group could receive one or more of the following: – Usual care – No treatment – Nonphysical activity intervention – Pharmacotherapy
Outcomes	Risk factors and other outcomes • Lipid-related measurements: LDL-C; HDL-C; triglycerides; non-HDL-C; ApoB; Lp (a); particle number (LDL-P); Apo A–1; and percent at lipid goal • BP-related measurements: systolic BP, diastolic BP, or hypertensive/nonhypertensive, and percent at BP goal • Incident hypertension
Setting	• Any geographic location • Any clinical or research setting • Any nontreatment setting

C. Literature Search Yield

A total of 42 systematic reviews and meta-analyses were identified that met I/E criteria and quality assessment requirements for CQ3. Of these, 16 studies were rated poor in quality assessment and were excluded from the final body of evidence for CQ3. Ten additional studies were rated fair, and 16 were rated good. Two studies were meta-analyses, and five were systematic reviews.

The CQ3 subcommittee members next identified the included systematic reviews and meta-analyses that contained detailed data on BP outcomes. They identified 11 studies with data on BP outcomes. Ten meta-analyses and one systematic review examined the effects of aerobic exercise. One study, a systematic review, looked at the effects of resistance training.

The CQ3 subcommittee members next identified the included systematic reviews and meta-analyses that contained detailed data on lipid outcomes. They identified 14 studies with data on lipid outcomes, including 10 meta-analyses and four systematic reviews.

The next step in the evidence review process for systematic reviews and meta-analyses was to develop evidence statements and recommendations from the included studies and present them to the full Lifestyle Workgroup for consideration and voting. Because these systematic review and meta-analysis articles each summarize evidence from a number of studies, NHLBI staff and Work Group members determined that the development of formal evidence tables and summary tables of individual articles was unnecessary. CQ3 subcommittee members developed evidence tables (CQ3 Summary Tables: Summary Table D–1: Aerobic Exercise and LDL-C, Summary Table D–2: Resistance Exercise and LDL-C, Summary Table D–3: Aerobic Exercise and HDL-C, and Summary Table D–4: Resistance Exercise and HDL-C) to summarize the evidence on physical activity and lipids.

D. CQ3 Evidence Statements

i. Physical Activity and Lipids

This section examines evidence supporting the use of physical activity alone (i.e., not in combination with other interventions, such as dietary interventions or weight loss) versus no physical activity or other type of intervention, for improvements in selected blood lipids (HDL-C, LDL-C, TG, and non-HDL-C. The 2008 *Physical Activity Guidelines Advisory Committee Report* was used as the starting point for evidence review.(106) Additionally, a systematic search identified eight recent (2001 onwards) meta-analyses and five systematic reviews rated fair to good that addressed this question and were included as the evidence base.

a. Aerobic exercise training and lipids

ES1. Among adults, aerobic physical activity, compared with control interventions, reduces LDL-C 3 to 6.0 mg/dL on average.

Strength of evidence: moderate

Rationale: Evidence from meta-analyses and systematic reviews was examined with regard to the effect of aerobic exercise on changes in LDL-C, along with conclusions of the Physical Activity Guidelines Advisory Committee.(106) A meta-analysis that included studies involving healthy adults ≥18 years of age or older showed a significant decrease in LDL-C of 6 mg/dL.(113) Studies involving only women ≥18 years of age showed a significant decrease in LDL-C of 4 mg/dL,(114) with the decrease in older adults being 4 mg/dL.(115) A nonsignificant decrease was observed in a meta-analysis of overweight and obese adults (3 mg/dL),(116) with a significant decrease of 6 mg/dL in a meta-analysis that included adults with type 2 diabetes.(117) In a meta-analysis of studies that included only patients with known CVD or who had undergone a medical procedure for CVD, a nonsignificant decrease in LDL-C of 8 mg/dL was observed.(118) These observed changes are present when exercise is ≥15 weeks in duration, >3 days per week, 35–50 minutes per session, at a vigorous intensity (>60 percent of maximal oxygen consumption). A systematic review also concluded that an average increase of 2,492 steps per day resulted in a significant reduction in LDL-C in outpatient adult studies.(119) However, other systematic reviews(120,121) have concluded that the effect of aerobic exercise on changes in LDL-C are inconsistent, with some studies showing a significant improvement in LDL-C and others not supporting these findings. The *Physical Activity Guidelines Advisory Committee Report* concluded that there is inconsistent

evidence of favorable improvements in LDL-C resulting from exercise.(106) While the results from 2 systematic reviews and the report of the Advisory Committee for the Physical Activity Guidelines for Americans are not consistent with the meta-analyses, the totality of the evidence suggests that there is a reduction in LDL-C from physical activity. This conclusion is based on the results from meta-analyses published between 2001 and 2011, which reported significant reductions in LDL-C with physical activity (113),(114),(115),(117); and an additional 2 meta-analyses that reported non-statistically significant reductions in LDL-C with physical activity that were of similar magnitude. Again, this conclusion is based on data from studies in which weight loss was not the primary outcome and when weight change was not ≥3%.

ES2. Among adults, aerobic physical activity alone, compared with control interventions, reduces non–HDL-C 6 mg/dL on average.

Strength of evidence: moderate

Rationale: Evidence from one meta-analysis was examined with regard to the effect of aerobic exercise on changes in non-HDL-C. This meta-analysis included studies involving healthy adults ≥18 years of age and showed a significant decrease in non-HDL-C of 6 mg/dL.(122) This observed change was present when aerobic exercise was 23 ±18 weeks in duration, 5 ±3 days per week, and 38 ±16minutes per session, at a vigorous intensity (65 ±9 percent of maximal oxygen consumption).

ES3. Among adults, aerobic physical activity alone, compared with control interventions, has no consistent effect on triglycerides.

Strength of evidence: moderate

Rationale: Evidence from five meta-analyses and four systematic reviews was examined with regard to the effect of aerobic exercise on TGs, along with a review of the conclusions of the Physical Activity Guidelines Advisory Committee.(106) A meta-analysis that included studies involving healthy adults ≥18 years of age showed that aerobic exercise led to nonsignificant increases in TGs of 0.2 mg/dL(122) and 1 mg/dL.(114) Studies involving only women ≥18 years of age showed a significant decrease of 4 mg/dL,(113) with the nonsignificant decrease in older adults being 7 mg/dL.(115) A significant decrease was observed in a meta-analysis of overweight and obese adults (16 mg/dL),(116) with a nonsignificant decrease of 10 mg/dL observed in a meta-analysis that included adults with type 2 diabetes.(117)

In a meta-analysis of studies that included only patients with known CVD or who had undergone a medical procedure for CVD, a significant decrease in TGs of –20 mg/dL was observed(118). These observed changes are present when exercise is ≥15 weeks in duration, >3 days per week, 35–50 minutes per session, at a vigorous intensity (>60 percent of maximal oxygen consumption). One systematic review(120) concluded that aerobic exercise has a consistent effect on reducing TG, whereas another systematic review concluded that the effect is inconsistent.(121) The *Physical Activity Guidelines Advisory Committee Report 2008* concluded that exercise results in favorable improvements in TGs.(106) A systematic review concluded that an average increase of 2,492 steps per day resulted in a nonsignificant decrease in TGs in outpatient adult studies.(119) These findings also show no deleterious effect of physical activity on triglycerides.

ES4. Among adults, aerobic physical activity alone, compared with control interventions, has no consistent effect on HDL-C.

Strength of evidence: moderate

Rationale: Evidence from eight meta-analyses and three systematic reviews published between 2001 and 2011 was examined with regard to the effect of aerobic exercise on changes in HDL-C, along with conclusions of the Physical Activity Guidelines Advisory Committee.(106) Meta-analyses that included studies involving healthy adults ≥18 years of age showed nonsignificant increases in HDL-C of 1mg/dL(114),(122). One meta-analysis of adults (≥20 years of age) that excluded studies in which participants may have been taking medication or prescribed a diet that may have influenced HDL-C reported a significant increase of 3 mg/dL.(118) Studies involving only women ≥18 years of age showed a significant increase of 2 mg/dL,(113) with the increase in older adults being 3 mg/dL.(115) A nonsignificant increase was observed in meta-analysis of overweight and obese adults (2 mg/dL),(116) with a nonsignificant increase of 1 mg/dL observed in a meta-analysis that included adults with type 2 diabetes.(117) In a systematic review of studies that included only patients with known CHD who engaged in exercise-based cardiac rehabilitation, a nonsignificant decrease in HDL-C of –1.9 mg/dL was observed.(123)

The observed changes in HDL-C reported in meta-analyses are present when exercise is ≥15 weeks in duration, >3 days per week, 35–50 minutes per session, at a vigorous intensity (>60 percent of maximal oxygen consumption). Systematic reviews(120,121) have concluded that the effect of aerobic exercise on increases in HDL-C are consistent, and the *Physical Activity Guidelines Advisory Committee Report 2008* concluded that exercise results in favorable improvements in HDL-C.(106) A systematic review concluded that an average increase of 2,492 steps per day resulted in a nonsignificant increase in HDL-C in outpatient adult studies.(119)

The conclusion of no inconsistent effect of physical activity on change in HDL-C may be a result of differences in patient demographics among the studies included in the meta-analyses and systematic reviews, the inability to examine meta-analyses or systematic reviews published prior to 2001 which may have limited the inclusion of earlier studies that showed a favorable influence on physical activity on HDL-C, or the insufficient dose of physical activity in some studies that would influence a change in HDL-C. These findings also show no deleterious effect of physical activity on HDL-C.

b. Resistance exercise training and lipids

ES5. Among adults, resistance training, compared with control interventions, reduces LDL-C, triglycerides, and non–HDL-C by 6 to 9 mg/dL on average and has no effect on HDL-C. Typical interventions shown to reduce LDL-C, triglycerides, and non-HDL-C and to have no effect on HDL-C include resistance physical activity programs that average 24 weeks' duration and include ≥3 days per week, 9 exercises performed for 3 sets and 11 repetitions at an average intensity of 70 percent of 1 maximal repetition.

Strength of evidence: low

Rationale:

LDL-C: Evidence from one meta-analysis and one systematic review was examined with regard to the effect of resistance exercise on changes in total cholesterol. The meta-analysis that included studies involving healthy adults ≥18 years of age showed a significant decrease in LDL-C of 6.1 mg/dL.(124) These observed changes are present when resistance exercise was 24±19weeks in duration and involved 2.9±0.4 days per week of exercise, with the average session lasting 48±12 minutes. Specifics of the resistance exercise sessions included performing 9±3different exercises, and engaging in 3 ±1sets of 12±7 repetitions for these exercises. The

intensity was 70 ±10 percent of one maximal repetition. A systematic review of the literature for the effects of resistance exercise on change in LDL-C in patients with type 2 diabetes concluded that studies generally showed an improvement in LDL-C with this form of exercise.(125) The resistance exercise in these studies was typically performed over a range of 4 weeks to 12 months and was typically performed 3 days per week. The dose of resistance exercise varied between the studies, with less detail provided in the systematic review.

Triglycerides: Evidence from one meta-analysis and one systematic review was examined with regard to the effect of **resistance exercise** on changes in lipids. The meta-analysis that included studies involving healthy adults ≥18 years of age showed a significant decrease in triglycerides of 8.1 mg/dL.(126) These observed changes are present when resistance exercise was 24.0±19.0 weeks in duration and involved 2.9±0.4 days per week of exercise with the average session lasting 48±12 minutes. Specifics of the resistance exercise sessions included performing 9.2±3.1 different exercises, and engaging in 3±1sets of 12±7 repetitions for these exercises. The intensity was 70±10percent of 1 maximal repetition. A systematic review of the literature for the effects of resistance exercise on change in triglycerides in patients with type 2 diabetes concluded that studies generally showed an improvement in triglycerides with this form of exercise.(125) The resistance exercise in these studies was typically performed over a range of 4 weeks to 12 months and was typically performed 3 days per week. The dose of resistance exercise varied between the studies with less detail provided in the systematic review.

Non-HDL-C: Evidence from one meta-analysis was examined with regard to the effect of **resistance exercise** on changes in non-HDL-C that included studies involving healthy adults ≥18 years of age, with results showing a significant decrease in non-HDL-C of 9 mg/dL.(126) These observed changes are present when resistance exercise was 24±19weeks in duration and involved 3 days per week of exercise with the average session lasting 48±12 minutes. Specifics of the resistance exercise sessions included performing 9±3different exercises, and engaging in 3±1 sets of 12±7 repetitions for these exercises. The intensity was 70±10percent of 1 maximal repetition.

HDL-C: Evidence from one meta-analysis and one systematic review was examined with regard to the effect of resistance exercise on changes in total cholesterol. The meta-analysis that included studies involving healthy adults ≥18 years of age showed a nonsignificant increase in HDL-C of 1mg/dL.(124) These observed changes are present when resistance exercise was 24±19 weeks in duration and involved 3 days per week of exercise, with the average session lasting 48±12 minutes. Specifics of the resistance exercise sessions included performing 9±3 different exercises and engaging in 3±1 sets of 12±7 repetitions for these exercises. The intensity was 707±10 percent of one maximal repetition. A systematic review of the literature for the effects of resistance exercise on change in HDL-C in patients with type 2 diabetes concluded that studies generally showed an improvement in HDL-C with this form of exercise.(125) The resistance exercise in these studies was typically performed over a range of 4 weeks to 12 months and was typically performed 3 days per week. The dose of resistance exercise varied between the studies, with less detail provided in the systematic review.

ii. Physical Activity and Blood Pressure

This section examines evidence supporting the use of physical activity alone (i.e., not in combination with other interventions, such as dietary interventions or weight loss) versus no physical activity or other types of intervention for BP reduction. The *Physical Activity Guidelines Advisory Committee Report 2008* was used as the starting point for evidence review.(106) Additionally, a systematic search identified 15 recent (2001 onwards) meta-analyses and reviews rated fair to good that addressed this question. Details of the search are provided in CQ3 search strategy).(123,127-139) Four of these were not used because: one examined a combination of exercise and diet versus usual recommendations;(137) one examined lifestyle counseling—as

opposed to intervention directly targeting physical activity—versus no counseling for blood pressure reduction;(135) one was a meta-analysis of observational studies, rather than RCTs;(129) and the relevant data from one review were obtained from a cross sectional study.(133) The remaining 11 meta-analyses and reviews were used as the basis for the evidence statements below.

a. Aerobic exercise training and blood pressure

ES1. Among adult men and women at all BP levels, including individuals with hypertension, aerobic physical activity decreases systolic and diastolic BP, on average by 2–5 and 1–4 mm Hg, respectively. Typical interventions shown to be effective for lowering BP include aerobic physical activity of, on average, at least 12 weeks' duration, 3 to 4 sessions per week, lasting on average 40 minutes per session and involving moderate- to vigorous-intensity physical activity.

Strength: high

Rationale: The 2008 Physical Activity Guidelines Advisory Committee reviewed the data from 10 meta-analyses and concluded that: "Both aerobic and progressive resistance exercise yields important reductions in systolic and diastolic BP in adult humans, although the evidence for aerobic exercise is more convincing. Traditional aerobic training programs of 40 minutes of moderate-to-high intensity exercise three to five times per week that involve more than 800 metabolic equivalent of task (MET)-minutes of aerobic exercise per week appear to have reproducible effects on BP reduction."(106) It is worth noting that the 2008 Physical Activity Guidelines Advisory Committee primarily focused on hard clinical endpoints, such as CVD, and BP was considered a secondary endpoint. Thus, evidence for physical activity and BP reduction was obtained from a search of reviews on the topic, with no assessment of the quality of the reviews used. For example, the committee placed emphasis on the most recent and inclusive meta-analysis,(140) which was not included in the present review because it was ranked "poor" in the current search strategy. Nonetheless, the conclusions of the Physical Activity Guidelines Advisory Committee Report 2008 are congruent with the conclusions from the present review, whose rationale is described in detail below.

For the present review of the meta-analyses and reviews rated fair to good that were identified in the systematic search described above for CQ6a, the largest was by Whelton et al.,(139) who conducted a meta-analysis that combined data from 54 RCTs lasting at least 2 weeks and included 2,419 subjects. The median trial duration was 12 weeks, and the average resting BP at baseline was 127/77. Three trials included patients on anti-hypertensives. Among all subjects, the average reductions in systolic and diastolic BP were 4 (3–5) and 3 (2–3) mmHg, respectively. When only trials with supervised exercise were included, larger reductions of 4 and 3 mmHg were observed.

Weight change in the intervention group was small (median: –0.4 kg; p=0.09). Among normotensive subjects, the corresponding reductions were 4 (3–5) and 2 (2–3) mmHg, respectively; among hypertensive subjects, reductions were 5 (3–7) and 4 (2–6) mmHg, respectively. There were no significant differences in the reductions achieved among: White, African American, or Asian subjects (p>0.2); among persons with different BMI (<24.5, 24.5–26.4, or >26.4 kg/m^2; p=0.12); or among persons with different net weight change during the trial (<–1.5, –1.5 to +0.2, or >0.2 kg; p>0.2). The characteristics of the training program did not predict BP change; shorter trials tended to show larger effects than longer trials (<10, 10–24, or >24 weeks; p=0.05). Because compliance typically declines with longer trial duration, this suggests that exercise needs to be sustained for BP reduction.

In addition to this meta-analysis, other meta-analyses have reached similar overall conclusions. Additional information provided by these other meta-analyses relates to:

- Specific modalities of exercise: walking and qigong (a practice of aligning breath, movement, and awareness for exercise, healing, and meditation);(128,131,134,136)
- Specific subgroups: older persons, postmenopausal women, and patients with CHD or type 2 diabetes.(123,127,130,132,138)

Two meta-analyses specifically examined walking interventions. Kelley et al.(131) pooled data from 16 studies and 650 subjects. Intervention subjects, whose baseline resting BP averaged 128/80, experienced significant decreases in systolic and diastolic BP of 3 (2–5) and 2 (1–3) mmHg, respectively. The average intervention was 25 weeks' duration, with intervention subjects walking 4 days per week for 42 minutes each day, at 63 percent of VO_2 max. Murphy et al.(136) also examined 24 RCTs of walking with 1,128 subjects in relation to cardiovascular risk factors. The average intervention was 35 weeks' duration, with intervention subjects walking 4days per week for 38 minutes each day, at 56 percent of VO_2 max. For the outcome of BP, data from nine studies with 356 total subjects were pooled. Subjects were primarily women (88 percent in the BP studies), and the baseline resting BP averaged 127/78. The pooled data showed that walking was not related to systolic BP change (–1 mmHg; p=0.32) but was related to diastolic BP change (–2 mmHg; p=0.03).

Two meta-analyses addressed qigong compared to no intervention (wait-list control), conventional aerobic exercise, or drug treatment with regard to BP, with several of the same trials used in both meta-analyses.(128,134) The data are limited because of the small number of studies included and the small number of subjects in each trial (e.g., a total of 130 subjects in the qigong, versus no intervention in Guo et al. 2008,(128) and 94 in Lee et al. 2007,(134) yielding results with wide confidence intervals. Investigators reported that qigong significantly reduced both systolic and diastolic BP compared with no intervention, but not compared with drug treatment or conventional aerobic exercise (jogging 4–5 km per day in one study; "exercise" 120 minutes per day, 2 days per week in another).

With regard to specific population groups, a meta-analysis examined data from RCTs of aerobic exercise training versus no exercise among persons aged ≥50 years.(132) A total of seven trials with 802 subjects were included; the mean age was 68.5 years. Initial mean BP was 128/77 in the intervention group. The average intervention was 35 weeks' duration, 3 days per week for 40 minutes each day, at 63 percent of VO_2 max. Exercise reduced systolic BP by 2 (1–4) mmHg; the reduction in diastolic BP was of borderline significance (change: –1 (–2 to 0) mmHg). There was no significant effect in changing the BMI of subjects.

A qualitative review of RCTs of exercise and BP in postmenopausal women provided mixed results.(127) Seven trials involving 976 women were reviewed. Aerobic exercise had no effect on BP in normotensive women; however, compliance with exercise sessions was only moderate (73 percent).

Among patients with CVD, Taylor et al.(123) pooled data from RCTs lasting ≥6 months of exercise-based cardiac rehabilitation versus comparison groups that did not involve exercise, but could include standard care involving drugs. For systolic BP, eight trials with a total of 744 patients were included; exercise-based cardiac rehabilitation (that also may have included targeting other risk factors such as diet, stress management, smoking, and group support) resulted in a decrease of 3 (1–5) mmHg. For diastolic BP, five trials with 482 patients were included. There was a decrease of 1.18 mmHg that was not statistically significant, possibly a consequence of the smaller sample (change: –1 (–3 to +0.32) mmHg). Jolly et al.(130) compared home-based cardiac rehabilitation with supervised rehabilitation. Based on only two studies, investigators found no significant difference with respect to systolic BP change with either type of program.

There are limited data on the effect of physical activity on BP in patients with type 2 diabetes. A meta-analysis examined this question, and included four RCTs with 127 patients for systolic BP, and three trials with 78 patients for diastolic BP.(138) Comparing exercise to no intervention, systolic BP decreased by 4.16 mmHg,

which is not statistically significant (change: –4 (–10 to +1.14) mmHg); diastolic BP showed little change (change: –0.13 (–4 to +3) mmHg).

Thus, although not all individual meta-analyses observed statistically significant decrements in systolic and diastolic BP with exercise—which likely are due to small total sample size (e.g., Thomas et al. 2006(138); 127 and 78 patients for systolic and diastolic BP data) or limited compliance (e.g., Asikainen et al. 2004(127))—the overall totality of evidence provides strong support for a role for aerobic exercise training in reducing BP.

b. Resistance exercise training and blood pressure

The 2008 Physical Activity Guidelines Advisory Committee focused on data from a meta-analysis of nine RCTs of resistance training that included 341 subjects.(141) However, in the systematic search described above for CQ3, given the limited parameters of the search, only one review was identified. A qualitative review of clinical trials—randomized, nonrandomized, and uncontrolled studies—examined resistance exercise training in relation to metabolic health among patients with type 2 diabetes.(125) Ten of these studies assessed BP. Investigators concluded that resistance exercise training resulted in beneficial changes in systolic BP, with benefits in diastolic BP less frequently observed. (The magnitude of reduction was not specified.)

Thus, the review of evidence did not provide consistent evidence on resistance exercise training for BP reduction.

c. Combination of aerobic and resistance exercise training and blood pressure

There have been no published meta-analyses or reviews specifically examining the effect of a combined regimen of aerobic exercise and resistance training on BP. However, in some of the meta-analyses and reviews described above, studies with aerobic and resistance components were included in pooled data related to aerobic exercise training.(127,138)

E. Physical Activity Recommendations

Lipids

1. In general, advise adults to engage in aerobic physical activity to reduce LDL-C and non-HDL-C: 3 to 4 sessions per week, lasting on average 40 minutes per session, and involving moderate- to vigorous-intensity physical activity.

   Grade: B (moderate)

Rationale: This recommendation was based on evidence from meta-analyses and reviews published from 2001 onwards and rated fair to good. This is also consistent with the findings of the literature review conducted for the *Physical Activity Guidelines Advisory Committee Report 2008*, in which it was found that it may require 12 MET (Metabolic Equivalent**)** -hours per week of exercise to favorably influence LDL-C. The amount of physical activity recommended above for reducing LDL-C and non-HDL-C is congruent with the amount of physical activity recommended in 2008 by the Federal Government for overall health: "Most health benefits occur with at least 150 minutes (2 hours and 30 minutes) a week of moderate intensity physical activity, such as brisk walking. Additional benefits occur with more physical activity."(142)

Blood pressure

2. In general, advise adults to engage in aerobic physical activity to lower BP: 3 to 4 sessions per week, lasting on average 40 minutes per session, and involving moderate- to vigorous-intensity physical activity.

   Grade: B (moderate)

Rationale: This recommendation was based on evidence from meta-analyses and reviews rated fair to good which were published from 2001 and later, as well as the *Physical Activity Guidelines Advisory Committee Report 2008*. The amount of physical activity recommended above for lowering BP is congruent with the amount of physical activity recommended in 2008 by the Federal Government for overall health: "Most health benefits occur with at least 150 minutes (2 hours and 30 minutes) a week of moderate intensity physical activity, such as brisk walking. Additional benefits occur with more physical activity."(143) It is worth noting that the present recommendation is congruent (i.e., expends approximately the same amount of energy), but not identical to the 2008 Federal guidelines. This is because the present recommendation is based on a review of meta-analyses of exercise in relation to BP *only* (hence, the specific regimens as used in the clinical trials), while the 2008 Federal guidelines targeted *overall* health (i.e., not just BP). Additionally, the 2008 Federal guidelines for overall health make it clear that any amount of physical activity is healthful ("Some physical activity is better than none"), and that there is a dose-response relationship ("For most health outcomes, additional benefits occur as the amount of physical activity increases through higher intensity, greater frequency, and/or longer duration").

F. Heart Healthy Nutrition and Physical Activity Behaviors

Overall, the Workgroup encourages heart healthy nutrition and physical activity behaviors for the entire adult population as stated in the *Dietary Guidelines for Americans, 2010* and the *2008 Physical Activity Guidelines for Americans*. The recommendations in Exhibit 1 are a consensus of the Workgroup, not a guideline, and generally consistent with the *2010 Dietary Guidelines for Americans* and the *2008 Physical Activity Guidelines for Americans*.

Exhibit 1. Heart Healthy Nutrition and Physical Activity Behaviors

Heart-Healthy Nutrition and Physical Activity Behaviors

The adult population should be encouraged to practice heart-healthy lifestyle behaviors including:
• Consume a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils, and nuts; and limits intake of sweets, sugar-sweetened beverages and red meats.
  ▪ Adapt this dietary pattern to appropriate calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical conditions (including diabetes).
  ▪ Achieve this pattern by following plans such as the DASH dietary pattern, the USDA Food Pattern, or the American Heart Association Diet.
• Engage in 2 hours and 30 minutes per week of moderate-intensity, or 1 hour and 15 minutes (75 minutes) per week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic physical activity. Aerobic activity should be performed in episodes of at least 10 minutes, preferably spread throughout the week.(143)
• Achieve and maintain a healthy weight. Refer to the 2013 Overweight and Obesity Expert Panel Report for recommendations on weight loss and maintenance (144).

8. Gaps in Evidence and Future Research Needs

A. Diet

- Interaction between dietary modification and statin treatment
- Relative effects of SFAs, MUFAs, PUFAs, *trans* fatty acids, omega–3 fatty acids and the type of carbohydrates on lipids, inflammation, microbiome, and other newer, potential CVD risk factors
- Relative effects of naturally occurring fiber (cereal [whole grains] and vegetable/fruit) and supplemental fiber on lipids, inflammation, microbiome, and other newer, potential CVD risk factors
- Effects of dietary cholesterol on LDL-C and HDL-C over the current ranges of cholesterol and saturated fat intakes (5th and 95th percentiles)
- Effects of minerals in combination other than sodium on BP
- Studies of HDL function in studies that modify HDL-C by changes in diet
- Is the minimal effect of dietary CHO on plasma triglycerides harmful?
- The effect of sodium reduction in patients with diabetes, heart failure, and chronic kidney disease
- Effect of dietary pattern and sodium intake in adults taking BP and/or lipid-lowering medications (effects on BP/lipids; achieving BP/lipid goals; medication needs/costs; outcomes).
- Effect of dietary pattern and sodium intake in adults with CVD (e.g., post-MI; post-stroke; with CAD, heart failure, chronic kidney disease)
- Strategies for effectively (and cost-effectively) implementing these evidence-based recommendations. How can primary care providers, health systems, public health agencies, local and Federal Government, community organizations, and other stakeholders help patients adopt these diet and sodium intake recommendations?

Increased understanding of racial/ethnic/socioeconomic factors that may influence (a) effect of dietary pattern and sodium on BP and lipids; (b) adoption of diet/sodium recommendations; and (c) method of diet assessment.

B. Physical Activity

- The results from recent meta-analyses and systematic reviews demonstrate that exercise, when performed at a sufficient dose and intensity, will reduce LDL-C and non-HDL-C. However, additional research is needed to understand the pattern of exercise that may be associated with the reduction in LDL-C and non-HDL-C, which may lead to improved understanding of whether exercise performed at a lower intensity or dose, or whether different modes of exercise, can impact these outcomes. It is also important to further understand the characteristics of individuals for whom exercise of a certain dose and/or intensity can reduce LDL-C and non-HDL-C.
- The results from recent meta-analyses and systematic reviews show inconsistent effects of exercise on HDL-C and TGs. It is important to understand the source of these inconsistent findings to better understand under what conditions exercise can increase HDL or decrease TGs. This may include additional research to understand the optimal dose that will result in the desired changes in these outcomes, or whether exercise

performed at a lower intensity or dose, or whether different modes of exercise, can impact these outcomes. It is also important to further understand the characteristics of individuals for whom exercise of a certain dose, intensity, or mode can increase HDL-C or reduce TGs.

- Although the data are clear in showing that physical activity lowers BP, most of the evidence comes from studies of Caucasian persons, with limited data on ethnic minorities. Additionally, it is unclear what specific aspects of an aerobic exercise program (i.e., length of program; frequency, duration, and intensity of physical activity) are related to greater reductions in BP; that is, it is unclear what the shape of the dose-response curve between physical activity and BP is. Further, there are limited data on whether resistance exercise training lowers BP, and whether a combination of aerobic and resistance exercise training offers any added BP lowering, compared to aerobic exercise only.
- Additional research is needed combining diet and physical activity regarding lipids and BP to determine how these behave synergistically.
- Effect of physical activity in adults taking BP and/or lipid-lowering medications (effects on BP/lipids; achieving BP/lipid goals; medication needs/costs; outcomes).
- Effect of physical activity in adults with CVD (e.g., post-MI; post-stroke; with CAD, heart failure, chronic kidney disease)
- Strategies for effectively (and cost-effectively) implementing these evidence-based recommendations. How can primary care providers, health systems, public health agencies, local and Federal Government, community organizations, and other stakeholders help patients adopt these physical activity recommendations?
- Increased understanding of racial/ethnic/socioeconomic factors that may influence (a) effect of physical activity on BP and lipids; and (b) adoption of physical activity recommendations.

9. Appendices

Appendix A.
Methods for Lifestyle Questions

Appendix A. Methods for Lifestyle Questions

i. Description of How Panel/Workgroup Members Were Selected

The NHLBI initiated a public call for nominations for Workgroup 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 Web site for several weeks and was also distributed to a Guidelines Leadership Group that 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 the close of the call for nominations, 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 persons being considered as chairs and co-chairs. The selected chairs then were formed into a Guidelines Executive Committee, which worked with the NHLBI to select Panel members from the list of nominees.

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 including primary care, nursing, pharmacology, nutrition, exercise, behavioral science, epidemiology, clinical trials, research methodology, evidence-based medicine, guideline development, guideline implementation, systems of care, or informatics. The Panels also include, as voting ex officio members, senior scientific staff from the NHLBI and other Institutes from the National Institutes of Health (NIH) who are recognized experts in the topics under consideration.

ii. Development and Prioritization of 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, primary care providers.

Proposed questions and topic areas were collected from Panel members over a period of several months. The number of critical questions was scoped, and questions were prioritized based on resource constraints. After group discussion, Panel members ranked priority critical questions through a combination of collaborative dialogue and voting. The rationale for each priority critical question is in the main body of the report.

With support from the methodologist and systematic review team, priority critical questions were formulated. I/E criteria were defined and formatted using the PICOTS framework. PICOTS is a framework for developing a structured research question. It includes the following components in the statement of the critical question or in the question's I/E criteria:

P Population
I Intervention, Exposure
C Comparator
O Outcome
T Timing
S Setting

I/E criteria define the parameters for the selection of literature for a particular critical question. I/E criteria were developed with input from the methodologist and systematic review team to ensure that criteria were clear and precise and could be applied consistently across literature identified in the search.

The final critical questions and criteria were submitted to the Literature Search team for search strategy development.

iii. 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 CVD risk reduction. Citations were acquired from the 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, Collexis, and Lucene. These engines were used for executing search strategies, and Lucene was used in correlating the search with screening results.

For every critical question, 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 specifying population, intervention, comparator, outcomes, timing, settings, and study design. The question and PICOTS components were translated into a search strategy involving Boolean and conceptual queries.

A Boolean query encodes both inclusion and exclusion 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 that was conducted by two independent reviewers 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 in support of application of I/E criteria. Frequently extracted and utilized data elements were study size and intervention followup 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 utilizes 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 the revised search strategy produced citations that did not undergo the screening process, then a new batch of citations was added for 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 search strategy was reviewed by the methodologist and Workgroup members, and was available for viewing and printing at any time by Workgroup members and staff collaborating on the systematic review. It was available for execution and supplying literature updates until the literature search and screening cut-off date.

Search strategies for a sample of questions were validated by an independent methodology team. This validation process involved the methodology team developing and executing a separate search strategy and screening a random sample of citations against I/E criteria; these results were compared to the search and screening results developed by the systematic review team. As an additional validation method, studies identified in systematic reviews and meta-analyses were cross-checked against a critical question's "include" list to ensure completeness of the search strategy.

iv. Process for Literature Review and Application of I/E Criteria

Using results from the search strategy, criteria were applied to screen literature for inclusion or exclusion in the evidence base for the critical question. I/E criteria address the parameters in the PICOTS framework and determine what types of studies are eligible and appropriate to answer the critical question. Additional criteria such as sample size restrictions were included by the Panel to fit the context of the critical question.

a. 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. Reviewers compared their results to ensure that I/E criteria were applied consistently. Discrepancies in votes were discussed, and clarification on criteria was sought from the Panel where appropriate. For example, if criteria were not specific enough to be clearly applied to include or exclude a citation, guidance was sought to more explicitly word criteria.

During this phase, reviewers provided feedback to the Literature Search team about the relevance of search strategy results; this feedback was used to further refine and optimize the search.

Phase 1: Title and abstract screening phase

After the completion of 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.

Titles and abstracts where one or both reviewers voted to include the publication advanced to Phase 2, Full-Text Screening. Titles and abstracts where both reviewers voted to exclude were excluded and not reviewed further; these citations were maintained in the VCW and marked as "excluded at title/abstract phase."

Phase 2: Full-text screening phase

Titles and abstracts where at least one reviewer voted to include were reviewed at the full-text level in phase 2. In this phase, two reviewers independently applied I/E criteria to the full-text article and voted for "include," "exclude," or "undecided." The reviewer had to specify the rationale for exclusion (i.e., population, intervention, etc.) in this phase.

Articles where both reviewers voted to include were moved to the "include" list. Articles where 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. Any article with discrepant votes (i.e., one include and one undecided, one include and one exclude, etc.) advanced to phase 3.

Phase 3: Resolution and consultation phase

In this phase, reviewers discussed their vote for "include," "exclude," or "undecided" and cited the relevant criteria for their decision. The two reviewers attempted to achieve consensus through collaborative discussion. If a decision was not reached between the two reviewers, input was sought from the methodologist. If a decision was not reached after consultation with the methodologist, input was sought from 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 critical question were maintained in the VCW with their reviewer voting status and all collected comments.

v. Quality Assessment of Individual Studies

The methodology team assessed the quality (internal validity) of all studies meeting the I/E criteria after the three-phase literature review process. Separate quality rating tools were used for each study design.

a. Design of the quality assessment tools

Appraisal of individual study quality was based on tailored quality assessment tools developed jointly by the NHLBI and Research Triangle International methodologists. The tools were based on quality assessment methods, concepts, and other tools developed by researchers in the Agency for Healthcare Research and Quality (AHRQ) Evidence-Based Practice Centers (EPCs), the Cochrane Collaboration, the U.S. Preventive Services Task Force, the Scottish Intercollegiate Guidelines Network, and the National Health Service Centre for Reviews and Dissemination, as well as consulting epidemiologists and others working in evidence-based medicine, with adaptations by methodologists and NHLBI staff for this project.

The tools were designed to assist reviewers in focusing on key concepts for critical appraisal of the internal validity of a study. The tools were not designed to provide a list of factors comprising a numeric score. The tools were specific to individual types of included study designs and are described in more detail below.

The tools included items for evaluating potential flaws in study methods or implementation, including sources of bias (e.g., patient selection, performance, attrition, and detection), confounding, study power, the strength of causality in the association between interventions and outcomes, and other factors. Quality reviewers could select "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 selected, reviewers were instructed to consider the potential risk of bias that could be introduced by that flaw in the study design or implementation. CD and NR were also noted as representing potential flaws.

Each of the quality assessment tools had a detailed guidance document, also developed by the methodology team and the NHLBI. The guidance documents were specific to each tool and provided more detailed descriptions and examples of application of the items, as well as justifications for each item's inclusion. For some items, examples were provided to clarify the intent of the question and the appropriate rater response. Copies of the six quality assessment tools and guidance documents are included in Tables A–1 through A–4 below.

b. Significance of the quality ratings of good, fair, or poor

Reviewers used the study rating tools on the range of items included in each tool to judge each study to be of "good," "fair," or "poor" quality. The ratings on the different items were used by the reviewers 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, and results are considered to be 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 critical question. The only exception allowed was if there was no other evidence available, then poor quality studies could be considered. However, this exception was not applied in this project because there were no situations found where only poor quality studies were available for a body of evidence for a particular critical question.

c. Training for application of the quality assessment tools

The methodology team conducted a series of training sessions on the use of four of the quality assessment tools. Initial training consisted of two 2-day, in-person training sessions. Training sessions provided instruction on 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 engaged in interactive evaluation of multiple example articles, both with the instructors and during group work. Reviewers were also instructed to refer to related articles on study methods if such papers were cited in the articles being rated.

Following the in-person training sessions, the methodology team assigned several articles with pertinent study designs to test the abilities of each reviewer. The reviewers were asked to individually identify the correct study design, complete the appropriate quality assessment tool, and submit it to the methodology team for grading against a methodologist-developed key. A second round of training sessions was then conducted via telephone to review the results and resolve any remaining misinterpretations. Based on the results of these evaluations, a third round of exercises and training sessions was sometimes convened.

The before-after and case series studies quality assessment tools were only applied for the Obesity Panel's CQ5 , which addresses bariatric surgery interventions. This CQ included those types of study designs due to the different types of issues addressed for this surgical intervention. As a result, a formal training program for use of these quality assessment tools was not conducted. The training efforts were more individual, focused on reviewing the tool and guidance document with staff working on quality assessment for this CQ.

d. Quality assessment process

For all studies except systematic reviews and meta-analyses, each article that met the CQ's inclusion criteria was independently rated for quality by two reviewers using the appropriate tool. If the ratings differed, the

reviewers discussed the article in an effort to reach consensus. If consensus was not achieved, the article was forwarded to a methodologist for quality adjudication.

Quality rating of systematic reviews and meta-analyses was performed independently by two methodologists. If ratings differed, reviewers discussed the article in an effort to reach consensus. When consensus was not achieved, the article was forwarded to a third methodologist for adjudication.

Panel members could appeal the quality of a particular study or publication, subsequent to the initial rating reported to the Panel members. However, to enhance the objectivity of the quality rating process, the final decision on quality ratings was made by the methodology team, and not by Panel members.

e. Quality assessment tool for controlled intervention studies

The quality assessment tool for controlled intervention studies is included below in Table A–1. The guidance document for that tool is also included in Table A–1. This tool was developed by the methodology team and the NHLBI based in part on criteria from AHRQ's Evidence-Based Practice Centers, the USPSTF, and the National Health Service Centre for Reviews and Dissemination.

This tool addresses 14 elements of quality assessment. They include randomization and allocation concealment, similarity of compared groups at baseline, use of intention-to-treat (ITT) analysis (i.e., all patients randomized were analyzed even if some were lost to followup), adequacy of blinding, the overall percentage of subjects lost to followup, the differential rates of loss to followup between the intervention and control groups, and other factors.

f. Quality assessment tool for systematic reviews and meta-analyses

The quality assessment tool for systematic reviews and meta-analyses is included below in Table A–2. The guidance document for that tool is also included in Table A–2. This tool was developed by the methodology team and the NHLBI based in part on criteria from AHRQ's Evidence-Based Practice Centers and the Cochrane Collaborative.

This tool addresses eight elements of quality assessment. They include the use of prespecified eligibility criteria, the 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.

g. Quality assessment tool for cohort and cross sectional studies

The quality assessment tool for cohort and cross sectional studies is included below in Table A–3. The guidance document for that tool is also included in Table A–3. This tool was developed by the methodology team and the NHLBI based in part on criteria from AHRQ's Evidence-Based Practice Centers, the U.S. Preventive Services Task Force, consultation with epidemiologists, and other sources.

This tool addresses 13 elements of quality assessment. They include the clarity of the research question or research objective; the definition, selection, composition, and participation of the study population; the definition and assessment of exposure and outcome variables; the measurement of exposures prior to outcome assessment; the study timeframe and followup; study analysis and power; and other factors.

h. Quality assessment tool for case-control studies

The quality assessment tool for case-control studies is included below in Table A–4. The guidance document for that tool is also included in Table A–4. This tool was developed by the methodology team and the NHLBI

based in part on criteria from AHRQ's Evidence-Based Practice Centers, consultation with epidemiologists, and other factors.

This tool includes 12 items for assessment of study quality. They include the clarity of the research objective or research question; the definition, selection, composition, and participation of the study population; definition and assessment of case or control status; exposure; outcome variables; use of concurrent controls; confirmation that the exposure occurred prior to the outcome; statistical power; and other factors.

Table 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?			
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, comorbid 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 intention-to-treat 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

vi. Guidance for Assessing the Quality of Controlled Intervention Studies

Descriptions by question number in the controlled intervention study tool:

Question 1. Described as randomized

Literally, was the study described as randomized? A study does not satisfy quality criteria as randomized simply because the authors call it *randomized*. But as a first step, did the authors of the study say it was randomized?

Questions 2 and 3. Treatment allocation—two interrelated pieces

- Adequate randomization: The 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).

Inadequate randomization: "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, then the answer is *no*.

There may be some tricky scenarios that will require careful reading and consideration for the role of chance in assignment. For example, sites are randomized to receive treatment or not so all individuals at the site are thereby assigned to a treatment group. This scenario was used for group-randomized trials (GRTs), which can be truly randomized, but often are "quasi-experimental" studies with comparison groups rather than true control groups. (We anticipate few if any GRTs in this evidence review.)

- 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. 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, etc.

Questions 4 and 5. Blinding

Blinding means that one does not know to which group—intervention or control—the participant is assigned. It is also sometimes called "masking." You are looking to see if each of the following is blinded to knowledge of treatment assignment: the person 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.); the person receiving the intervention (e.g., the patient or volunteer participant); and the person 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 often be blinded only to the outcome assessors. Sometimes the person providing the intervention is the same person doing the outcome assessment. If so, make note of it in your comments section.

Question 6. Similarity of groups at baseline

This question relates to whether the intervention and control groups have similar characteristics on average. The whole point of doing a randomized trial is to create similar groups to enable valid comparisons of intervention effects between groups. If there is a significant difference, you should see it when you abstract baseline characteristics. 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. If you have any concerns about baseline difference in the groups, write them down in the comments section and consider them in your overall determination of the study quality.

Questions 7 and 8. Drop-out

By "drop-out" we mean participants for whom there are no endpoint measurements—the most common reason being that they dropped out of the study (for whatever reason) and were lost to followup.

Generally, an acceptable overall dropout rate is considered 20 percent or less of participants who were randomized/allocated into each group, and an acceptable *differential drop-out* is considered an absolute difference between groups of 15 percentage points at most (calculated by subtracting the drop-out rate of one group minus the drop-out rate of the other group). However, these are general rates. Higher overall drop-out rates may be acceptable. If you are conducting a systematic review on comparative efficacy on antidepressants, then setting the cap at 20 percent for overall drop-out makes sense. On the other hand, if you are looking at joint space narrowing for targeted immune modulators (TIMs), you may be able to raise the cap for what you define as an overall acceptable drop-out rate. Studies comparing TIMs for this outcome are going to be of longer duration, which means drop-outs are more likely. This is the kind of thing that should be decided by the experts for your systematic review. It may or may not be the same cap for all Panels for the NHLBI systematic reviews.

Differential drop-out, however, is not flexible. Stick with the 15 percent cap. If you have a differential drop-out rate of 15 percent or higher between arms, then you have serious potential for bias, and this constitutes a fatal flaw resulting in a *poor* quality rating for the study.

Question 9. Adherence

Did participants in each treatment group adhere to the protocols for assigned interventions? For example, if Group 1 was assigned to 10 mg/day of Drug A, did most of them take 10 mg/day of Drug A? Another example is a study evaluating the difference between a 30-pound weight loss and a 10-pound weight loss on specific clinical outcomes (say heart attacks), but the 30-pound weight loss group did not achieve its intended weight loss target. A third example is whether a large percentage of participants assigned to one group "crossed over" and got the intervention provided to the other group. A final example is when 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. Avoid other interventions

Changes that occur in the study outcomes being assessed should be attributable to the interventions being compared in the study. If participants in any of the groups receive other interventions that are not part of the study protocol and that could affect the outcomes being assessed, and they receive these interventions differentially, there is cause for concern, as it could bias the results. For example, if you had a study comparing two different dietary interventions on serum cholesterol, but one of the groups had a significantly higher percentage of participants taking statin drugs, it could unduly influence the results of the study because you would not know whether the difference in outcome was due to the dietary intervention or the drugs.

Question 11. Outcome measures assessment

What tools or methods were used to measure outcomes in the study? Were the tools/methods accurate and reliable—for example, have they been 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 whether the outcomes were

assessed in the same manner within groups and between groups. One example is that a self-report of dietary salt intake is not as valid and reliable as testing urine for sodium content. Another example is measurement of BP that only uses clinicians' usual measurement approaches rather than measurers being trained on a standard approach using the same instrument and taking BP multiple times. In each of these cases, the question would get a "no" for the former and a "yes" for the latter scenario. Another example of a "no" is when an intervention group is seen much more often, enabling more opportunities to report clinical events, than the control group.

Question 12. Power calculation

Generally, a paragraph in the methods section of the study will explain 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 anything about power.

Question 13. Prespecified outcomes

Outcomes reported in the study must have been prespecified in order to be hypothesis testing—which is the whole purpose of doing a RCT. If they are not prespecified, then the study may be reporting ad hoc analyses, simply looking for differences that support the findings they wanted. In addition to outcomes, the subgroups being examined should be prespecified in order to be considered hypothesis testing. 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. Intention-to-treat (ITT) 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 doing an ITT analysis preserves the reason for doing a randomized trial—that is, to compare groups that differ only in the intervention being tested. Once the ITT philosophy is not followed, you are not really sure that the main reason for doing an RCT is upheld as the groups being compared may no longer be the same. If a study does not use an ITT analysis, it should probably be rated as poor. However, if some other analysis is used and you think it is valid, explain in the "other" box of the quality review form. Some studies will use a *completers analysis* (analyzes only the participants that completed the intervention and the study), which introduces significant potential for bias. Characteristics of participants who do not complete the study are unlikely to be the same as those who do. The likely impact of participants who withdraw from the study treatment must be considered carefully. ITT analysis provides a more conservative (potentially less biased) estimate of effectiveness.

Some general guidance for determining the overall quality rating

The questions on the form are designed to help you focus on the key concepts for evaluating the internal validity of a study. They are not intended to create a list that you simply tally up to arrive at a summary judgment of quality.

Internal validity is the extent to which the results (effects) reported in a study can truly be attributed to the intervention being evaluated and not to flaws in the design or conduct of the study—in other words, the ability for the study to make causal conclusions about the effects of the intervention being tested. Any 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 throughout the questions above). High potential for risk of bias translates to a rating of poor quality.

Low potential for 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.)

Fatal flaws: If a study has a "fatal flaw," then risk of bias is significant and the study is of poor quality. Examples of fatal flaws in RCTs include high drop-out, high differential drop-out, no ITT analysis or/unsuitable statistical analysis (e.g., completers-only analysis).

Generally, when you evaluate a study, you will not see a fatal flaw, but you will find some risk of bias. By focusing on the concepts underlying the questions in the tool, you should ask yourself about the potential for bias in the study you are critically appraising. For any box where you check "no," you should ask what the potential for bias is as a result. That is, does this factor cause you to doubt the results that are reported in the study?

We can provide some background reading for you on critical appraisal, but the best approach is for you to think about the questions in the tool and how each tells you something about the potential for bias for any study. We are reluctant to give you general rules as each study has nuances. The more you familiarize yourself with the key concepts, the more comfortable you will be with critical appraisal.

We will provide you some examples of studies that fall into each of the categories: good/fair/poor. But again, these will be examples. Each study must be assessed on its own given the details that are reported.

Table 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 prespecified?			
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?			
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 meta-analyses.)			
Quality Rating (Good, Fair, or Poor):			
Reviewer #1 initials:	Reviewer #2 initials:		
Comments:			

*CD: cannot determine; NA: not applicable; NR: not reported

vii. Guidance for Quality Assessment of Systematic Reviews and Meta-Analyses

A systematic review is a study that attempts to answer a question by synthesizing the results of primary studies using strategies to limit bias and random error.(145-148) 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.

Systematic reviews 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 systematic review 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.

The guidance below is organized by question number from the companion tool for quality assessment of systematic reviews and meta-analyses.

Question 1. Focused question

The review should be based on a question that is clearly stated and well formulated. An example would be a question that uses the PICO (Population, Intervention, Comparator, and Outcome) format, with all the components clearly described.

Question 2. Eligibility criteria

The eligibility criteria used to determine whether studies were included or excluded from the review should be clearly specified and predefined. It should be clear to the reader why studies were included or excluded.

Question 3. Literature search

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 should supplement the electronic searches.

Additional search strategies that may be used to improve the yield include the following:

- 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 the grey literature, which includes technical reports and other papers from government agencies or scientific groups or committees, presentations and posters from scientific meetings, conference proceedings, unpublished manuscripts, etc. A search of the grey literature is important (whenever feasible) because sometimes only positive studies with significant findings are published in the peer-reviewed literature, which can bias the results of a review.

The literature search strategy should be described clearly in the review and be reproducible by others with similar results.

Question 4. Dual review for determining which studies to include and exclude

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. Disagreements between the reviewers should be resolved by discussion and consensus or with third party involvement. The process for review, including methods for adjudicating disagreements, should be clearly stated.

Question 5. Quality appraisal for 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, this should be done by at least two independent reviewers. However, because there is not one commonly accepted, standardized tool for rating the quality of studies, what we are looking for is that individual study quality was assessed, and details as to how this was done should be clearly stated by the authors.

Question 6. List and describe included studies

All of the included studies should be listed in the review, along with descriptions of their key characteristics. This can be presented in narrative or table format.

Question 7. Publication bias

Publication bias is when studies with positive results have a higher likelihood of being published, being published rapidly, being published in higher impact journals, being published in English, being published more than once, or being cited by others.(145,146) Publication bias can be linked to favorable or unfavorable treatment of research findings due to the investigators, editors, industry, commercial interests, or peer reviewers. A strategy that can minimize the potential for publication bias is to conduct a very comprehensive literature search that includes the strategies discussed in Question 3.

A funnel plot is a commonly used graphical method for detecting publication bias. The funnel plot is a scatter plot of component studies in a meta-analysis. The graph looks like a symmetrical inverted funnel if there is no significant publication bias.

The likelihood of publication bias should be assessed in the review. This can be done in a number of different ways, but an assessment should be conducted and clearly described.

Question 8. Heterogeneity

Heterogeneity is used to describe important differences in the included studies of a meta-analysis that may make it inappropriate to combine the studies.(147) Heterogeneity can be clinical (e.g., important differences between study participants, baseline disease severity, 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).

Clinical or methodological heterogeneity is usually assessed qualitatively by determining whether it makes sense to combine studies.

For example:

- Should a study evaluating the effects of an intervention on CVD risk that involves elderly male smokers with hypertension be combined with a study that involves healthy adults age 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 and 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.

An assessment for heterogeneity should be conducted and clearly described. If the studies are found to be heterogeneous, the investigators should explore and explain the causes of the heterogeneity, and they should determine what influence, if any, the study differences had on the overall study results.

Table 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. Were sample size justification, power description, or variance and effect estimates provided?			
5. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
6. Was the timeframe 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 followup 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

viii. Guidance for Assessing the Quality of Cohort and Cross Sectional Studies

The descriptions below are by question number from the cohort and cross sectional study quality assessment tool.

Question 1. Research question

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. Study population

Did the authors describe the group of people from which the study participants were selected or recruited, using demographics, location, and time period? If you were to conduct this study again, would you know who to recruit, from where, and from what time period?

An example would be 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. In this example, the population is clearly described as: (1) who (men over 40 years old with type 2 diabetes); (2) where (Phoenix Good Samaritan Hospital); and (3) when (between January 1, 1990 and December 31, 1994). Another example is women aged 34 to 59 years of age in 1980 who were in the nursing profession and 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.

You may need to look at prior papers on methods in order to make the assessment for this question. Those papers are usually in the reference list.

Question 3. Groups recruited from the same population and uniform eligibility criteria

Were the inclusion and exclusion criteria developed prior to recruitment or selection of the study population? Were the same underlying criteria used for all of the subjects involved? This issue is related to the description of the study population, above, and you may find the information for both of these questions in the same section of the paper.

Most cohort studies begin with the selection of the cohort; participants in this cohort are then measured or evaluated to determine their exposure status. However, some cohort studies may recruit or select exposed participants in a different time or place than unexposed participants, especially retrospective cohort studies—which is when data are obtained from the past (retrospectively), but the analysis examines exposures prior to outcomes. For example, one research question could be whether diabetic men with clinical depression are at higher risk for cardiovascular disease than those without clinical depression. So, diabetic men with depression might be selected from a mental health clinic, while diabetic men without depression might be selected from an internal medicine or endocrinology clinic. This study recruits groups from different clinic populations, so this example would get a “no.”

However, the women nurses described in the question above were selected based on the same inclusion/exclusion criteria, so that example would get a “yes.”

Question 4. Sample size justification

Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Do they note or discuss the statistical power of the study? This question is about whether or not the study had enough participants to detect an association if one truly existed.

A paragraph in the methods section of the article may explain the sample size needed to detect a hypothesized difference in outcomes. You may also find a discussion of power in the discussion section (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 of these cases, the answer would be "yes."

However, observational cohort studies often do not report anything about power or sample sizes because the analyses are exploratory in nature. In this case, the answer would be "no." This is not a "fatal flaw." It just may indicate that attention was not paid to whether the study was sufficiently sized to answer a prespecified question—i.e., it may have been an exploratory, hypothesis-generating study.

Question 5. Exposure assessed prior to outcome measurement

This question is important because, in order to determine whether an exposure causes an outcome, the exposure must come before the outcome.

For some prospective cohort studies, the investigator enrolls the cohort and then determines the exposure status of various members of the cohort (large epidemiological studies like Framingham used this approach. However, for other cohort studies, the cohort is selected based on its exposure status, as in the example above of depressed diabetic men (the exposure being depression). Other examples include a cohort identified by its exposure to fluoridated drinking water and then 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 of these types of cohort studies, the cohort is followed forward in time (i.e., prospectively) to assess the outcomes that occurred in the exposed members compared to nonexposed members of the cohort. Therefore, you begin the study in the present by looking at groups that were exposed (or not) to some biological or behavioral factor, intervention, etc., and then you follow them forward in time to examine outcomes. If a cohort study is conducted properly, the answer to this question should be "yes," since the exposure status of members of the cohort was determined 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 them forward in time, the investigators go back in time (i.e., retrospectively) and select a cohort based on their exposure status in the past and then follow them forward to assess the outcomes that occurred in the exposed and nonexposed cohort members. Because in retrospective cohort studies the exposure and outcomes may have already occurred (it depends on how long they follow the cohort), it is important to make sure that the exposure preceded the outcome.

Sometimes cross sectional studies are conducted (or cross sectional analyses of cohort-study data), where the exposures and outcomes are measured during the same timeframe. 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 should be "no."

Question 6. Sufficient timeframe to see an effect

Did the study allow 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? In the examples given above, if clinical depression has a biological effect on increasing risk of CVD, such an effect may take years. In the other example, if higher dietary sodium increases blood pressure, a short timeframe may be sufficient to assess its association with blood pressure, but a longer timeframe would be needed to examine its association with heart attacks.

The issue of timeframe is important to enable meaningful analysis of the relationships between exposures and outcomes to be conducted. This often requires at least several years, especially when looking at health outcomes, but it 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 those would get a "no" response.

Question 7. Different levels of the exposure of interest

If the exposure can be defined as a range (examples: drug dosage, amount of physical activity, amount of sodium consumed), were multiple categories of that exposure assessed? (for example, for drugs: not on the medication, on a low dose, medium dose, high dose; for dietary sodium, higher than average U.S. consumption, lower than recommended consumption, between the two). Sometimes discrete categories of exposure are not used, but instead exposures are measured as continuous variables (for example, mg/day of dietary sodium or blood pressure values).

In any case, studying different levels of exposure (where 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. The presence of trends or dose-response relationships lends credibility to the hypothesis of causality between exposure and outcome.

For some exposures, however, this question may not be applicable (e.g., the exposure may be a dichotomous variable like living in a rural setting versus an urban setting, or vaccinated/not vaccinated with a one-time vaccine). If there are only two possible exposures (yes/no), then this question should be given a NA, and it should not count negatively towards the quality rating.

Question 8. Exposure measures and assessment

Were the exposure measures defined in detail? Were the tools or methods used to measure exposure accurate and reliable—for example, have they been validated or are they objective? This issue is important as it influences confidence in the reported exposures. When exposures are measured with less accuracy or validity, it is harder to see an association between exposure and outcome even if one exists. Also as important is whether the exposures were assessed in the same manner within groups and between groups; if not, bias may result.

For example, 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. Another example is measurement of BP, where there may be quite a difference between usual care, where clinicians measure BP however it is done in their practice setting (which can vary considerably), and use of trained BP assessors using 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). In each of these cases, the former would get a "no" and the latter a "yes."

Here is a final example that illustrates the point about why it is important to assess exposures consistently across all groups: If people with higher BP (exposed cohort) are seen by their providers more frequently than those without elevated BP (nonexposed group), it also increases the chances of detecting and documenting changes in health outcomes, including CVD-related events. Therefore, it may lead to the conclusion that higher BP leads to more CVD events. This may be true, but it could also be due to the fact that the subjects with higher BP were seen more often; thus, more CVD-related events were detected and documented simply because they had more encounters with the health care system. Thus, it could bias the results and lead to an erroneous conclusion.

Question 9. Repeated exposure assessment

Was the exposure for each person measured more than once during the course of the study period? Multiple measurements with the same result increase our confidence that the exposure status was correctly classified. Also, multiple measurements enable investigators to look at changes in exposure over time, for example, people who ate high dietary sodium throughout the followup period, compared to those who started out high then reduced their intake, compared to those who ate low sodium throughout. Once again, this 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. Outcome measures

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 issue is important because it influences confidence in the validity of study results. Also important is whether the outcomes were assessed in the same manner within groups and between groups.

An example of an outcome measure that is objective, accurate, and reliable is death—the outcome measured with more accuracy than any other. But even with a measure as objective as death, there can be differences in the accuracy and reliability of how death was assessed by the investigators. Did they base it on an autopsy report, death certificate, death registry, or report from a family member? Another example is a study of whether dietary fat intake is related to blood cholesterol level (cholesterol level being the outcome), and the cholesterol level is measured from fasting blood samples that are all sent to the same laboratory. These examples would get a "yes." An example of a "no" would be self-report by subjects that they had a heart attack, or self-report of how much they weigh (if body weight is the outcome of interest).

Similar to the example in Question 9, results may be biased if one group (e.g., people with high BP) is seen more frequently than another group (people with normal BP) because more frequent encounters with the health care system increases the chances of outcomes being detected and documented.

Question 11. Blinding of outcome assessors

Blinding means that outcome assessors did not know whether the participant was exposed or unexposed. It is also sometimes called "masking." The objective is to look for evidence in the article that the person(s) assessing the outcome(s) for the study (for example, examining medical records to determine the outcomes that occurred in the exposed and comparison groups) is masked to the exposure status of the participant. 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 because they also took measurements of exposures. If so, make a note of that in the comments section.

As you assess this criterion, think about whether it is likely that the person(s) doing the outcome assessment would know (or be able to figure out) the exposure status of the study participants. If the answer is no, then

blinding is adequate. An example of adequate blinding of the outcome assessors is to create a separate committee, whose members were not involved in the care of the patient and had no information about the study participants' exposure status. The committee would then be provided with copies of participants' medical records, which had been stripped of any potential exposure information or personally identifiable information. The committee would then review the records for prespecified outcomes according to the study protocol. If blinding was not possible, which is sometimes the case, mark NA and explain the potential for bias.

Question 12. Followup rate

Higher overall followup rates are always better than lower followup rates, even though higher rates are expected in shorter studies, whereas lower overall followup rates are often seen in studies of longer duration. Usually, an acceptable overall followup rate is considered 80 percent or more of participants whose exposures were measured at baseline. However, this is just a general guideline. For example, a 6-month cohort study examining the relationship between dietary sodium intake and BP level may have over 90 percent followup, but a 20-year cohort study examining effects of sodium intake on stroke may have only a 65 percent followup rate.

Question 13. Statistical analyses

Were key potential confounding variables measured and adjusted for, such as by statistical adjustment for baseline differences? Logistic regression or other regression methods are often used to account for the influence of variables not of interest.

This is a key issue in cohort studies, because statistical analyses need to control for potential confounders, in contrast to an RCT, where the randomization process controls for potential confounders. All key factors that may be associated both with the exposure of interest and the outcome—that are not of interest to the research question—should be controlled for in the analyses.

For example, in a study of the relationship between cardiorespiratory fitness and CVD events (heart attacks and strokes), the study should control for age, BP, blood cholesterol, and body weight, because all of these factors are associated both with low fitness and with CVD events. Well-done cohort studies control for multiple potential confounders.

General guidance for determining the overall quality rating

The questions on the form are designed to help you focus on the key concepts for evaluating the internal validity of a study. They are not intended to create a list that you simply tally up to arrive at a summary judgment of quality.

Internal validity for cohort studies is the extent to which the results reported in the study can truly be attributed to the exposure being evaluated and not to flaws in the design or conduct of the study—in other words, the ability of the study to draw associative conclusions about the effects of the exposures being studied on outcomes. Any such flaws can increase the risk of bias.

Critical appraisal involves considering the 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. (Thus, 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 whether 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, sufficient timeframe to see an effect, and appropriate control for confounding—all concepts reflected in the tool.

Generally, when you evaluate a study, you will not see a "fatal flaw," but you will find some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, you should ask yourself about the potential for bias in the study you are critically appraising. For any box where you check "no" you should ask, "What is the potential risk of bias resulting from this flaw in study design or execution?" That is, does this factor cause you to doubt the results that are reported in the study or doubt the ability of the study to accurately assess an association between exposure and outcome?

The best approach is to think about the questions in the tool and how each one tells you something about the potential for bias in a study. The more you familiarize yourself with the key concepts, the more comfortable you will be with critical appraisal. Examples of studies rated good, fair, and poor are useful, but each study must be assessed on its own based on the details that are reported and consideration of the concepts for minimizing bias.

Table 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 timeframe)?			
5. Were the definitions, inclusion and exclusion criteria, 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?			

Quality Rating (Good, Fair, or Poor):	
Reviewer #1 initials:	Reviewer #2 initials:
Comments:	

*CD: cannot determine; NR: not reported; NA: not applicable

ix. Guidance for Assessing the Quality of Case-Control Studies

The descriptions are by question number in the case-control study quality assessment tool.

Question 1. Research question

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. Study population

Did the authors describe the group of people from which the cases and controls were selected or recruited, using demographics, location, and time period? If you were to conduct this study again, would you know exactly who to recruit, from where, and from what time period?

Case-control study populations are determined by the location, time period, and inclusion criteria for cases (people with the disease or problem) and controls (people without the disease or health problem). An example population for a study of lung cancer and chemical exposure would be all incident cases of lung cancer diagnosed in patients aged 35–79 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 which case the populations are people in the area covered by the disease registry, or included in a cohort study (i.e., nested case-control or case-cohort). For example, 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.

You may need to look at prior papers on methods in order to make this assessment. Those papers are usually in the reference list.

Question 3. Sample size justification

Did the authors discuss their reasons for selecting or recruiting the number of people included? Do they discuss the statistical power of the study? This question concerns whether or not the study was sufficiently sized to see an association if one exists.

Generally, a paragraph in the methods section of the article will explain sample size needed to detect differences in exposures. However, you may also find a discussion of power in the discussion section.

Question 4. Groups recruited from the same population

In order 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, cases and controls are recruited from hospitals in a given region. It may be reasonable to 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 controls are recruited or selected from a different region or time period, then the cases and controls are recruited from different populations.

Another example: Eligible cases may be men and women between the ages of 18 and 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 18–39 years of age living in Perth (population-based controls); they could also be sampled from patients without atherosclerosis at the same hospitals (hospital-based controls). As long as the controls are people that would have been eligible to be included in the study as cases (if they had been diagnosed with atherosclerosis), then the controls are considered to be selected appropriately from the same source population as cases.

In a prospective case-control study, people are enrolled as cases at the time they are found to have the outcome of interest; the number of cases usually increases as time progresses. In this type of study, controls may be recruited or selected from the population without the outcome of interest at the time the case is diagnosed. Cases may be identified or recruited through a surveillance system, with controls selected from the population covered by that surveillance system—this would be an example of population-based controls. Controls may also be sampled from a cohort study population, in which cases should be the cases that are identified in that cohort study population, and controls should be selected from outcome-free individuals in the same cohort study. This is known as a nested case-control study.

Question 5. Inclusion and exclusion criteria prespecified and applied uniformly

Were the inclusion and exclusion criteria developed prior to recruitment or selection of the study population? Were the same underlying criteria used for all of the groups involved? The same selection criteria should be used except, of course, for whether or not they had the disease/condition, which would be different for cases and controls by definition. Often, therefore, the same age (or age range), gender, race, etc., is used to select cases and controls. This issue is related to the description of the study population, above, and you may find the information for both of these questions in the same section of the paper.

Question 6. Case and control definitions

Was a specific description of "case" and "control" provided? Is there a discussion of the validity of the case and control definitions and the processes or tools used to identify study participants as such? Were the tools or methods accurate, reliable, and objective? For example, cases might be identified as "adult patients admitted to a Veterans Administration hospital from January 1, 2000 to December 31, 2009, with an ICD–9 discharge diagnosis code of acute myocardial infarction and at least one of the following confirmatory findings in their medical records: at least 2 mm of ST elevation changes in two or more ECG leads, 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. Study results cannot be used to draw valid conclusions unless the distinction between cases and controls is accurate and reliable.

Question 7. Random selection of study participants

If a case-control study did not use 100 percent of eligible cases and controls (e.g., not all *disease-free participants* were included as controls), did the authors indicate that random sampling was used to select controls? 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. If consecutive sampling was used, as frequently occurs for cases in prospective studies, then study participants were not randomly selected, so the answer would be "no." This would not be considered a fatal flaw.

If all eligible cases and controls were included as study participants, then mark "NA."

Question 8. 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. This can be done in both prospective case-control studies and retrospective case-control studies. For example (assuming our study of adenocarcinoma of the colon was performed retrospectively using data from hospital records), if hospital records indicate that Person A was diagnosed with adenocarcinoma of the colon on June 22, 2002, then one or more controls would be selected from the population of patients *without* adenocarcinoma of the colon on June 22, 2002. One might also imagine this study to have been performed using patient records from a cohort study instead of from a hospital database, in which case it would be a nested case-control study.

The use of concurrent controls can be done in the presence or absence of matching, and vice versa. Just because a study incorporates matching, does not mean that concurrent controls were used.

Question 9. Exposure assessed prior to outcome measurement

Because case or control status is determined first (based on presence or absence of outcome of interest), and then exposure history of the case or control is assessed, it is important to make sure that the exposure preceded the outcome. For example, if tissue samples were used to determine exposure, were the tissue samples collected from patients prior to their diagnosis? If hospital records were used, did investigators verify that the date that a patient was exposed (e.g., received medication for atherosclerosis) occurred prior to the date that a person became a case (e.g., was diagnosed with type 2 diabetes)? In order for an association between an exposure and an outcome to be considered causal, the exposure *must* occur prior to the outcome.

Question 10. Exposure measures and assessment

Were the exposure measures defined in detail? Were the tools or methods used to measure exposure accurate and reliable—for example, have they been validated, or are they objective? This is important as it influences confidence in the reported exposures. As important is whether the exposures were assessed in the same manner within groups and between groups.

For example, 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. Another example is measurement of blood pressure in a study assessing BP as an exposure potentially affecting a particular outcome. There may be quite a difference in BP measurements between usual care, where clinicians measure BP as it is done is their practice setting, and use of trained BP assessors using 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).

Question 11. Blinding of exposure assessors

Blinding means that persons assessing the exposure status of study participants did not know whether the participant was a case or control. It is also sometimes called "masking." The objective is to look for evidence in the article that the person assessing the exposure(s) (for example, examining medical records to determine the exposures that occurred in the cases and controls) is masked to the case/control status of the participant. Sometimes the person measuring the exposure is the same person conducting case ascertainment. If so, make a note of that in the comments section.

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 controls. As you assess this criterion, think about whether it is likely that the person doing the exposure assessment would know whether the study participant was a case or control. If the answer is no, then the blinding should be adequate. For example, if the investigators were using medical records to assess exposure, you would want them to: (1) Not be directly involved in the care of the study subjects, because they would probably have knowledge of the conditions of their patients; and (2) If the medical record contained information on the patient's condition that identified him/her as a case (which is likely), that information would have to be removed before the exposure assessors reviewed the records.

If blinding was not possible, which is sometimes the case, mark "NA" and explain the potential for bias.

Question 12. Statistical analysis

Were key potential confounding variables measured and adjusted for, such as by statistical adjustment for baseline differences? Logistic regression or other regression methods are often used to account for the influence of variables not of interest.

This is a key issue in case-control studies, because the statistical analyses need to control for potential confounders, in contrast to a randomized controlled trial where the randomization process controls for potential confounders. All key factors that may be associated both with the exposure of interest and the outcome should be controlled for in the analyses. For example, in a study of the relationship between smoking and CVD events (heart attacks and strokes), the investigators need to control for age, gender, and body weight, because those are all associated both with smoking and with CVD events. Well-done case-control studies control for multiple potential confounders.

Matching is a technique used in an effort to improve study efficiency and control for known confounders. For example, in the study of smoking and CVD events, one 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) *should be controlled for in the analysis*.

General Guidance for Determining the Overall Quality Rating

The questions on the form are designed to help you focus on the key concepts for evaluating the internal validity of a study. They are not intended to create a list that you simply tally up to arrive at a summary judgment of 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 and not 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 being studied on outcomes? Any such flaws can increase the risk of bias. Critical appraisal involves considering the 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. Thus, 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 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 you evaluate a study, you will not see a "fatal flaw," but you will find some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, you should ask yourself about the potential for bias in the study you are critically appraising. For any box where you check "no," you should ask, "What is the potential risk of bias resulting from this flaw in study design or execution?" That is, does this factor cause you to doubt the results that are reported in the study?

The best approach is to think about the questions in the tool and how each one tells you something about the potential for bias in a study. Specific rules are not useful, as each study has nuances that are a bit different. The more you familiarize yourself with the key concepts, the more comfortable you will be with critical appraisal. Examples of studies rated good, fair, and poor are useful, but each study must be assessed on its own based on the details that are reported and consideration of the concepts for minimizing bias.

x. Policy and Procedures for the Use of Existing Systematic Reviews and Meta-Analyses

Systematic reviews (SRs) and meta-analyses (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. Guidance on using existing SRs has been published by AHRQ as a chapter of the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* and helped to inform the development of the NHLBI criteria.(149)

To use existing SRs or MAs to inform the NHLBI guideline recommendations, the project needed to identify: (1) those SRs and MAs relevant to the topic of interest, (2) those where the risk of bias was low, and (3) those that were recent. Examining the research question and component studies in the SRs or MAs as they related to the NHLBI critical questions (CQs) addressed the first issue, using a quality assessment tool addressed the second issue, and examining publication dates addressed the third issue.

In general, for this project:

- Eligibility of SRs and MAs was determined by the methodologists, consulting with Expert Panels and Workgroups as needed.
- Data was not abstracted from SRs or MAs, so they were not included in evidence tables. However, if an SR or MA was used to make a recommendation, a summary of the evidence was provided in the text, information from the SR or MA was included in a summary table or appendix, and the citation was included in the reference list.
- SRs or MAs were rated using the quality assessment tool for this project. SRs or MAs were used to develop recommendations if they were rated "good" or "fair" or were comprehensive reviews commissioned by the

Federal Government. SRs or MAs 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 MAs addressing the same topic were identified through a systematic search to minimize bias. The SRs or MAs used were summarized in text, tables, or appendices.
- Rating the body of evidence followed the same system used for the de novo systematic reviews conducted for this project and resulted in a high [SRs/MAs rated good only], moderate, or low rating based on number, type, and quality of the studies in the MA or SR.
- Recommendation strength took into account whatever evidence was available in the SR or MA used to make the recommendation, including issues like strength of the evidence, applicability of the evidence, consistency of the evidence, etc. 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/MAs used to make the recommendation are rated as Good), Grade B (Moderate), Grade C (Weak), Grade D (Against), Grade E (Expert Opinion), and Grade N (No recommendation.)

Additional criteria were used in to determine when SRs or MAs could be used. They are described in Situations 1–3 below.

SITUATION #1—When an SR or MA addresses a topic relevant to the NHLBI CVD guidelines that was not covered by an existing CQ (example, effects of physical activity on CVD risk):

A. In order 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 are relevant, those relevant portions that are reported separately could be used. For example, in the Department of Health and Human Services' (HHS) 2008 systematic review on physical activity, the effects of physical activity on CVD were relevant and were 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 MAs could be used if they were recent (i.e., published within 3 years of the end date of the NHLBI systematic review publication window of 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 deliberations on recommendations. If the end date of the SR or MA literature search was prior to December 31, 2009, Panels or Workgroups had the option of conducting a bridging literature search through December 31, 2009, if the Panel or Workgroup members believed it was necessary because relevant studies were published after the end date of the SR or MA. In this situation, the bridging literature search could only cover the time period up to 1 year prior to the literature search cut-off date of the SR or MA and extend to no later than December 31, 2009.

SITUATION #2—If the NHLBI literature review identified an existing SR or MA that could possibly replace NHLBI's review of a CQ or subquestion:

A. The SR or MA was examined for consistency between the SR's or MA's included studies and the CQ I/E criteria. Component studies had to meet the CQ I/E criteria; however, smaller sample sizes were allowed, as were studies published prior to the beginning of the NHLBI project's search date window, as long as a truly systematic approach was used.

B. SRs or MAs could be used if they were recent (i.e., published within 3 years of the end date of the NHLBI systematic review publication window), or identified by the Panel or Workgroup if published after the end date of the project literature search and before the panel began deliberations on recommendations. If the end date of the SR or MA literature search was prior to December 31, 2009, Panels or Workgroups could conduct a bridging literature search through December 31, 2009, if the Panel or Workgroup members believed it was necessary because relevant studies were published after the end date of the SR or MA. In this situation, the bridging literature search could only cover the time period up to 1 year prior to the literature search cut-off date of the SR or MA and extend to 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).

xi. 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 was developed by the methodologist 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 were checked for accuracy, completeness, and the use of standard formatting.

xii. Development of Evidence Tables and Summary Tables

a. Evidence tables

For each critical question, methodologists worked with the Panel/Workgroup members to identify the key data elements needed to answer the question. Using the PICOTS criteria as the foundation, Panel/Workgroup members determined what information was needed from each study to be able to understand the design, sample, and baseline characteristics in order 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 review by the Panel/Workgroup to ensure that all of the 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 critical question.

Only studies rated "good" and "fair" were included in the evidence tables.

Templates varied by each individual critical question 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: inclusion/exclusion criteria, primary outcome, secondary outcome, composite outcomes

- Study Design Details: treatment groups, descriptions of interventions, duration of treatment, duration of followup, run-in, washout, intervention n's
- Baseline Population Characteristics: demographics, biomarkers, other measures relevant to the outcomes
- Results: outcomes of interest for the critical question with between group *p* values or confidence intervals for risk ratios, adverse events, attrition, adherence

Studies are presented in alphabetical order by the study name (if none, the first author's last name was used). Some Panels combined all of 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.

b. Summary Tables

To enable a more targeted focus on the specific aspects of a critical question, methodologists developed summary tables, or abbreviated evidence tables, in concert with the Panels or Work Groups. A summary table might be designed to address a general population or a specific subpopulation, such as diabetes, women, or the elderly, but it only presents concise data elements. All of the available data in the evidence tables were reviewed to determine a consistent format to present the specific outcome of interest. For example, some lifestyle interventions have lengthy descriptions in the evidence tables, but only the key features would be concisely stated in the summary tables. Within an outcome, the time periods are clearly identified and the order of the different measures is consistently applied. For example, weight loss is always listed in order of percentage change, followed by kilogram change, and lastly by number of subjects losing a certain percent of their body weight. Templates varied by each aspect of the critical question 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 and baseline characteristics
- Study Design Details: intervention doses and duration
- Results: change in outcomes by time periods, attrition, adherence

Each Panel/Workgroup 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 listed by the type or characteristics of the intervention.

xiii. Process for the Development of Evidence Statements, Recommendations, and Panel Voting

Using the summary tables (and evidence tables as needed), evidence statements were collaboratively written by Work group or Panel members with input from methodology staff and oversight of the process by NHLBI staff. Evidence statements aimed to summarize key messages from the evidence that could be provided to primary care physicians 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, or low), and the Panels used this guidance to grade each evidence statement. This guidance is documented in the following section.

Panel members who had 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 and contractors did not vote.

Once evidence statements were finalized, attention turned to developing recommendations. Recommendations were developed using a similar process to evidence statements. For approval of a recommendation rated E (expert opinion), at least 75 percent of the Workgroup/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 facilitate further discussion and revisions to address areas of disagreement (e.g., by wordsmithing or dividing an evidence statement into more than one statement). Voting could be by confidential ballot if the group chose.

For both evidence statements and recommendations, a record of the vote count (for, against, or recusal) was made without attribution. The ideal was 100 percent consensus, but a two-thirds majority was considered acceptable.

xiv. Grading the Body of Evidence

The NHBLI Adult Cardiovascular Disease Guidelines Project applied related but distinct processes for grading the bodies of evidence for critical questions, for bodies of evidence for different outcomes included within critical questions, and for the subsequent strength of recommendations developed from those bodies of evidence. Each of these processes is described in turn below.

In developing the system for grading the body of evidence, the NHLBI reviewed a number of systems, including GRADE, the U.S. Preventive Services Task Force (USPSTF), AHRQ Evidence-based Practice Centers, 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 resulting system was strongly supported by Expert Panel and Workgroup members. In using the system, decisions about evidence rating were made by the Panels and Workgroups and the methodology team working collaboratively to apply the system and guidance in a thoughtful manner.

Two approaches were used for summarizing the body of evidence for each critical question. The first process was to conduct a de novo literature search and literature review for all of the individual studies that met a critical question's inclusion and exclusion criteria. This was used for most of the critical questions. The second process, developed in response to resource limitations for the project overall, was to focus the literature search on existing systematic reviews and meta-analyses, that themselves summarized a broad range of the scientific literature. This was used for several critical questions across Panels and Workgroups. Additional information on the use of SRs and MAs is provided in the following section.

Once the Panel and Workgroup members reached consensus on the wording of the evidence statement, the next step was to assign a grade to the strength of the body of evidence to provide guidance to primary care physicians and other stakeholders on how much support the evidence provided for the evidence statement. Three options were identified for grades for the strength of evidence: High, Moderate, or Low.

The table below describes the types of evidence that were used to grade the strength of evidence as high, moderate, or low by the Panel and Workgroup members, with assistance from methodologists.

Table A–5. Types of Evidence Used To Grade 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; • Meta-analyses 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; • Meta-analyses 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; • Meta-analyses 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.

Guidance was provided by methodologists to the Panels and Workgroup 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.(150,151) 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:

a. 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 Workgroup 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.

b. 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 (e.g., 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 confidence intervals, 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 where 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.

c. 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.

d. 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 confidence intervals. Precise estimates enable firm conclusions to be drawn about an intervention's effect relative to another intervention or control. An imprecise estimate is where the confidence interval 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 a meta-analysis, precision is reflected by the confidence interval around the summary effect size. For systematic reviews, where there are 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, other considerations were also examined in some cases. For example, the objectivity of an outcome measure can be an issue in some cases. Total mortality is a very objective measure as it is usually recorded accurately. Determination of angina is less objective and may be considered to result in lower strength of evidence. Similarly, urinary sodium excretion is a more objective measure than dietary sodium intake reported by study subjects through recall. Another example is measured height and weight used to calculate a study subject's BMI versus self-reported weight and height that provide less reliable data.

Following the conclusion of review and discussion of this range of factors by the Panel or Workgroup members, a vote was next taken 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, although in most cases the Panels and Workgroups discussed the results if there were dissenting opinions until consensus or large majorities were achieved for the votes on the strength of evidence.

xv. Search Strategy Overview and Syntax of Queries

This section provides a description of 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–6 shows examples of queries and a description of results. A complete list of attributes used in search strategies with their explanation is listed in Table A–7. Commonly used macro queries are defined in Table A-8.

Table A–6. Examples of Simple Queries

Query	Results
title=blood pressure	Articles with phrase “blood pressure” in article title
title,abstract=blood pressure	Articles with phrase “blood pressure” in article title or its abstract
blood pressure	When attribute name is skipped, “title, abstract” is assumed; therefore, the results are equivalent to query: title,abstract=blood pressure
title=(blood pressure or cholesterol)	Articles with phrases “blood pressure” or “cholesterol” in article title
title=blood pressure and abstract=(mortality or morbidity)	Articles with “blood pressure” in the title and words “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,’ random, etc.
abstract=?cholesterol?	Articles with abstracts including any word that includes subword ‘cholesterol,’ e.g., hypocholesterolemia
not journalTitle=“ACP journal club”	Exclude articles from “ACP journal club”
publicationYear >1997 and publicationYear <2010	Articles from 1998 to 2009
(CVD %2 event?)	Articles with ‘CVD’ word in proximity of two words from word stem ‘event’

Table A–7. Attributes, Their Values, and Explanation

Attribute	Values
Abstract	Text of abstract
Title	Text of title
<no attribute specified>	Combined text of title and abstract
journalTitle	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
majorSubject	MeSH major subject headings
qualifier	MeSH subheadings
substance	MeSH substances
RecordContentSource	e.g,. ‘Pubmed,’ ‘embase,’ ‘cinahl’
recordStatus	e.g., ‘delete’
pubmedid	Pubmed identifier
uuid	Internal unique identifier

Table A–8. Common Macro Queries Used in Search Strategies

Macro Name	Query
RCT	(((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 (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

In order 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 in order to be retrieved. The inclusion/exclusion criteria for each question, which was defined using the PICOTS structure (population, intervention, comparator, outcomes, timing, and setting), 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, systematic reviews, prospective cohort studies, etc.)
- Boolean search: implements expressions for population, intervention, outcomes, timing, and settings
- 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.

Appendix B.
Question 1 Methods

Appendix B. Question 1 Methods

i. Search Strategy

a. Among adults, what is the effect of dietary patterns and/or macronutrient composition on CHD/CVD risk factors or health outcomes, when compared to no treatment or to other types of interventions?

The search strategy presented here reflects original (broad) I/E criteria. The final criteria did not include hard outcomes as well as interventions pertaining to nondietary patterns.

b. Study type query

Study types eligible for this question: RCTs, systematic reviews or meta-analyses of RCTs or controlled clinical trials, observational or epidemiologic studies with time difference between interventions/exposures and outcomes (e.g., cohort studies, case-control studies).

Sample size: For biomarker assessment and risk factor studies, sample size >=100

- (RCT) OR (Systematic Review) OR
- genre= (Controlled Clinical Trial) OR
- (subject= ("Controlled Clinical Trials as Topic") **and** (subject,abstract,title= (random?) or systematic? or 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")) OR
- (subject,title,abstract= (Case-Control Stud? or Retrospective Stud? or Cohort Stud? or Followup Stud? or Longitudinal Stud? or Prospective Stud? or Observational Stud?))

c. Boolean search

(

- (publicationYear>1997 and publicationYear<2010 and language=eng)
- AND (qualifier="diet therapy"
- or subject,title,abstract= (diet? %3 (pattern? or habit? or preference?))
- or subject= (Diet or "Diabetic Diet" or "Diet, Carbohydrate-Restricted" or "Diet Fads" or "Diet, Fat-Restricted" or "Diet, Gluten-Free" or "Diet, Mediterranean" or "Diet, Protein-Restricted" or "Diet, Reducing" or "Diet, Sodium-Restricted" or "Diet, Vegetarian" or "Diet, Macrobiotic" or "Energy Intake" or "Caloric Restriction" or "Ketogenic Diet" or "Diet Therapy")
- or isocaloric diet? or "DASH diet" or "OMNI diet" or Mediterranean diet? or therapeutic lifestyle change? or vegetarian diet? or vegan diet? or "Ornish diet" or Pritikin diet or "American Diabetes Association Diet" or "ADA Diet" or low-fat diet? or high protein diet? or high carbohydrate diet? or high-CHO or low carbohydrate diet? or low-CHO or high fiber diet? or low glycemic index diet? or "glycemic load" or "Atkins diet" or "portfolio diet" or Ketogenic diet or "NCEP diet" or "AHA Diet" or (step %2 diet) or meal replacement or adventist diet? or raw food diet?
- or (macronutrient %3 intervention) or isocaloric or controlled diet?
- or subject,title,abstract= ("Dietary Fats" or Butter or "Cholesterol, Dietary" or "Dietary Fats, Unsaturated" or "Cod Liver Oil" or "Corn Oil" or "Cottonseed Oil" or "Fatty Acids, Omega–3" or "alpha-Linolenic Acid"

or "Docosahexaenoic Acids" or "Eicosapentaenoic Acid" or "Safflower Oil" or "Sesame Oil" or "Soybean Oil" or "Fat Emulsions, Intravenous" or Margarine or "Dietary Carbohydrates" or "Dietary Sucrose")

- or saturated fatty acid? or unsaturated fatty acid? or polyunsaturated fatty acid? or monounsaturated fatty acid? or trans fatty acid? or dietary cholesterol or sugar-sweetened beverages or ((complex or plant-based or animal based) %3 fiber?) or glycemic index
- or subject,abstract,title= (Dietary Proteins or "Egg Proteins, Dietary" or Conalbumin or Ovalbumin or Ovomucin or Phosvitin or Milk Proteins or Caseins or Lactalbumin or Lactoglobulins or Vegetable Proteins)
- or MeSHSubjectPhrase= ("Food" or "Food Preferences" or "Food Habits"))
- AND (subject,qualifier,title,abstract=mortality or death? or died or fatal? or subject= ("Cause of Death" or "Fatal Outcome" or "Survival Rate")
- or subject,title,abstract= ("Acute Coronary Syndrome" or "Myocardial Infarction" or "Shock Cardiogenic" or "Myocardial Stunning" or "No Reflow Phenomenon" or "Heart Arrest" or "Death Sudden Cardiac" or "Angina, Unstable" or "Heart Attack") or STEMI or NSTEMI or myocardial infarctions or unstable angina? or acute coronary syndromes
- or subject,abstract,title= ("Stroke" or "Brain Infarction" or "Brain Stem Infarctions" or "Lateral Medullary Syndrome" or "Cerebral Infarction" or "Dementia, Multi-Infarct" or "Infarction Anterior Cerebral Artery" or "Infarction Middle Cerebral Artery" or "Infarction Posterior Cerebral Artery")
- or ((CVD or CHD or HF or CHF or cardiovascular or coronary or heart failure or cardiac) and (subject,abstract,title= (hospitalization) or hospitalization? or rehospitalization? or subject,abstract,title= (inciden? or morbidity or prevalence)))
- or ((subject= (Cardiovascular Diseases or Coronary Disease or Coronary Artery Disease or Myocardial Infarction or Heart Failure or Cerebrovascular Disorders)) with (qualifier=complications))
- or (lifetime %3 risk) or subject="Severity of Illness Index"
- or subject,title,abstract= (Angioplasty or Revascularization or Coronary Artery Bypass or Coronary Angiography or Stents or Endarterectomy) or CABG
- or subject= ("Kidney Failure, Chronic" or "Renal Insufficiency, Chronic") or Chronic Kidney Failure or CKD or Chronic Kidney Disease or End Stage Renal or ESRD or ((kidney or renal) %5 stage %5 (3 or 4 or 5 or III or IV or V))
- or risk score
- or subject="Metabolic Syndrome X" or metabolic syndrome
- or subject,abstract,title= (inciden? and (diabet? or hypertension))
- **or ((**
- ((subject="C-Reactive Protein") with (qualifier= (metabolism or analysis))) or hs-CRP or CRP or hsCRP or "C-reactive protein"
- or inflammatory marker? or subject,title,abstract= (Fibrinogen) or prothrombotic factor?
- 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 LDL particle number or LDL-P or (LDL and subject,abstract,title="Particle Size") or lipid goal? or ?cholesterol? or ?lipid? or lipoprotein? or LDL-cholesterol or LDL-C or non-HDL-cholesterol or anticholesterol?
- or ((subject= (Hypertension or Cholesterol or Diabetes or Metabolic Syndrome X)) with (qualifier= (blood or diagnosis)))

- or subject,title,abstract= ("Blood pressure" or systol? or diastol?) or BP or SBP or DPB or hypertensive or nonhypertensive or blood pressure 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=Obesity) with (qualifier=prevention)) or subject= ("Obesity, Abdominal" or "Obesity, Morbid") or subject,title,abstract= (Anthropometry or "Body Mass Index" or "Waist Circumference" or "Body Fat Distribution") or BMI or BMIs or weight change
- or Carotid intima-medial wall thickness or subject,abstract,title= ((carotid or tunica) and (intima medial or wall thickness?)) or (IMT? not (muscle training or memory task? or intensive mixture or intramuscularly or intrathecal morphine or myofibroblastic or tyrosine or immune modulation or immunotherapy or immunomodulat? or microthombosis or idiopathic macular))
- or Coronary calcium or ((calcium or Agatston) %2 score?)
- **)**
- **and (** subject,title,abstract= (risk? or marker? or biomarker? or indicator? or level? or concentration? or end point? or endpoint? or Treatment Outcome) **))**
)

)

NOT majorSubject= ("Dietary Supplements")

NOT majorSubject= (Fruit or Vegetables or Margarine or Butter or Phytotherapy or Phenols or Flavonoids or Carotenoids or "Diet, Sodium-Restricted")

NOT title= (fruit? or vegetable? or ((antioxidants or vitamin? or sodium or salt or potassium or magnesium or calcium or folate) %2 (dietary or intake or supplement? or consumption)) or tocopherol or phenol? or beta-carotene or caroten? or resveratrol or polyphenol or proanthocyanidins or selenium or garlic or chocolate or Phytosterol? or Ecdysteroid? or Ergosterol or Withanolid? or Sitosterol? or Stigmasterol or plant sterol? or campesterol? or sitostanol or campestanol? or Isoflavone? or flavonoid? or genestein or daidzein or equol)

NOT ((subject= (Fruit or Vegetables or Calcium or Magnesium or Potassium or Phytotherapy or Plant Extracts or Vitamins or Ascorbic Acid or Antioxidants or Carotenoids or Tocopherols or beta Carotene or Allyl Compounds or "Calcium, Dietary" or "Sodium, Dietary" or "Sodium Chloride, Dietary" or Phytosterol? or Ecdysteroid? or Ergosterol or Withanolid? or Sitosterol? or Stigmasterol)) with (qualifier= (administration or therapeutic use or pharmacology)))

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 majorSubject= ("Research Design")

NOT subject= (Animals or Venoms)

NOT title,abstract,subject=flax?

NOT ((?dialysis %5 patients) or subject= (renal dialysis) or hemodialysis)

NOT title= (Alcohol or red wine or Coffee)

NOT subject,title= (pregnan?)

Boolean Filter

None

ii. Search Strategy Results and PRISMA Diagram

The below listed databases were searched for RCTs, controlled clinical trials, and observational or epidemiologic studies with a time difference between interventions/exposures and outcomes (i.e., cohort studies, case-control studies) and systematic reviews and meta-analyses of these study designs to answer Question 1. Observational and epidemiologic studies or systematic reviews of such studies were eligible for hard health outcomes only.

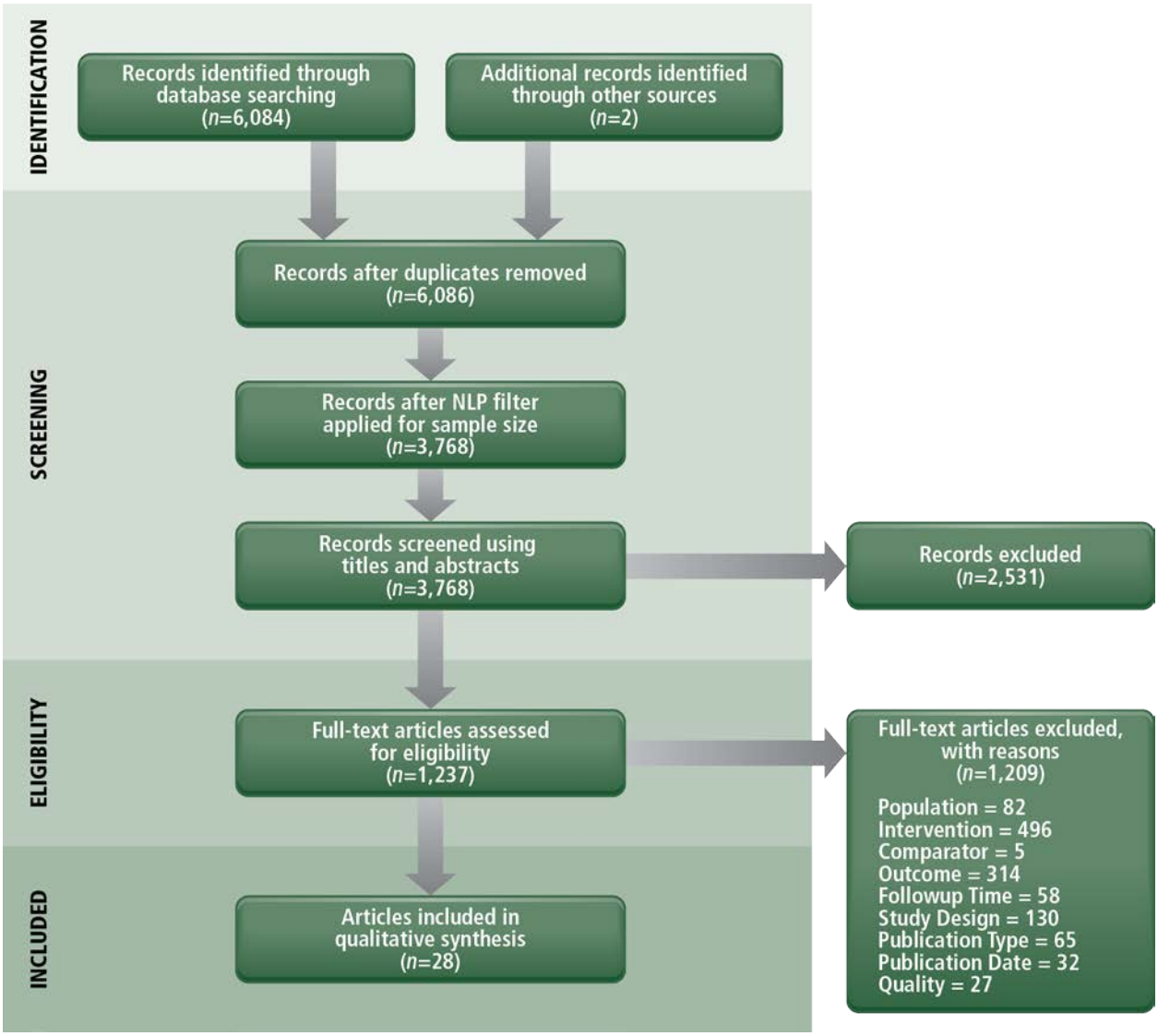
- PubMed from January 1998 to December 2009
- CINAHL from January 1998 to July 2008
- EMBASE from January 1998 to July 2008
- PsycInfo from January 1998 to July 2008
- EBM (Evidence-based Medicine) Cochrane Libraries from January 1998 to July 2008
- Biological Abstracts from January 2004 to July 2008
- Wilson Social Sciences Abstracts from January 1998 to July 2008

Duplicate citations which arise from the same citation being found in more than one database were removed from the Central Repository prior to screening. The search produced 6,084 citations. This number of citations includes results from a supplemental search of PubMed for systematic reviews and meta-analyses focused on fatty acids, with publication dates between 1990 and 2009.

A natural language processing (NLP) filter was used to identify studies with sample sizes less than 500, for studies reporting hard health outcomes and sample sizes less than 50, for biomarker assessment and risk factor studies. The NLP filter was executed against titles and abstracts, and 2,318 publications were automatically excluded because they were of studies with less than the required sample size. The titles and abstracts of the 3,768 remaining publications were screened against the inclusion/exclusion criteria independently by two reviewers, which resulted in the retrieval of 1,237 full-text papers. These papers were independently screened by two reviewers and 1,209 of these publications were excluded on one or more of the I/E criteria. An additional 27 publications were excluded because they were rated as poor quality; 17 were RCTs, 4 were cohort studies, and 6 were systematic reviews or meta-analyses. Twenty-eight articles were included in the Question 1

Evidence Base. Twenty-four were RCTs, 1 was a cohort study, and 3 were systematic reviews or meta-analyses. This information can be found in Figure B–1, below.

Figure B–1. PRISMA Diagram Showing Selection of Articles for Lifestyle Question 1



iii. CQ1 Studies Rated as Poor With Rationale

Table B–8. CQ1 Studies Rated as Poor with Rationale

Study	Design	Primary Reasons for Poor Quality Rating
Ammerman et al. 2003(152)	RCT	High LTF (Lost-to-Followup), no ITT (Intent-to-Treat analysis), no information on power calculations or adherence
Appleby et al. 1999(153)	Observational cohort	No information on LTF or confounding factors
Aquilani et al. 1999(154)	RCT	No information on blinding procedures, power, differential LTF rates
Asztalos et al. 2000(155)	RCT	Poorly described randomization process, high LTF, low adherence, information on differential LTF and power analysis was not reported
Bo et al. 2008(156)	RCT	Inadequately powered, LTF, and subgroups were not prespecified
Chrysohoou et al. 2004(157)	RCT	No information on randomization procedure, LTF, or ITT
de Lorgeril et al. 1999(158)	Observational cohort	High LTF, unclear description of intervention, no information on sample size justification or power, no statistical testing was reported for risk factors
Furtado et al. 2008(159)	RCT	High LTF, no ITT
Griffin et al. 2006(160)	RCT	No ITT, inadequate randomization and power
Hjerkinn et al. 2004(161)	RCT	No ITT, LTF or information on power analysis
Hunninghake et al. 2000(162)	RCT	High LTF, no information on randomization procedure and power analysis
Kolovou et al. 2003(163)	Observational Cohort	No information on LTF or sample size justification
Kuller et al. 2001(164)	RCT	No information on sample size justification, power analysis, LTF or ITT
Lagström et al. 1999(165)	RCT	No ITT, LTF or information on blinding procedures, sample size calculation or power analysis
Morgan et al. 2009(166)	RCT	High LTF, no ITT or power calculation
Rasmussen et al. 2006(167)	RCT	No information on randomization procedure or power analysis
Søndergaard et al. 2003(168)	RCT	Inadequate randomization and blinding procedures; no information on LTF or power analysis; No ITT

Study	Design	Primary Reasons for Poor Quality Rating
Stefanick et al. 1998(169)	RCT	No ITT analysis, no information on LTF, power analysis, or adherence
Toobert et al. 2003(170)	RCT	Inadequate randomization procedure; no information on blinding procedure or power analysis
Witana et al. 2005(171)	Observational cohort	No information on power analysis, sample size justification; unclear definition of exposure measure
Xiao et al. 2003(172)	RCT	No ITT; no information on LTF or power analysis

Key
LTF: Lost-to-followup
ITT: Intent-to-treat analysis

Appendix C.
Question 2 Methods

Appendix C. Question 2 Methods

i. Search Strategy

Among adults, what is the effect of dietary intake of other nutrients (not macronutrients, but including electrolytes, minerals, vitamins, etc.) on CHD/CVD outcomes and risk factors, when compared to no treatment or to other types of interventions?

a. Study type query

Study types eligible for this Question: RCTs, systematic reviews or meta-analyses of RCTs or controlled clinical trials, observational or epidemiologic studies with time difference between interventions/exposures and outcomes (e.g., cohort studies, case-control studies).

- (RCT) OR (Systematic Review) OR
- genre= (Controlled Clinical Trial) OR
- (subject= ("Controlled Clinical Trials as Topic") **and** (subject,abstract,title= (random?) or systematic? or 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")) OR
- (subject,title,abstract= (Case-Control Stud? or Retrospective Stud? or Cohort Stud? or Followup Stud? or Longitudinal Stud? or Prospective Stud? or Observational Stud?))

b. Boolean search

- (publicationYear >1997)
- **AND** subject,title,abstract,qualifier= (diet? or food? or fruit? or vegetable? or life style or lifestyle or ((sodium or potassium) intake?))
- **AND** (MeSHSubjectPhrase= ("Sodium" or "Sodium, Dietary" or "Diet, Sodium-Restricted" or "Sodium Chloride, Dietary" or "Potassium" or "Potassium, Dietary" or "Calcium, Dietary" or "Calcium" or "Vitamin D?" or "Sweetening Agents" or Sucrose or "Dietary Sucrose" or "Dietary Carbohydrates" or "Dairy Products" or Butter or Cheese or Ice Cream or Margarine or Milk or Yogurt)
  - OR "dietary sodium" or "dietary potassium" or "dietary calcium" or "vitamin d?" or (vitamin? !4 (d or d2 or d3)) or "Sweetening Agents" or Sucrose or sugar or "Dietary Sucrose" or "Dietary Carbohydrates" or "Dairy Products" or Butter or Cheese or Ice Cream or Margarine or Milk or Yogurt or yoghurt
  - OR (subject,abstract,title= (sodium or potassium or calcium or salt) and (electrolyte? or mineral? or subject,abstract,title=micronutrient? or nutrient? or intake?))
  - OR (subject,abstract,title= (fruit? or vegetable?) and (electrolyte? or mineral? or subject,abstract,title=micronutrient?)))
- **AND** (subject,qualifier,title,abstract=mortality or death? or died or fatal? or subject= ("Cause of Death" or "Fatal Outcome" or "Survival Rate")
- or subject,title,abstract= ("Acute Coronary Syndrome" or "Myocardial Infarction" or "Shock Cardiogenic" or "Myocardial Stunning" or "No Reflow Phenomenon" or "Heart Arrest" or "Death Sudden Cardiac" or "Angina, Unstable" or "Heart Attack" or "Heart Failure") or STEMI or NSTEMI or myocardial infarctions or unstable angina? or acute coronary syndromes

- or subject,abstract,title= ("Stroke" or "Brain Infarction" or "Brain Stem Infarctions" or "Lateral Medullary Syndrome" or "Cerebral Infarction" or "Dementia, Multi-Infarct" or "Infarction Anterior Cerebral Artery" or "Infarction Middle Cerebral Artery" or "Infarction Posterior Cerebral Artery")
- or ((CVD or CHD or HF or CHF or cardiovascular or coronary or heart failure or cardiac) and (subject,abstract,title= (hospitalization) or hospitalization? or rehospitalization? or subject,abstract,title= (inciden? or morbidity or prevalence)))
- or ((subject= (Cardiovascular Diseases or Coronary Disease or Coronary Artery Disease or Myocardial Infarction or Heart Failure or Cerebrovascular Disorders)) with (qualifier=complications))
- or subject,title,abstract= (Angioplasty or Revascularization or Coronary Artery Bypass or Coronary Angiography or Stents or Endarterectomy) or CABG
- or subject= ("Kidney Failure, Chronic" or "Renal Insufficiency, Chronic") or Chronic Kidney Failure or CKD or Chronic Kidney Disease or End Stage Renal or ESRD or ((kidney or renal) %5 stage? %5 (3 or 4 or 5 or III or IV or V))
- or (composite %5 (index or score or outcome?))
- **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 LDL particle number or LDL-P or (LDL and subject,abstract,title="Particle Size") or lipid goal? or lipid level?
    - or ((subject= (Hypertension or Cholesterol)) with (qualifier= (blood or diagnosis or prevention)))
    - 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 (urin? %2 (albumin or sodium or potassium))
    - or subject,title,abstract= ("Glomerular Filtration Rate" or "Albuminuria") or GFR or eGFR or estGFR
    - or (change %3 (medication or dose or dosage))
    - **)**
    - **and (** subject,title,abstract= (risk? or factor? or marker? or biomarker? or indicator? or level? or concentration? or end point? or endpoint? or Treatment Outcome or response) **))**
)
-)
- **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= (Practice Guidelines as Topic or Pilot Projects or Cross Sectional Studies)
- **NOT** majorSubject= ("Research Design")
- **NOT** subject= (Animals or Venoms)
- **NOT** title,abstract,subject=flax?
- **NOT** ((?dialysis %5 patients) or subject= (renal dialysis) or hemodialysis)
- **NOT** title= (Alcohol or red wine or Coffee or Case study or "design and baseline characteristics" or "Summaries for patients")
- **NOT** subject,title= (pregnan?)
- **NOT** (recordStatus=delete)

c. Boolean filter

The Boolean filter in the Lifestyle 2 search strategy implements an extension of the search period for sodium and hard outcomes from 2010 to April 2012.

- (publicationYear >1997 and publicationYear<2010) **OR** (
- (publicationYear >2009)

  - **AND** (MeSHSubjectPhrase= ("Sodium" or "Sodium, Dietary" or "Diet, Sodium-Restricted" or "Sodium Chloride, Dietary") OR "dietary sodium" OR (subject,abstract,title= (sodium or salt) and (electrolyte? or mineral? or subject,abstract,title=micronutrient? or nutrient? or intake)))
  - **AND** (
    subject,qualifier,title,abstract=mortality or death? or died or fatal? or
    subject= ("Cause of Death" or "Fatal Outcome" or "Survival Rate") or
    subject,title,abstract= ("Acute Coronary Syndrome" or "Myocardial Infarction" or "Shock Cardiogenic" or "Myocardial Stunning" or "No Reflow Phenomenon" or "Heart Arrest" or "Death Sudden Cardiac" or "Angina, Unstable" or "Heart Attack" or "Heart Failure") or
    STEMI or NSTEMI or myocardial infarctions or unstable angina? or acute coronary syndromes or
    subject,abstract,title= ("Stroke" or "Brain Infarction" or "Brain Stem Infarctions" or "Lateral Medullary Syndrome" or "Cerebral Infarction" or "Dementia, Multi-Infarct" or "Infarction Anterior Cerebral Artery" or "Infarction Middle Cerebral Artery" or "Infarction Posterior Cerebral Artery") or
    ((CVD or CHD or HF or CHF or cardiovascular or coronary or heart failure or cardiac) and (subject,abstract,title= (hospitalization) or hospitalization? or rehospitalization? or subject,abstract,title= (inciden? or morbidity or prevalence))) or
    ((subject= (Cardiovascular Diseases or Coronary Disease or Coronary Artery Disease or Myocardial Infarction or Heart Failure or Cerebrovascular Disorders)) with (qualifier=complications)) or
    subject,title,abstract= (Angioplasty or Revascularization or Coronary Artery Bypass or Coronary Angiography or Stents or Endarterectomy) or CABG or
    subject= ("Kidney Failure, Chronic" or "Renal Insufficiency, Chronic") or
    Chronic Kidney Failure or CKD or Chronic Kidney Disease or End Stage Renal or ESRD or ((kidney or renal) %5 stage? %5 (3 or 4 or 5 or III or IV or V)) or
    (composite %5 (index or score or outcome?))
)
)

ii. Search strategy results and PRISMA diagram

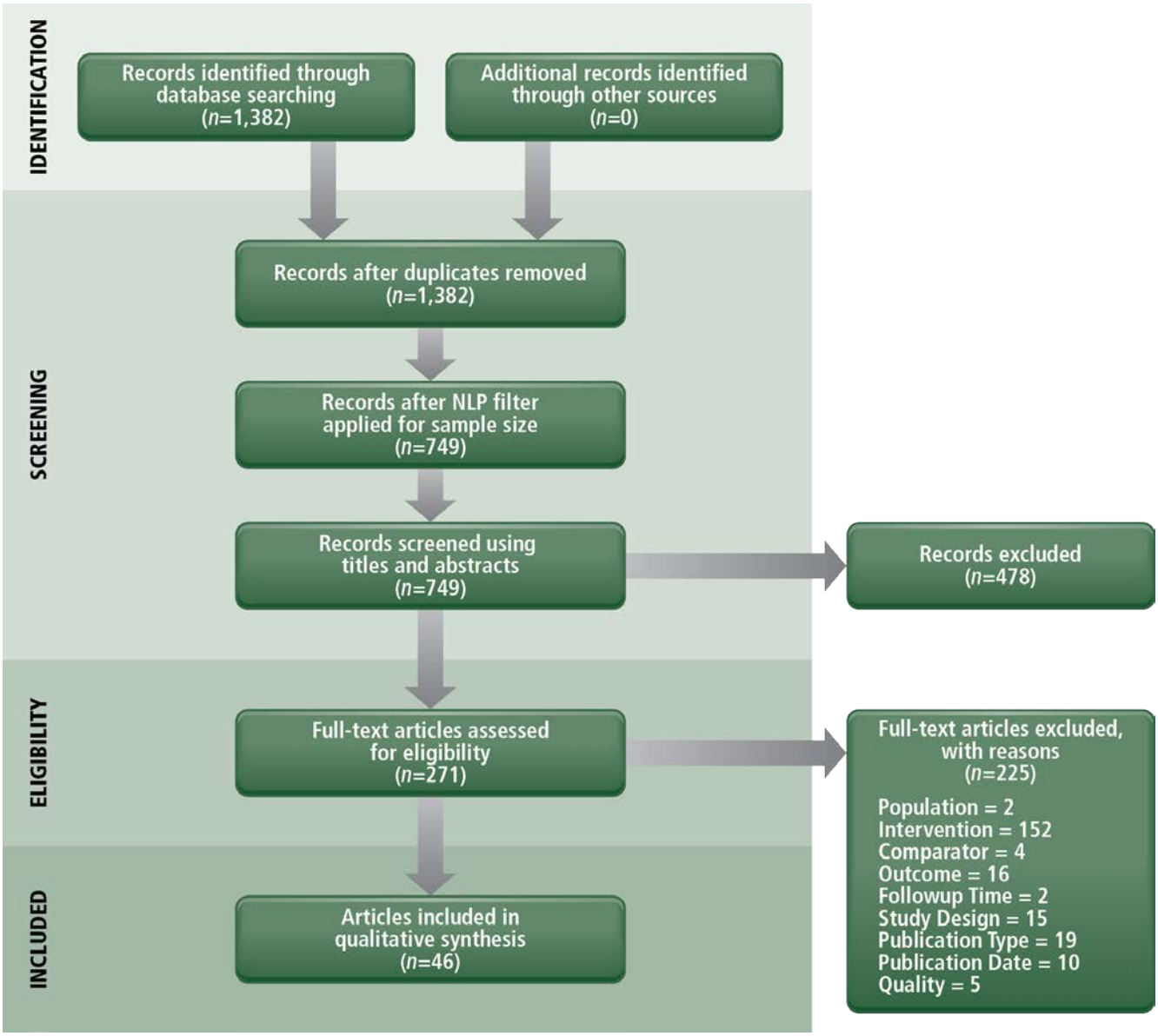
The below listed databases were searched for RCTs, controlled clinical trials, and observational or epidemiologic studies with a time difference between interventions/exposures and outcomes (i.e., cohort studies, case-control studies) and systematic reviews and meta-analyses of these study designs to answer Question 2. Observational and epidemiologic studies or systematic reviews of such studies were eligible for hard health outcomes only.

- PubMed from January 1998 to April 2012
- CINAHL from January 1998 to July 2008
- EMBASE from January 1998 to July 2008
- PsycInfo from January 1998 to July 2008
- EBM (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

Duplicate citations which arise from the same citation being found in more than one database were removed from the Central Repository prior to screening. The search produced 1,382 citations. This number of citations includes results from a supplemental search of PubMed that was extended to April 2012, and which was focused on sodium and hard health outcomes.

A natural language processing (NLP) filter was used to identify studies with sample sizes less than 500 for studies reporting hard health outcomes and for sample sizes less than 50 for biomarker assessment and risk factor studies. The NLP filter was executed against titles and abstracts. Six hundred and thirty-three publications were automatically excluded using the NLP filter because they were of studies with less than the required sample size. The titles and abstracts of the 749 remaining publications were screened against the inclusion/exclusion criteria independently by two reviewers, which resulted in the retrieval of 271 full-text papers. These papers were independently screened by two reviewers and 225 of these publications were excluded on one or more of the inclusion/exclusion criteria. An additional 5 publications were excluded because they were rated as poor quality; all 5 poor quality studies were RCTs. 46 articles were included in the Question 2 Evidence Base. Sixteen were RCTs, 25 were cohort studies, 1 was a case-control study, and 4 were systematic reviews or meta-analyses.

Figure C–1. PRISMA Diagram Showing Selection of Articles for Lifestyle Question 2



iii. CQ2 Studies Rated as Poor With Rationale

Table C–9. CQ2 Studies Rated as Poor with Rationale

Study	Design	Primary Reason for Poor Quality Rating
Forrester et al. 2005(173)	RCT	Sample size justification, power analysis and LTF not reported
He, Feng et al. 2005(174)	RCT	Post hoc analysis, small sample size and no power, sample size justification, adherence or LTF reported
Manios et al. 2006(175)	RCT	Information on randomization procedures, blinding, differential drop-out rates and power not reported
Roberts 2006(176)	RCT	Small sample size; information on randomization procedures, differential drop-out rate and adherence not reported.
Takahashi et al. 2006(177)	RCT	No ITT; high LTF
Tuekpe et al. 2006(178)	RCT	No ITT; high LTF

Key
LTF: Lost-to-Followup
ITT: Intent-to-Treat Analysis

Appendix D.
Question 3 Methods

Appendix D. Question 3 Methods

i. Search Strategy

Among adults, what is the effect of physical activity on hypertension and cholesterol when compared to no treatment, or to other types of interventions?

a. Study type query

Study types eligible for this question: Systematic reviews and meta-analyses

- (Systematic Review)

b. Boolean search

(

- (publicationYear>2000)
- AND (subject,title,abstract= ("Physical Fitness" OR "Motor Activity" or "Exercise Tolerance" OR "Metabolic Equivalent" OR "Exercise Test" or Life Style or Lifestyle) OR subject= (Exercise or Training or Walking) OR VO2? OR "maximal MET" OR (METs not "metabolic syndrome mets") OR physical activity or "maximal metabolic" OR metabolic equivalent? or graded exercise test? OR GXT)
- AND (subject,title,abstract= (?cholesterol? or ?lipid? or lipoprotein? or triglyceride? or LDL-cholesterol or HDL-cholesterol or HDL-C or LDL-C or non-HDL-cholesterol or ApoB or Lp (a) or LDL-P or Apo A–1 or anticholesterol? or blood pressure or systol? or diastol? or hypertension or antihypertens? or hypertensive or non-hypertensive or metabolic syndrome or Risk Factors or Biological Markers or ((cardiovascular or CVD or coronary or CHD or stroke or myocardial infarction or cerebrovascular or heart disease?) and (risk? or confound? or predict? or marker? or incidence))))

)

NOT subject= ((child or adolescent or infant) not (adult or aged))
NOT recordStatus=delete

c. Boolean filter

None

ii. Search strategy results and PRISMA diagram

Lifestyle Question 6 was restricted to systematic reviews and meta-analyses. The following databases were searched for evidence to answer this question:

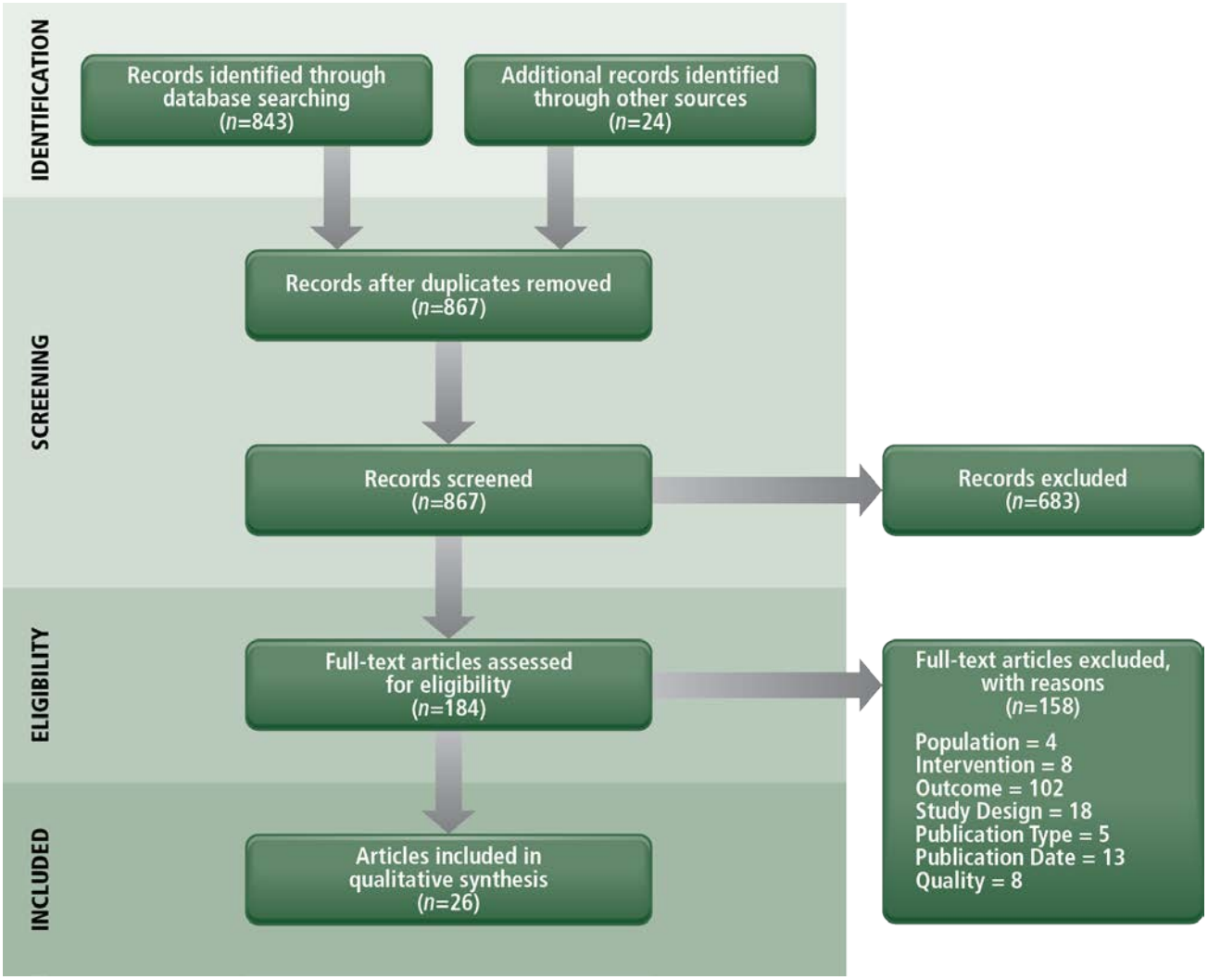
- PubMed from January 2001 to January 2010
- CINAHL from January 2001 to July 2008
- EMBASE from January 2001 to July 2008
- PsycInfo from January 2001 to July 2008
- EBM (Evidence-based Medicine) Cochrane Libraries from January 2001 to July 2008
- Biological Abstracts from January 2001 to July 2008
- Wilson Social Sciences Abstracts from January 2001 to July 2008

Duplicate citations which arise from the same citation being found in more than one database were removed from the Central Repository prior to screening. The search produced 843 systematic reviews and meta-analyses. An additional 24 citations published between January 2010 and May 2011 were retrieved from PubMed for review.

The titles and abstracts of these 867 publications were screened against the inclusion/exclusion criteria independently by two reviewers which resulted in the retrieval of 184 full-text papers. These papers were independently screened by two reviewers, and 158 of these publications were excluded on one or more of the inclusion/exclusion criteria. The majority of full-text articles that were excluded were excluded because the outcomes did not meet those specified in the criteria. An additional 16 publications were excluded because they were rated as poor quality using the NHLBI Quality Assessment Tool for Systematic Reviews and Meta-Analyses. Twenty-six systematic reviews and meta-analyses were eligible for inclusion in the Question 3 Evidence Base.

Twenty-five of the 26 included systematic reviews and meta-analyses were published between January 2001 and January 2010. One systematic review by Lin et al. that was published in December 2010 was retained in the body of evidence.(135)

Figure D–1. PRISMA Diagram Showing Selection of Articles for Lifestyle Question 3



iii. CQ3 Studies Rated as Poor With Rationale

Table D–7. CQ3 Studies Rated as Poor with Rationale

Study	Design	Primary Reason for Poor Quality Rating
Bartlo et al. 2007(179)	SR/MA	Unclear if review of citations and quality of component citations were completed by two independent reviewers; search strings not well described
Cornelissen et al. 2005(140)	SR/MA	Results based on search of one electronic database; Unable to determine if dual review or assessment of internal validity was completed
Cornelissen et al. 2005(141)	SR/MA	Unclear if review of citations and quality of component citations were completed by two independent reviewers
Fagard 2001(180)	SR/MA	No quality assessment of component studies, heterogeneity testing, or sensitivity analyses was performed
Haennel et al. 2002(181)	SR/MA	Results based on search of one electronic database; Unable to determine if dual review or assessment of internal validity was completed
Hamer et al. 2006(182)	SR/MA	No quality assessment of component studies, heterogeneity testing, or sensitivity analyses was performed
Tambalis et al. 2009(183)	SR/MA	Results based on search of one electronic database (PubMed); Unable to determine if dual review or quality assessment of component studies was performed
Yang 2007(184)	SR/MA	No dual review; unclear assessment of quality of component studies

Key
LTF: Lost-to-Followup
ITT: Intent-to-Treat Analysis

Appendix E. Summary Tables for Critical Questions

CQ1 Summary Tables

CQ1 Summary Table B–1. Mediterranean Style Dietary Pattern

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
Jula et al. 2002(23) RCT, crossover Turku, Southwestern Finland, 5 industrial plants and government offices Fair	**TREATMENT GROUPS:** G1: Modified Mediterranean-style diet G2: Habitual diet G1: <10% energy from saturated and *trans* unsaturated fatty acids; cholesterol ≤250 mg/d; omega–3 fatty acid intake of plant origin (α-linolenic acid) and marine origin ≥4 g/d and ratio of omega–6/omega–3 polyunsaturated fatty acids <4; increase intake of fruits, vegetables, and soluble fiber Rapeseed margarine and oil, oat bran (20 g/d) and frozen berries (50 g/d) supplied free Individual session and 2 group counseling sessions at the beginning of the treatment and 5 subsequent monthly group 'brush-up' sessions during the dietary treatment G2: subjects advised to continue eating usual diet during study period; no formal intervention after baseline **DURATION:** **Placebo run-in:** 4–6 weeks **Treatment:**12 weeks **Second randomized:** simvastatin vs. placebo	Adult males 35 to 64 years of age, previously untreated hypercholesterolemia (>232 mg/dL), BMI<32 ***N*:** G1: 60 G2: 60 **MEAN AGE, YRS (SD):** G1: 48.0 (6.2) G2: 48.4 (6.2) **WEIGHT, KG (SD):** G1: 82.4 (9.3) G2: 81.4 (9.7) **TOTAL CHOLESTEROL, MG/DL (SD):** G1: 250 (21) G2: 259 (24) *p*=0.04 **HDL-C, MG/DL (SD):** G1: 52 (12) G2: 49 (12) **LDL-C, MG/DL (SD):** G1: 175 (22)	NR (Authors note that BP not affected by diet or simvastatin (data not presented)	**AT 12 WEEKS** Mean (SE) [95% CI] G1–G2 **LDL-C, MG/DL** –19 (3) [–25 to –14] *p*<0.001 **HDL-C, MG/DL** –2 (1) [–4 to –0.4] *p*=0.01 **TRIGLYCERIDES, MG/DL** –1 (5) [–12 to 10] *p*=0.90 **APO A1, MG/DL** –3 (2) [–7 to 0] *p*=0.08 **APO B, MG/DL** –8 (2) [–13 to –3] *p*=0.003	**WITHDRAWALS, *N* (%):** G1: 0 (0) G2: 2 (3.3) **ADHERENCE:** NR (Descr' as 'good') **ACTUAL NUTRIENT INTAKE:** **Fat,% of total energy (SD):** G1: 34.8 (5.6) G2: 36.9 (4.6) **CHOLESTEROL, MG/D (SD):** G1: 214 (82) G2: 313 (101) **SFA, % OF TOTAL ENERGY (SD):** G1: 9.3 (2.1) G2: 14.6 (2.7) **MUFA, % OF TOTAL ENERGY (SD):** G1: 14.1 (3.0) G2: 12.6 (1.9) **PUFA, % OF TOTAL ENERGY (SD):** G1: 8.1 (1.6) G2: 5.9 (1.5)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
		G2: 183 (23) *p*=0.05 **APO B, MG/DL (SD):** G1: 129 (17) G2: 139 (21) *p*=0.01			**FIBER, G/DAY (SD)** G1: 27.2 (7.8) G2: 19.6 (6.1)

CQ1 Summary Table B–1. Mediterranean Style Dietary Pattern (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
Michalsen et al. 2006(24) RCT Germany, outpatient medical setting Fair	**TREATMENT GROUPS:** G1: Mediterranean-style diet G2: Control G1: Dietary recommendations for a diet rich in ALA, marine n–3 PUFA, MUFA, phytochemicals, and low in SFA. ≤5 portions of fruits and vegetables; daily emphasis on root and green vegetables (high ALA); >2 portions of fatty fish per week; whole-grains, flaxseed and walnuts; limit meat and sausage to 3 servings/wk; replace beef, pork, lamb with poultry, fish, or vegetarian dishes; olive, canola, flaxseed, and walnut oils encouraged; margarine discouraged (unless from olive oil as no ALA-based products were available) **Duration:** **Treatment:** 1 year **INTERVENTION DELIVERY:** G1: 3-day nonresidential retreat that included group counseling followed by weekly 3-hr meetings for 10 weeks. Thereafter, 2-hr meetings took place every other week for 9 months. Participants were intensively (100 h/yr) informed about the	CAD patients treated with statins, aspirin, Coumadin, beta blockers or ACE inhibitors ***N*:** G1: 53 G2: 48 **AGE, MEAN YEARS (SD):** G1: 59.0 (8.7) G2: 59.8 (8.6) **SEX, *N** (%):** Male G1: 42 (79.2) G2: 36 (75.5) **RACE/ETHNICITY:** NR **WEIGHT:** NR	NR	**AT 1 YEAR** **MEAN CHANGE IN HDL-C, MMOL/L (SD):** G1: 1.45 (0.37) G2: 1.39 (0.29) G1 vs. G2: 0.03 (95% CI): (–0.04,0.10) *p*=0.360 **MEAN CHANGE IN LDL-C, MMOL/L (SD):** G1: 3.12 (1.12) G2: 3.02 (0.72) G1 vs. G2: 0.22 (95% CI): (–0.10, 0.56) *p*=0.224 **MEAN CHANGE IN NON-HDL-C, MMOL/L (SD):** G1: 3.44 (1.25) G2: 3.38 (0.82) G1 vs. G2: 0.22	**WITHDRAWALS, *N* (%):** G1: 2 (3.77) G2: 1 (2.08) **ADHERENCE:** NR **ACTUAL NUTRIENT INTAKE:** **AT 1 YEAR** **ENERGY KJ (SD):** G1: 9371 (2130) G2: 9351 (2254) **FAT,% OF ENERGY (SD):** G1: 32.2 (6.1) G2: 35.2 (6.1) **CHO, % OF ENERGY (SD):** G1: 46.6 (6.4) G2: 43.4 (6.3) **PROTEIN, % OF ENERGY (SD):**

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
	Mediterranean diet, including group discussions, cooking classes, and group meals. If necessary a 1-hr individual session presented customized instructions. Also received a practical stress management program. G2: Patients received less detailed written information about Mediterranean diet and lifestyle advice (stress reduction) leaflet by mail.	**BMI, KG/M^2 (SD):** G1: 26.1 (3.2) G2: 27 (2.8) **SBP, MMHG (SD):** G1: 145.1 (19.1) G2: 145.1 (17.5) **DBP, MMHG (SD):** G1: 84.7 (13.4) G2: 82.7 (11.9)		(95% CI): (–0.12,0.58) *p*=0.289 **MEAN CHANGE IN TG, MMOL/L (SD):** G1: 1.45 (0.82) G2: 1.57 (0.95) G1 vs. G2:–0.03 (95% CI): (–0.34, 0.28) *p*=0.646	G1: 16.8 (2.6) G2: 17.0 (3.1) **SFA, % OF FAT (SD):** G1: 31.4 (7.2) G2: 36.8 (5.8) **MUFA, % OF FAT (SD):** G1: 32.8 (5.5) G2: 34.6 (4.2) **PUFA, % OF FAT (SD)** G1: 19.0 (6.2) G2: 21.0 (6.3) DHA and EPA increased **FIBER, G/DAY (SD):** G1: 33.1 (9.2) G2: 30.9 (12.6)

CQ1 Summary Table B–1. Mediterranean Style Dietary Pattern (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
PREDIMED Estruch et al., 2006(35) RCT Spain, outpatient centers Good	**TREATMENT GROUPS:** G1: Mediterranean diet with virgin olive oil G2: Mediterranean diet with mixed nuts G3: Recommended low-fat diet **DURATION:** **Treatment:** 3 months **Followup:** 4 yrs **INTERVENTION DELIVERY:**	Men 55 to 80 years, Women 60 to 80 years, Type 2 DM; or 3 or more CHD risk factors; 77% were hypertensive ***N*:** G1: 257 G2: 258 G3: 257 **AGE, MEAN YEARS (SD):**	**At 3 months** **MEAN CHANGES IN SBP, MMHG:** G1: –4.8 G2: –6.5 G3: 0.64 G1 vs. G3: –5.9 95% CI: (–8.7, –3.1); *p*<0.001 G2 vs. G3: –7.1 95% CI: (–10.0, –4.1); *p*<0.001	**At 3 months** **MEAN CHANGE IN HDL-C MMOL/L:** G1: 0.62 G2: 0.02 G3: 0.01 G1 vs. G3: 0.08 95% CI: (0.04, 0.10) *p*<0.001 G2 vs. G3: 0.04	**WITHDRAWALS, *N* (%)** G1: 0 (0) G2: 1 (0.38) G3: 2 (0.77) **ADHERENCE:** NR **Actual nutrient intake—Mean change from baseline at 3 months**

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
	All groups: Dietitian had a 30-min personalized session with each participant, and provided recommendations on the desired frequency of intake of specific foods. G1 & G2: 1 week after inclusion, the dietitian delivered a 1-hr group session with separate sessions for each Mediterranean diet group. Afterwards participants had free and continuous access to their center dietitian for advice and consultation. G1 & G2 also received free "3-month supplies (with additional supplies for those in families) of typical" sources of Mediterranean fats (virgin olive oil or nuts (walnuts, hazelnuts, almonds) based on group assignment). G3: Reduce fat intake and given AHA leaflet. No further intervention.	G1: 68.6 (6.9) G2: 68.5 (6.2) G3: 69.5 (6.1) **SEX, *N* (%):** Male G1: 102 (40) G2: 128 (50) G3: 109 (42) **RACE/ETHNICITY:** NR **WEIGHT:** NR **BMI ≥25 *N* (%)** G1: 232 (90) G2: 233 (90) G3: 231 (90) **BMI:** NR **SBP:** NR **DBP:** NR	**MEAN CHANGES IN DBP, MMHG (95% CI)** G1: –2.5 G2: –3.6 G3: –0.85 G1 vs. G3: –1.60 95% CI: (–3.00, –0.01); *p*=0.048 G2 vs. G3: –2.6 95% CI: (–4.2, 1.0); *P*=0.001	95% CI: (0.01, 0.07) *p*=0.006 **MEAN CHANGES IN LDL-C, MMOL/L:** G1: –0.15 G2: –0.10 G3: –0.15 G1 vs. G3: –0.10 95% CI: (–0.25, 0.04) *p*=0.177 G2 vs. G3: –0.09 95% CI: (–0.23, 0.05) *p*=0.119 **MEAN CHANGES IN TG, MMOL/L (95% CI):** G1: –0.03 G2: –0.09 G3: 0.03 G1 vs. G3: –0.08 95% CI: (–0.20, 0.04); *p*=0.21 G2 vs. G3: –0.15 95% CI: (–0.26, –0.02) *p*=0.022	**ENERGY, KCAL:** G1: –180 G2: –34 G3: –197 G1 vs. G3: 4.5 95% CI: (–139.0, 148.0); *p*=0.95 G2 vs. G3: 161 95% CI: (12, 310); *p*=0.034 **ENERGY FROM TOTAL PROTEIN, %:** G1: 0.36 G2: –0.28 G3: 0.83 G1 vs. G3: –0.47 95% CI: (–1.07, 0.13); *p*=0.122 G2 vs. G3: –1.00 95% CI: (–1.60, –0.38) *p*=0.002 **ENERGY FROM TOTAL CARBOHYDRATE, %:** G1: 0.33 G2: –2.9 G3: –0.36 G1 vs. G3: 0.22 95% CI: –1.30, 1.70); *p*=0.84 G2 vs. G3: –3.6 95% CI: (–5.2, –2.1); *p*<0.001 *(continued in next table)*

CQ1 Summary Table B–1. Mediterranean Style Dietary Pattern (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
PREDIMED Estruch et al., 2006(35) *(continued)*					*(continued from previous table)* **FIBER, G/D:** G1: 0.98 G2: 3.8 G3: 0.60 G1 vs. G3: 0.49 95% CI: (–1.91, 2.90); *p*=0.69 G2 vs. G3: 2.00 95% CI: (–0.54, 4.50); *p*=0.124 **ENERGY FROM TOTAL FAT, %:** G1: –0.75 G2: 3.4 G3: –1.40 G1 vs. G3: 0.45 95% CI: (–1.00, 1.90); *p*=0.55 G2 vs. G3: 5.0 95% CI: (3.5, 6.5) *p*<0.001 **SFA,%:** G1: –0.77 G2: –1.00 G3: –0.74 G1 vs. G3: –0.09 95% CI: (–0.55, 0.36); *p*=0.69 G2 vs. G3: 0.07 95% CI: (–0.40, 0.54); *p*=0.78 **MUFA, %:** G1: 0.15 G2: 1.38 G3: –0.52 G1 vs. G3:0.58 95% CI: (–0.30, 1.45); *p*=0.198 G2 vs. G3: 1.9 95% CI: (1.0, 2.8); *p*<0.001 *(continued in next table)*

CQ1 Summary Table B–1. Mediterranean Style Dietary Pattern (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
PREDIMED Estruch et al., 2006(35) *(continued)*					*(continued from previous table)* **PUFA, %:** G1: –0.11 G2: 3.0 G3: 0.14 G1 vs. G3: 0.03 95% CI: (0.53, 0.58); *p*=0.93 G2 vs. G3: 3.0 95% CI: (2.4, 3.5); *p*<0.001
SUN Núñez-Córdoba et al. 2009 (37) Prospective cohort study Spain, University Fair	**TREATMENT GROUPS:** G1: High adherence (score 7–9) G2: Moderate adherence (score 3–6) G3: Low adherence (score 0–2) Adherence scores assessed degree of adherence to the traditional Mediterranean dietary pattern. The score includes 9 components: vegetables, legumes, fruits and nuts, cereals, fish, meat and meat products, dairy products, alcohol, and the ratio of MUFA to SFA. Values of 0 or 1 were assigned to each of the 9 components. Consumption of vegetables, legumes, fruits and nuts, cereals, and fish: ≥median =1 pt; < the median = 0 pts. Consumption of meats, meat products and dairy: < median = 1 pt; ≥ median = 0 pts. Alcohol intake: 10–50 g/day for men, 5–25 g/day for women= 1 pt. MUFA:SFA ratio: < median = 0 pts; ≥ median= 1 pt. **FRUITS: MEAN (SD) SERVINGS/DAY:** G1: 3.5 (2.3) G2: 2.3 (1.9) G3: 1.2 (0.9) **Vegetables: Mean (SD) servings/day:** G1: 3.1 (1.5) G2: 2.2 (1.4) G3: 1.4 (0.8) *(continued in next table)*	Healthy adults ***n*:** G1: 1,143 G2: 6,730 G3: 1,535 **Mean years (SD):** G1: 41 (12) G2: 36 (10) G3: 32 (9) **Sex, *n*:** NR by group For overall population Male: 5,825 Female: 3,583 **Race/ethnicity:** NR **Weight:** NR **BMI, kg/m^2 (SD):** G1: 24 (3) G2: 23 (3) G3: 23 (3) **SBP:** NR **DBP:** NR	**At 6 years** ***N* (THOSE WITHOUT HTN AT BASELINE):** G1: 175 G2: 1,109 G3: 229 **SBP, mean absolute change, mmHg:** G1: –0.5 G2: 0 G3: 1.3 *p*=NR **SBP mean relative change, mmHg (multivariate adjusted[†]):** G1: –3.1 G2: –2.4 G3: 0 *p* for trend=0.01 **DBP, mean absolute change, mmHg:** G1: 0.2 G2: 0.1 G3: 0 *p*=NR *(continued in next table)*	NR	**WITHDRAWALS, *N* (%):** 9,190 participants completed 2-year follow-up questionnaire 6,428 completed 4-year follow-up questionnaire 3,509 completed 6-year follow-up questionnaire **ADHERENCE:** NR **ACTUAL NUTRIENT INTAKE:** NR

CQ1 Summary Table B–1. Mediterranean Style Dietary Pattern (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
SUN Núñez-Córdoba et al. 2009 (37) *(continued)*	*(continued from previous table)* **Legumes: Mean (SD) servings/day:** G1: 0.5 (0.3) G2: 0.4 (0.3) G3: 0.3 (0.3) **Nuts and dried fruits: Mean (SD) servings/day:** G1: 0.3 (0.4) G2: 0.2 (0.3) G3: 0.1 (0.1) **Cereals: Mean (SD) servings/day:** G1: 2.5 (1.4) G2: 1.9 (1.3) G3: 1.4 (1.1) **Meat: Mean (SD) servings/day:** G1: 1.5 (0.7) G2: 1.9 (0.9) G3: 2.2 (0.9) **Fish: Mean (SD) servings/day:** G1: 1.0 (0.4) G2: 0.7 (0.4) G3: 0.5 (0.3) **Eggs: Mean (SD) servings/day:** G1: 0.4 (0.2) G2: 0.4 (0.3) G3: 0.4 (0.3) **Dairy products: Mean (SD) servings/day:** G1: 1.0 (0.8) G2: 1.7 (1.3) G3: 2.4 (1.4) **Low-fat dairy products: Mean (SD) servings/day:** G1: 1.7 (1.5) G2: 1.3 (1.4) G3: 0.8 (1.2) *(continued in next table)*		*(continued from previous table)* **DBP mean relative change, mmHg (multivariate adjusted[†]):** G1: –1.9 G2: –1.,3 G3: 0 *p*=0.05 [†]adjusted for age, sex, BMI, family history of HTN, basal BP, hypercholesterolemia, caffeine intake, total energy intake, PA and smoking **Incident HTN # of participants / # of incident cases:** G1: 1,143/80 G2: 6,730/359 G3: 1.535/62 **Incident HTN, HR:*** G1: 1.17 G2: 1.11 G3: 1.00 *p* for trend=0.46 *Age- and sex-adjusted **Incident HTN, HR (95% CI), multivariate adjusted*** G1: 1.12 G2: 1.10 G3: 1.00 *p* for trend=0.41 *adjusted for age, sex, BMI, family history of HTN, hypercholesterolemia, caffeine intake, sodium intake, total energy intake, physical activity, and smoking		

CQ1 Summary Table B–1. Mediterranean Style Dietary Pattern (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence Actual Nutrient Intake
SUN Núñez-Córdoba et al. 2009 (37) *(continued)*	*(continued from previous table)* **Alcohol intake: Mean (SD) g/day:** G1: 9 (9) G2: 6 (10) G3: 4 (7) **SFA: Mean (SD) % of energy intake:** G1: 10 (2) G2: 13 (3) G3: 15 (3) **MUFA: Mean (SD) % of energy intake:** G1: 15 (4) G2: 16 (4) G3: 16 (3) **CHO: Mean (SD) % of energy intake:** G1: 47 (7) G2: 43 (7) G3: 41 (7) **Protein: Mean (SD) % of energy intake:** G1: 18 (3) G2: 18 (3) G3: 18 (3) **Kcal: Mean (SD):** G1: 2,528 (548) G2: 2,387 (615) G3: 2,261 (580) **Duration:** **Followup:** median period of 4.2 years (range, 1.9–7.9) **Intervention delivery:** Dietary habits at baseline assessed using a semi-quantitative food frequency questionnaire with 136 items. After baseline, participants received biennial questionnaires about diet, lifestyle, risk factors, and medical conditions.				

CQ1 Summary Table B–2. DASH Dietary Pattern and DASH Variations

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27); Obarzanek et al. 2001(28) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9 g fiber, and 300 mg/d of cholesterol G1: Diet rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein. Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, and 3,000 mg sodium. G2: Diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium, 3,000 mg sodium G3: Control diet typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was and was kept stable by changing calorie level. Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal. **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks *(continued in next table)*	Adults ≥22 years; SBP <160 mmHg and a DBP of 80–95 mmHg ***N*:** G1: 151 G2: 154 G3: 154 **AGE, MEAN YEARS (SD):** G1: 44 (10) G2: 45 (11) G3: 44 (11) **SEX, *N** (%):** Male G1: 74 (49.0) G2: 79 (51.3) G3: 81 (52.6) Female G1: 77 (51.0) G2: 75 (48.7) G3: 73 (47.4) **RACE/ETHNICITY, *N* (%):** Black G1: 93 (61.1) G2: 90 (58.4) G3: 92 (59.7) Non-minority G1: 47 (31.1) G2: 55 (35.7) G3: 54 (35.1) Other Minority G1: 11 (7.3) G2: 9 (5.8) G3: 8 (5.2) *(continued in next table)*	**At 8 weeks** **MEAN CHANGE IN CLINIC SBP, MMHG:** G1 vs. G3: –5.5, *p*=S G2 vs. G3: –2.8 *p*=NR **MEAN CHANGE IN CLINIC DBP, MMHG:** G1 vs. G3: –3.0 *p*=S G2 vs. G3: –1.1 *p*=NR **MEAN CHANGE IN AMBULATORY SBP, MMHG:** G1 vs. G3: –4.5, *p*=S G2 vs. G3: –3.1 *p*=NR **MEAN CHANGE IN AMBULATORY DBP, MMHG:** G1 vs. G3: –2.7 *p*=S G2 vs. G3: –2.1 *p*=NR **MEAN CHANGE IN SBP, MMHG (97.5% CI):** G1 vs. G2: –2.7 (–4.6, –0.9) *p*=0.001 G1 vs. G3: –5.5 (–7.4, –3.7) *p*<0.001 G2 vs. G3:–2.8 (–4.7, –0.9) *p*<0.001 *(continued in next table)*	**At 8 weeks** *N*=436* **HDL-C MMOL/L, NET CHANGE (95% CI):** G1 vs. G3: –0.09 (–0.13, –0.06) *p*< 0.0001 G2 vs. G3: –0.005 (–0.04, 0.030) *p*=NS **LDL-C MMOL/L, NET CHANGE (95% CI):** G1 vs. G3: –0.28 (–0.40, –0.16) *p*<0.0001 G2 vs. G3: –0.05 (–0.17, 0.07) *p*=NS *436 participants (95% of the 459) who provided fasting blood samples at baseline and end of the intervention	**WITHDRAWALS, *N* (%):** G1: 2 (1.3) G2: 4 (2.6) G3: 7 (4.5) **ADHERENCE:*** assessed by percent attendance at onsite meals **ONSITE MEAL ATTENDANCE, %:** G1: 96.1 G2: 95.4 G3: 95.8 Adherence was also assessed by percent of days per person with perfect adherence to study diets. Perfect adherence was defined as all study foods consumed and no nonstudy foods consumed. **MEAN % OF DAYS WITH PERFECT ADHERENCE PER PERSON:** G1: 93.2 G2: 93.9 G3: 94.6 *Procedures for adherence to the diets were revised after first participant groups completed the program. Data on adherence is for the 362 participants enrolled after the first participant group completed the program.

CQ1 Summary Table B–2. DASH Dietary Pattern and DASH Variations (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27); Obarzanek et al. 2001(28) *(continued)*	*(continued from previous table)* **INTERVENTION DELIVERY:** Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages and up to 2 servings of specific alcoholic beverages were allowed. *Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal.	*(continued from previous table)* **MEAN WEIGHT, KG:** G1: 83.4 G2: 81.8 G3: 81.5 **MEAN BMI, KG/M^2:** G1: 28.5 G2: 28.2 G3: 28.0 **SBP, MMHG (SD):** G1: 131.2 (10.0) G2: 132.3 (10.5) G3: 132 (10.7) **DBP, MMHG (SD):** G1: 85.1 (3.6) G2: 84.8 (3.9) G3: 85.3 (4.0)	*(continued from previous table)* **MEAN CHANGE IN SBP, MMHG (97.5% CI):** G1 vs.G2: –1.9 (–3.3, –0.6) *p*=0.002 G1 vs. G3: –3.0 (–4.3, –1.6) *p*<0.001 G2 vs. G3: –1.1 (–2.4, 0.3) *p*=0.07		

CQ1 Summary Table B–2. DASH Dietary Pattern and DASH Variations (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Harsha et al. 2004(30) RCT, crossover design within each diet USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Typical American Diet Run-in: Control diet + high sodium level, 50 mmol/d G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol. Emphasis on fruits, vegetables, and low-fat dairy foods, includes whole grains, poultry, fish, and nuts, and is reduced in fats, red meat, sweets, and sugar-containing beverages. G2: Control diet: 37% fat, 16% SF13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION:** **Run-in:** 2 wks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were high (H; 150 mmol/d), intermediate (I; 100 mmol/d), and low (L; 50 mmol/d).All food was provided. Weight was kept stable.	Adults ≥22 years; target of 50% enrollment of Blacks and women ***N*:** G1: 208 G2: 204 **AGE, MEAN YEARS (SD):** G1: 47 (10) G2: 49 (10) **SEX, *N** (%)** Male G1: 85 (41) G2: 93 (46) Female G1: 123 (59) G2: 111 (54) **n* from Vollmer WM, Sacks FM, Ard J et al. 2001(45) **RACE, *N* (%)** Black G1: 118 (57) G2: 114 (56) Non-Hispanic White G1: 83 (40) G2: 81 (40) Asian or other G1: 6 (3) G2: 10 (5) **WEIGHT:** NR	**At 30 days** **SBP, MMHG (95% CI):** G1 H vs. G2 H: –5.9 (–8.0, –3.7) *p*<0.001 G1 I vs. G2 I: –5.0 (–7.6, –2.5) *p*<0.001 G1 L vs. G2 L: –2.2 (–4.4, –0.1) *p*<0.05 **DBP, MMHG (95% CI):** G1 H vs. G2 H: –2.9 (–4.3, –1.5) *p*<0.001 G1 I vs. G2 I: –2.5 (–4.1, –0.8) *p*<0.01 G1 L vs. G2 L: –1.0 (–2.5, 0.4) *p*=NS	**At 30 days** **MEAN CHANGE IN LDL-C MMOL/L, AT 30 DAYS BY NA LEVEL (95% CI)**:** G1 H vs. G2 H: –0.33 (–0.45, –0.21) *p*<0.0001 G1 I vs. G2 I: –0.30 (–0.45, –0.16) *p*<0.0001 G1 L vs. G2 L:–0.37 (–0.49, –0.24) *p*<0.0001 **MEAN CHANGE IN HDL-C MMOL/L, AT 30 DAYS BY NA LEVEL (95% CI)*:** G1 H vs. G2 H: –0.10 (0.14, –0.06) *p*<0.0001 G1 I vs. G2 I: –0.09 (–0.14, –0.05) *p*<0.0001 G1 L vs. G2 L: –0.08 (–0.11, –0.04) *p*<0.0001 **MEAN CHANGE IN TG MMOL/L, AT 30 DAYS BY NA LEVEL (95% CI):**** G1 H vs. G2 H: 0.06 (–0.05, 0.18) *p*=0.3 G1 I vs. G2 I: –0.02 (–0.16, 0.11) *p*=0.7 G1 L vs.G2 L: 0.03 (–0.09, 0.15) *p*=0.6 **n*=390 ***n*=379	**WITHDRAWALS, *N* (%):** G1: 10 (95) G2: 12 (94) **ADHERENCE:** NR **Actual nutrient intake:** **Energy kcal/day, mean (SD):** G1: 2576 (511) G2: 2576 (493) **TOTAL FAT, % OF ENERGY (SD):** G1: 27.4 (0.2) G2: 38.6 (4.2) **TOTAL CHO, % OF ENERGY (SD):** G1: 58.5 (0.3) G2: 49.2 (0.3) **PROTEIN, G:** NR **SF, % OF ENERGY (SD):** G1: 6.2 (0.1) G2: 15.0 (0.2) **MUFA, % OF ENERGY (SD):** G1: 11.2 (0.1) G2: 12.5 (0.3) **PUFA, % OF ENERGY (SD):** G1: 8.0 (0.2)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
		MEAN BMI KG/M^2 (SD): G1: 29 (5) G2: 30 (5) *(continued in next table)*			G2: 7.4 (0.3) **FIBER, G/DAY, MEAN (SD):** G1: 35.0 (6.1) G2: 17.3 (18.0) *(continued in next table)*

CQ1 Summary Table B–2. DASH Dietary Pattern and DASH Variations (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Harsha et al. 2004(30) *(continued)*		*(continued from previous table)* **MEAN SBP, MMHG (SD):** G1: 134 (10) G2: 135 (10) **MEAN DBP, MMHG (SD):** G1: 86 (5) G2: 86 (4)			*(continued from previous table)* **CHOLESTEROL, MG/DAY, MEAN (SD):** G1: 194 (48) **G2: 324 (62.7)**
DASH-Sodium, Ancillary study Erlinger et al. 2003(31) RCT, crossover USA: outpatient medical center Fair	**TREATMENT GROUPS:** G1: DASH diet G2: Control diet Run-in: 37% fat, 16% SF,13% MUFA, 8% PUFA, 300 mg/d cholesterol G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION** **Run-in:** 2 wks Treatment: 14 wks **INTERVENTION DELIVERY:** Run-in is equivalent to control diet at highest sodium level. All food was provided. Weight was kept stable. There were three 30-day feeding periods, 1 at each of the 3 sodium levels, 150, 100, 50 mmol/d* in a random order. There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. *Sodium levels presented are representative of the diets at the energy level of 2,100 kcal.	Adults ≥22 years of age; SBP of 120–159 mmHg & DBP of 80–95 mmHg ***N*:** G1: 50 G2: 50 **AGE, MEAN YEARS (SD):** G1: 50 (1.4) G2: 53 (1.3) **SEX FEMALE, *N* (%):** Female G1: 31 (62) G2: 21 (42) **RACE/ETHNICITY, *N* (%):** Black G1: 41 (82) G2: 34 (68) **WEIGHT:** NR **BMI, KG/M^2 (SD):** G1: 29.3 (0.5)	NR	**At 14 weeks** **MEAN CHANGE IN HDL, MMOL/L:** G1 vs. G2:–0.12 *p*<0.001 **MEAN CHANGE IN LDL, MMOL/L:** G1 vs. G2: –0.29 *p*<0.001 **MEAN CHANGE IN TG, MMOL/L:** G1 vs. G2: +0.05 *p*=0.21	**WITHDRAWALS, *N* (%):** G1: 17 (34) G2: 19 (38) **ADHERENCE:** NR **ACTUAL NUTRIENT INTAKE:** NR

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
		G2: 30.1 (0.6) **SBP:** NR **DBP:** NR			

CQ1 Summary Table B–2. DASH Dietary Pattern and DASH Variations (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
OmniHeart Appel et al. 2005(36) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH-type diet G2: Protein rich diet G3: Diet rich in unsaturated fat G1: The carbohydrate diet similar to DASH, 58% CHO 27% total fat, 6% SF, 13% MUFA, 8% PUFA, protein 15%, fiber >30g, TC <150 mg/d. G2: The protein rich diet with varied proteins (meat, poultry, egg product substitutes, and dairy products); approximately ½ protein from plant sources like legumes, grains, nuts, and seeds. 48% CHO, 27% fat, 6% SF, 13% MUFA, 8% PUFA, 25% protein, fiber >30 mg/d, cholesterol < 150 mg/d G3: The unsaturated fat diet emphasized monounsaturated fats like olive, canola, and safflower oils, and a variety of nuts and seeds. 48% CHO, 37% fat, 6% SF, 21% MUFA, 10% PUFA, 15% protein, fiber >30 mg/d, cholesterol <150 mg/d 5 caloric levels of each diet: 1,600, 2,100, 2,600, 3,100, and 3,600 kcal. The goal was to keep weight within 2% of baseline. *nutrient targets based on 2,100 kcal version of diets **DURATION** **Treatment:** 6 weeks for each of the 3 feeding periods **Washout:** 2 to 4 weeks **INTERVENTION DELIVERY:** Participants ate each diet for a total of 3 feeding periods. All food was provided. On each weekday, participants ate their main meal onsite. All other meals were consumed offsite. Washout of 2 to 4 wks between feeding periods; participants ate their own food during washout.	Adults ≥30 years; BP range included individuals with pre-HTN (SBP 120–139 mmHg or DBP 80–89 mmHg) and stage 1 HTN (SBP 140–159 mmHg or DBP 90–99 mmHg) Baseline population characteristics not reported by treatment group ***N*:** Total: 164 **AGE, MEAN YEARS (SD):** 53 (10) **SEX, *N** (%)** Male: 92 (56) Female: 73 (44) **RACE, *N* (%)** African American: 90 (55) **WEIGHT:** NR **MEAN BMI KG/M^2 (SD)*:** 30.4 (6.1) * BMI representative of women sample only **MEAN SBP, MMHG (SD):** 131.2 (9.4) **MEAN DBP, MMHG (SD):** 77.0 (8.2)	**At 6 weeks** **MEAN CHANGE IN SBP, MMHG:** G1: –8.2 G2: –9.5 G3: –9.3 G1 vs. G2: –1.4; P= 0.002 G1 vs. G3: –1.3 *p*=0.005 G2 vs. G3:–0.1 *p*=0.90 **MEAN CHANGE IN DBP, MMHG (95% CI):** G1:–4.1 G2:–5.2 G3:–4.8 G1 vs. G2: –1.2 *p*<0.001 G1 vs. G3:–0.4 *p*=0.20 G2 vs. G3:–0.8 *p*=0.02	**At 6 weeks** **MEAN CHANGE IN LDL-C, MG/DL (95% CI):** G1:–11.6 G2:–14.2 G3:–13.1 G1 vs. G2: –3.3 *p*=0.01 G1 vs. G3:–1.5 *p*=0.24 G2 vs. G3:–0.8 *p*=0.02 **MEAN CHANGE IN HDL-C, MG/DL (95% CI):** G1: –1.4 G2: –2.6 G3: –0.3 G1 vs. G2: –1.3 *p*=0.02 G1 vs. G3 1.1 *p*=0.03 G2 vs. G3: –2.3 *p*<0.001 **MEAN NON-HDL-C, MG/DL (95% CI):** G1: –11.0 G2: –17.3 G3: –15.1 G1 vs. G2: –6.5 *p*<0.001 G1 vs. G3:–2.6 *p*=0.054 G2 vs. G3 –4.2 *p*=0.002	**WITHDRAWALS:** 161 included in analysis of G2 vs. G1 161 included in analysis of G3 vs. G1 160 included in analysis of G3 vs. G2 **ADHERENCE, %:** G1: 96 G2: 95 G3: 96 Adherence defined as % days of perfect adherence. Perfect adherence is self-report of all study food eaten and no nonstudy food eaten expressed as a percentage of person-days of feeding. **ACTUAL NUTRIENT INTAKE:** **ENERGY INTAKE, MEAN (SD), KCAL/D:** G1: 2599 (578) G2: 2558 (538) G3: 2564 (556)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
				(continued in next table)	

CQ1 Summary Table B–2. DASH Dietary Pattern and DASH Variations (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
OmniHeart Appel et al. 2005(36) *(continued)*				*(continued from previous table)* **MEAN CHANGE IN TG, MG/DL (95% CI):** G1: –0.1 G2: –16.4 G3: –9.3 G1 vs. G2: –15.7 *p*<0.001 G1 vs. G3 –9.6 *p*=0.02 G2 vs. G3:–7.1 *p*=0.03	

CQ1 Summary Table B–3. DASH Pattern Subgroups: Sex

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis Appel et al. 1997(26); Svetkey 1999(41); Obarzanek et al. 2001(28) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9 g fiber, and 300 mg/d of cholesterol G1: Diet rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein. Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol,	Adults ≥22 years; SBP <160 mmHg and a DBP of 80–95 mmHg ***N*:** G1: 151 G2: 154 G3: 154 **SEX , *N* (%):** Male G1: 74 (49.0) G2: 79 (51.3)	**At 8 weeks** Male, *n*=234 Female, *n*=225 **NET CHANGE IN SBP IN FEMALES, MMHG:*** G1 F:–6.4 G2 F: –2.2 G3 F: NR *(continued in next table)*	**At 8 weeks** *N*=436 **MEAN CHANGE IN HDL-C, MMOL/L:** G1 F: –0.09 G1 M: –0.10 G2 F: 0.01 G2 M: –0.03 *p*=NR **MEAN CHANGE IN LDL-C,**	**WITHDRAWALS:** NR by subgroup **ADHERENCE:** NR by subgroup **ACTUAL NUTRIENT INTAKE:** NR by subgroup

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
	4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, and 3,000 mg sodium. *(continued in next table)*	G3: 81 (52.6) Female G1: 77 (51.0) G2: 75 (48.7) G3: 73 (47.4)		**MMOL/L:** G1 F: –0.14 G1 M: –0.43 G2 F: 0.05 G2 M: –0.12 *p*=NR	

CQ1 Summary Table B–3. *DASH Pattern Subgroups: Sex (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis Appel et al. 1997(26); Svetkey 1999(41); Obarzanek et al. 2001(28) *(continued)*	*(continued from previous table)* G2: Diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium, 3,000 mg sodium G3: Control diet typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was kept stable Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks **INTERVENTION DELIVERY:** Participants attended the clinic each weekday to be		*(continued from previous table)* **MEAN CHANGE IN SBP IN FEMALES, MMHG (97.5 CI%)** G1 F vs. G2 F:–3.9 (–6.9, –1.0) *p*=0.003 G1 F vs. G3 F: 6.2 (–9.2, –3.3) *P*<0.001 G2 F vs. G3 F:–2.3 (–5.3, 0.7) *P*=0.08 **NET CHANGE IN SBP IN MALES, MMHG:*** G1 M: –4.8 G2 M: –3.4 G3 M = NR **MEAN CHANGE IN SBP IN MALES, MMHG (97.5 CI%):** G1 M vs. G2 M:–1.6 (–4.0, 0.8) *p*=0.13 G1 M vs. G3 M:–4.9 (–7.3, –2.5) *p*<0.001 G2 M vs. G3 M: –3.3 (–5.6, –0.9)		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
	weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages and up to 2 servings of specific alcoholic beverages were allowed.		*p*=0.002 **NET CHANGE IN DBP IN FEMALES, MMHG:*** G1 F: –2.9 G2 F: –0.1 G3 F: NR **MEAN CHANGE IN DBP IN FEMALES, MMHG (97.5 CI%):** G1 F vs. G2 F:–2.5 (–4.6, –0.5) *p*=0.006 G1 F vs. G3 F: –2.7 (–4.8, –0.7) *P*=0.003 G2 F vs. G3 F: –0.2 (–2.3, 1.9) *p*=0.83 *(continued in next table)*		

CQ1 Summary Table B–3. DASH Pattern Subgroups: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis Appel et al. 1997(26); Svetkey 1999(41); Obarzanek et al. 2001(28) *(continued)*			*(continued from previous table)* **NET CHANGE IN DBP IN MALES, MMHG:*** G1 M: –3.3 G2 M: –2.0 G3 M: NR **MEAN CHANGE IN DBP IN MALES, MMHG:** (97.5 CI%) G1 M vs. G2 M: –1.3 (–3.2, 0.5) *p*=0.10		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
			G1 M vs. G3 M: –3.3 (–5.1, –1.5) *p*<0.001 G2 M vs. G3 M:–2.0 (–3.7,–0.2) *p*=0.01 *adjusted for site and cohort effects		
DASH subgroup analysis Moore et al. 1999(42) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9 g fiber, and 300 mg/d of cholesterol G1: Diet rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein. Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, and 3,000 mg sodium. G2: Diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium, 3,000 mg sodium *(continued in next table)*	Participants in DASH cohorts 2–5 in which ABP was measured and run-in ABPM was satisfactory ***N*:** G1: 115 G2: 121 G3: 118 **SEX , *N* (%):** Male G1: NR (50) G2: 68 (56) G3: 63 (53) Female G1: NR (50) G2: 53 (44) G3: 55 (47)	**At 8 weeks** **MEAN SBP RESPONSE (95% CI):** G1 M vs. G3 M:–4.4 (–6.6, –2.1) *p*=0.0002 G1 F vs. G3. F:–4.6 (–7.3, –1.9) *p*=0.0011 **MEAN DBP RESPONSE (95% CI):** G1 M vs. G3 M:–2.4 (–4.1, –0.7) *p*=0.0050 G1 F vs. G3. F:–3.2 (–5.2, –1.1) *p*=0.0025	NR	**WITHDRAWALS:** NR by subgroup **ADHERENCE:** NR by subgroup **ACTUAL NUTRIENT INTAKE:** NR by subgroup

CQ1 Summary Table B–3. DASH Pattern Subgroups: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis	*(continued from previous table)* G3: Control diet typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8%				

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
Moore et al. 1999(42) *(continued)*	PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was kept stable. *Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal. **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks **INTERVENTION DELIVERY:** Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages and up to 2 servings of specific alcoholic beverages were allowed.				

CQ1 Summary Table B–3. DASH Pattern Subgroups: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium subgroup analysis Vollmer, et al. 2001(45) RCT, crossover USA, outpatient medical setting Fair	**TREATMENT GROUPS:** G1: DASH diet G2: Typical American diet Run-in: Control diet + high sodium level, 50 mmol/d G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol. Emphasis on fruits, vegetables, and low-fat dairy foods, includes whole grains, poultry, fish, and nuts, and is reduced in fats, red meat, sweets, and sugar-containing beverages. G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol. **DURATION:** **Run-in:** 2 wks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were high (H; 150 mmol/d), intermediate (I; 100 mmol/d), and low (L; 50 mmol/d). All food was provided. Weight was kept stable. There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was kept stable. *Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal.	Adults ≥22 years; target of 50% enrollment of Blacks and women ***N*:** G1: 208 G2: 204 **SEX, *N* (%)** Male G1: 85 (41) G2: 93 (46) Female G1: 123 (59) G2: 111 (54)	**MEAN CHANGE IN SBP, MMHG AT HIGHER SODIUM INTAKE LEVEL (95% CI):*** G1 F vs. G2 F: –6.6 *p*=NR G1 M vs. G2 M: –5.1 *p*=NR **MEAN CHANGE IN DBP, MMHG AT HIGHER SODIUM INTAKE LEVEL (95% CI):*** G1 F vs. G2 F: –3.0 *p*=NR G1 M vs. G2 M: –2.7 *p*=NR *Analyses are unadjusted for other groups. All models included adjustment for baseline BP, study site, feeding cohort, and carryover effects.	NR	**WITHDRAWALS:** NR by subgroup **ADHERENCE:** NR by subgroup **ACTUAL NUTRIENT INTAKE:** NR

CQ1 Summary Table B–4. DASH Pattern Subgroups: Race/Ethnicity

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27), Svetkey et al. 1999(41); Obarzanek et al. 2001(28) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet G1: DASH. Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9 g fiber, and 300 mg/d of cholesterol Treatment: rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, 3,000 mg sodium G2: Fruits and vegetables diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium, 3,000 mg sodium. G3: Control diet: typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium *Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal. **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks *(continued in next table)*	Adults ≥22 years; SBP of <160 mmHg and DBP 80 to 95 mmHg ***N*:** G1: 151 G2: 154 G3: 154 **RACE/ETHNICITY, *N* (%):** Black G1: 92 (61.1) G2: 90 (58.4) G3: 92 (59.7) Non-minority G1: 48 (31.1) G2: 55 (35.7) G3: 54 (35.1) Other Minority G1: 11 (7.3) G2: 9 (5.8) G3: 8 (5.2) Minority, *n*=303 Non-Minority, *n*=156	**At 8 weeks** **MEAN CHANGE IN SBP, MMHG** G1 AA:–6.9 G1 W:–3.3 *p*=NR **MEAN CHANGE IN DBP, MMHG:** G1 AA: –3.7 G1 W: –2.4 *p*=NR **MEAN CHANGE IN SBP IN MINORITY POPULATION, MMHG (97.5%):** G1 vs. G2=–3.2 (–5.6, –0.8) *p*=0.003 G1 vs. G3= –6.8 (–9.2, –4.4) *p*<0.001 G2 vs. G3= –3.6 (–6.1, –1.2) *p*=0.001 **MEAN CHANGE IN SBP IN NON-MINORITY POPULATION, MMHG (97.5%):** G1 vs. G2=–1.9 (–4.8, 1.0) *p*=0.13 G1 vs. G3= –3.0 (–5.9, –0.1) *p*=0.02 G2 vs. G3= –1.1 (–3.9, 1.7) *p*=0.38 *(continued in next table)*	**At 8 weeks** *n*=436 **MEAN CHANGE IN HDL-C MMOL/L (95% CI):** G1 AA: –0.09 G1 non AA: –0.10 G2 AA: –0.02 G2 non AA: 0.01 *p*=NR **MEAN CHANGE IN LDL-C MMOL/L (95% CI):** G1 AA: –0.29 G1 non AA: –0.28 G2 AA: 0.00 G2 non AA: –0.09 *p*=NR **MEAN CHANGE IN TG MMOL/L (95% CI):** G1 AA: 0.02 G1 non AA: 0.05 G2 AA: –0.05 G2 non AA: –0.14 *p*=NR	**WITHDRAWALS:** NR for subgroup **ADHERENCE:** NR for subgroup **ACTUAL NUTRIENT INTAKE:** NR for subgroup

CQ1 Summary Table B–4. DASH Pattern Subgroups: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27), Svetkey et al. 1999(41); Obarzanek et al. 2001(28) *(continued)*	*(continued from previous table)* **INTERVENTION DELIVERY:** Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages (coffee, tea, and sugar-free, caffeine free soft drinks) and up to 2 servings of specific alcoholic beverages (beer, white wine, and spirits) were allowed. THERE WERE FOUR CALORIE LEVELS OF 1,600, 2,100, 2,600, OR 3,100 KCALS FOR EACH DIET. WEIGHT WAS AND WAS KEPT STABLE.		*(continued from previous table)* **MEAN CHANGE IN DBP IN MINORITY POPULATION, MMHG (97.5%):** G1 vs. G2: –2.1 (–3.8, –0.4) *p*=0.007 G1 vs. G3: –3.5 (–5.2, –1.8) *p*< 0.001 G2 vs. G3: –1.4 (–3.2, 0.3) *p*=0.07 **MEAN CHANGE IN SBP IN NON-MINORITY POPULATION, MMHG (97.5%):** G1 vs. G2: –1.6 (–3.8, 0.5) *p*=0.09 G1 vs. G3: –2.0 (–4.2, 0.2) *p*=0.04 G2 vs. G3: –0.4 (–2.5, 1.7) *p*=0.70 **NET CHANGE IN SBP, MMHG:*** G1 AA: –6.9 G1 W: –3.3 G2 AA: –3.5 G2 W: –0.9 *p*=NR **NET CHANGE IN DBP, MMHG:*** G1 AA:–3.7 G1 W:–2.4 G2 AA: –1.4 G2 W: –0.3 *p*=NR *adjusted for site and cohort effects		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
			(continued in next table)		

CQ1 Summary Table B–4. DASH Pattern Subgroups: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27), Svetkey et al. 1999(41); Obarzanek et al. 2001(28) *(continued)*			*(continued from previous table)* **At 8 weeks** **MEAN CHANGE IN SBP IN AFRICAN AMERICANS, MMHG:** G1 H: –13.2 G1 no H: –4.3 G2 H: –8.0 G2 no H: –1.3 **MEAN CHANGE IN SBP IN WHITES, MMHG** G1 H: –6.3 G1 no H: –2.0 G2 H: –5.9 G2 no H: 0.8 **MEAN CHANGE IN DBP IN AFRICAN AMERICANS, MMHG** G1 H: –6.1 G1 no H: –2.6 G2 H: –3.4 G2 no H: –0.3 **MEAN CHANGE IN SBP IN WHITES, MMHG:** G1 H: –4.4 G1 no H: –1.2		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
			G2 H: –3.1 G2 no H: 0.4		

CQ1 Summary Table B–4. DASH Pattern Subgroups: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Moore et al.1999(42) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet G1: DASH. Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9g fiber, and 300 mg/d of cholesterol. Treatment: Rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, 3,000 mg sodium G2: Fruits and vegetables diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium, 3,000 mg sodium G3: Control diet: typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium *Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal. **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks *(continued in next table)*	Participants in DASH cohorts 2–5 in which ABP was measured. Run-in ABPM was satisfactory ***N*:** G1: 115 G2: 121 G3: 118 **RACE/ETHNICITY, *N* (%):** Other [Minority]: G1: 74 (64) G2: 73 (60) G3: 72 (61)	**At 8 weeks** **MEAN SBP RESPONSES IN NON-MINORITY POPULATION, MMHG (95% CI):** G1 vs. G3: –2.7 (–5.5, 0.2) *p*=0.0668 **MEAN SBP RESPONSES IN MINORITY POPULATION, MMHG (95% CI):** G1 vs. G3:–5.6 (–7.8, –3.4) *p*=0.0001 **MEAN DBP RESPONSES IN NON-MINORITY POPULATION, MMHG (95% CI):** G1 vs. G3:–1.8 (–3.9, 0.4) *p*=0.0998 **MEAN DBP RESPONSES IN MINORITY POPULATION, MMHG (95% CI):** G1 vs. G3: –3.4 (–5.0, –1.7) *p*=0.0001	NR	**WITHDRAWALS:** NR for subgroup **ADHERENCE:** NR for subgroup **ACTUAL NUTRIENT INTAKE:** NR for subgroup

CQ1 Summary Table B–4. DASH Pattern Subgroups: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Moore et al.1999(42) *(continued)*	*(continued from previous table)* **INTERVENTION DELIVERY:** Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages (coffee, tea, and sugar-free, caffeine free soft drinks) and up to 2 servings of specific alcoholic beverages (beer, white wine, and spirits) were allowed. **THERE WERE FOUR CALORIE LEVELS OF 1,600, 2,100, 2,600, OR 3,100 KCALS FOR EACH DIET. WEIGHT WAS AND WAS KEPT STABLE.**				
DASH-Sodium Vollmer et al. 2001(45); Bray et al. 2004(44) RCT: crossover USA, outpatient medical setting Fair	**TREATMENT GROUPS:** G1: DASH diet G2: Typical American diet Run-in: Control diet + high sodium level, 50 mmol/d G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol. Emphasis on fruits, vegetables, and low-fat dairy foods, includes whole grains, poultry, fish, and nuts, and is reduced in fats, red meat, sweets, and sugar-sweetened beverages. G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION:** **Run-in:** 2 wks **Treatment:** 90 days, 30 days per sodium condition *(continued in next table)*	Adults ≥22 years; target of 50% enrollment of Blacks and women ***N*:** G1: 208 G2: 204 **RACE, *N* (%)*** African American G1: 119 (57) G2: 115 (56) Total: 234 (57) White G1: NR G2: NR Total: 162 (39) *(continued in next table)*	**MEAN CHANGE IN SBP, MMHG AT HIGHER SODIUM INTAKE LEVEL (95% CI):*** G1 AA vs. G2 AA: –5.9 *p*=NR G1 Non-AA vs. G2 Non-AA: –5.6 *p*=NR **MEAN CHANGE IN DBP, MMHG AT HIGHER SODIUM INTAKE LEVEL (95% CI):*** G1 AA vs. G2 AA: –3.1 *p*=NR G1 Non-AA vs. G2 Non-AA: –2.4 *p*=NR	NR	**WITHDRAWALS:** NR for subgroup **ADHERENCE:** NR for subgroup **ACTUAL NUTRIENT INTAKE:** NR

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
			(continued in next table)		

CQ1 Summary Table B–4. DASH Pattern Subgroups: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Vollmer et al. 2001(45); Bray et al. 2004(44) *(continued)*	*(continued from previous table)* **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were high (H; 150 mmol/d), intermediate (I; 100 mmol/d), and low (L; 50 mmol/d).All food was provided. Weight was kept stable.	*(continued from previous table)* Other G1: NR G2: NR Total: 16 (4) Non-African American G1: 89 (43) G2: 89 (44) Total: 178 (76) ***N*:** AA H: 56 AA no H: 129 White H: 24 White no H: 77 Baseline characteristics reported for race and reported for HTN but not for both race + HTN	*(continued from previous table)* *Analyses are unadjusted for other groups. All models included adjustment for baseline BP, study site, feeding cohort and carryover effects. **At 30 days** **MEAN CHANGE IN SBP, MMHG (HIGHER TO LOWER SODIUM):*** African American G1 H: –5.7 G1 no H: –2.0 G2 H: –9.4 G2 no H: –6.9 *p*=NR Non-African American G1 H: –3.7 G1 no H: –1.4 G2 H: –6.8 G2 no H: –4.0 *p*=NR **N*=412		

CQ1 Summary Table B–5. DASH Pattern Subgroup: Hypertension Status

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27); Svetkey 1999(41) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet G1: DASH. Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9g fiber, and 300 mg/d of cholesterol Treatment: Rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein. Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, 3,000 mg sodium G2: Fruits and vegetables diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium, 3,000 mg sodium G3: Control diet: typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium *Nutrient values presented for all diets are representative of the diets at the energy level of 2100 kcal. **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks *(continued in next table)*	Adults ≥22 years; SBP of <160 mmHg and DBP 80 to 95 mmHg ***N*:** G1: 151 G2: 154 G3: 154 **HTN, *N* (%):** G1: 37 (25) G2: 49 (32) G3: 47 (31) ***N*/TOTAL SAMPLE (%):** 133/459 (29)	**At 8 weeks** **MEAN CHANGE IN SBP, MMHG (97.5% CI):** G1 HTN vs.G2 HTN: –4.1 (–8.6, 0.3) *p*= 0.04 G1 HTN vs. G3 HTN: –11.4 (–15.9, –6.9) *p*< 0.001 G3 HTN vs. G2 HTN: –7.2 (11.4, 3.0) *p*< 0.001 G1 no HTN vs. G2 no HTN: –2.7 (–4.5, –0.8) *p*= 0.001 G1 no HTN vs. G3 no HTN: –3.5 (–5.3, –1.6) *p*< 0.001 G3 no HTN vs. G2 no HTN: –0.8 (–2.7, 1.1) *p*=0.33 **MEAN CHANGE IN DBP, MMHG (97.5% CI):** G1 HTN vs.G2 HTN: –2.6 (–5.4, 0.1) *p*=0.03 G1 HTN vs. G3 HTN: –5.5 (–8.2, –2.7) *p*<0.001 G3 HTN vs. G2 HTN: –2.8 (–5.4, –0.3) *p*=0.01 G1 no HTN vs. G2 no HTN: –1.8 (–3.4, –0.3) *p*=0.009	NR	**WITHDRAWALS:** NR by subgroup **ADHERENCE:** NR by subgroup **ACTUAL NUTRIENT INTAKE:** NR by subgroup

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
			(continued in next table)		

CQ1 Summary Table B–5. *DASH Pattern Subgroup: Hypertension Status (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27); Svetkey 1999(41) *(continued)*	*(continued from previous table)* **INTERVENTION DELIVERY:** Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages (coffee, tea, and sugar-free, caffeine free soft drinks) and up to 2 servings of specific alcoholic beverages (beer, white wine, and spirits) were allowed. There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was kept stable		*(continued from previous table)* **MEAN CHANGE IN DBP, MMHG (97.5% CI):** G1 no HTN vs. G3 no HTN: –2.1 (–3.6, –0.5) *p*=0.003 G3 no HTN vs. G2 no HTN: –0.3 (–1.9, 1.3) *p*=0.71 **NET CHANGE IN SBP, MMHG:*** G1 HTN: –11.6 G1 no HTN: –3.5 *p*≤0.008 G2 HTN: –7.1 G2 no HTN: –0.09 *p*=0.001 **NET CHANGE IN DBP, MMHG:*** G1 HTN: –5.3 G1 no HTN: –2.2 *p*≤0.008 G2 HTN: –2.8 G2 no HTN: –0.4 *p*=0.07 * net change values adjusted for site and cohort effects		

CQ1 Summary Table B–5. DASH Pattern Subgroup: Hypertension Status (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis Moore et al 1999(42) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet G1: DASH, Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9 g fiber, and 300 mg/d of cholesterol Treatment: Rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, 3,000 mg sodium G2: Fruits and vegetables diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium, 3,000 mg sodium G3: Control diet: typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium *Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal. **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks *(continued in next table)*	Participants in DASH cohorts 2–5 in which ABP was measured. Run-in ABPM was satisfactory ***N*:** G1: 115 G2: 121 G3: 118 **HTN, *N* (%):** G1:31 (27) G2:36 (30) G3:36 (31)	**At 8 weeks** **MEAN SBP RESPONSE (95% CI):** G1 HTN vs. G3 HTN: –10.1 (–13.9,–6.2) *p*=0.0001 G1 no HTN vs. G3 no HTN: –2.3 (–4.1,–0.5) *p*= 0.0121 **MEAN DBP RESPONSE (95% CI):** G1 HTN vs. G3 HTN: –5.5 (–8.2, –2.7) *p*=0.0001 G1 no HTN vs. G3 no HTN: –1.6 (–3.1,–0.2) *p*=0.0234	NR	**WITHDRAWALS:** NR by subgroup **ADHERENCE:** NR by subgroup **ACTUAL NUTRIENT INTAKE:** NR

CQ1 Summary Table B–5. DASH Pattern Subgroup: Hypertension Status (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis Moore et al 1999(42) *(continued)*	*(continued from previous table)* **INTERVENTION DELIVERY:** Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages (coffee, tea, and sugar-free, caffeine free soft drinks) and up to 2 servings of specific alcoholic beverages (beer, white wine, and spirits) were allowed. There were four calorie levels of 1.600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was and was kept stable.				
DASH Subgroup Analysis Conlin et al. 2000(43) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet G1: DASH, Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9 g fiber, and 300 mg/d of cholesterol Treatment: rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, 3,000 mg sodium. G2: Fruits and Vegetables diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium,	Participants in DASH with SBP of 140 to 159 mmHg and/or DBP of 90 to 95 mmHg ***N*:** G1: 37 G2: 49 G3: 47 **HTN, *N** (%)** G1: (65) G2 (55) G3: (64)	**At 8 weeks** **MEAN BETWEEN DIET DIFFERENCES IN SBP, MMHG:*** G1 vs. G3: –11.6 (–15.5, –7.6) *p*<0.001 G1 vs. G2: –4.5 (–8.4, –0.7) *p*=0.023 G2 vs. G3: –7.0 (–10.7, –3.4) *p*<0.001 **MEAN BETWEEN DIET DIFFERENCES IN DBP, MMHG:*** G1 vs. G3: –5.9 (–8.3, –3.4) *p*<.001 G1 vs. G2: –2.9 (–5.3, –0.5) *p*=.020 G2 vs. G3: –3 (–5.3, –0.7) *p*=.010		**WITHDRAWALS:** NR **ADHERENCE, %:** G1: 100 G2: 96 G3: 94 **ACTUAL NUTRIENT INTAKE:** NR

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
	3,000 mg sodium *(continued in next table)*		*adjusted for Clinical Centers, gender, race, age, ETOH, and baseline SBP		

CQ1 Summary Table B–5. DASH Pattern Subgroup: Hypertension Status (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Subgroup Analysis Conlin et al. 2000(43) *(continued)*	*(continued from previous table)* G3: Control diet: typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium *Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal. **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks **INTERVENTION DELIVERY:** Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages (coffee, tea, and sugar-free, caffeine free soft drinks) and up to 2 servings of specific alcoholic beverages (beer, white wine, and spirits) were allowed.				

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
	There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was and was kept stable.				

CQ1 Summary Table B–5. DASH Pattern Subgroup: Hypertension Status (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Vollmer et al. 2001(45) RCT: crossover USA, outpatient medical setting Fair	**TREATMENT GROUPS:** G1: DASH diet G2: Typical American diet Run-in: Control diet + high sodium level, 50 mmol/d G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol. Emphasis on fruits, vegetables, and low-fat dairy foods, includes whole grains, poultry, fish, and nuts, and is reduced in fats, red meat, sweets, and sugar-containing beverages. G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION:** **Run-in:** 2 wks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were high (H; 150 mmol/d), intermediate (I; 100 mmol/d), and low (L; 50 mmol/d). All food was provided. Weight was kept stable.	Adults ≥22 years; target of 50% enrollment of Blacks and women ***N*:** G1: 208 G2: 204 **HTN, *N* (%):** G1: 85 (40) G2: 83 (40)	**MEAN CHANGE IN SBP, MMHG AT HIGHER SODIUM INTAKE LEVEL (95% CI):*** G1 HTN vs. G2 HTN: –6.6 *p*=NR G1 Non-HTN vs. G2 Non-HTN: –5.4 *p*=NR **MEAN CHANGE IN DBP, MMHG AT HIGHER SODIUM INTAKE LEVEL (95% CI):*** G1 HTN VS. G2 HTN: –3.2 *p*=NR G1 Non-HTN vs. G2 Non-HTN: –2.7 *p*=NR *Analyses are unadjusted for other groups. All models included adjustment for baseline BP, study site, feeding cohort, "and carryover effects."	NR	**WITHDRAWALS:** NR by subgroup **ADHERENCE:** NR by subgroup **Actual Nutrient Intake:** NR

CQ1 Summary Table B–6. DASH Pattern Subgroup: Age

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis Svetkey et al. 1999 RCT USA, Outpatient Medical Setting Good	**Treatment Groups:** G1. DASH diet G2. Fruits and vegetables diet G3. Control diet G1: DASH, Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9g fiber, and 300 mg/d of cholesterol Treatment: rich in fruits, vegetables, and low fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein. Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4700mg potassium, 500mg magnesium, 1240mg calcium, 3,000mg sodium G2: Fruits and Vegetables diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4770mg potassium, 500mg magnesium, 450mg calcium, 3,000mg sodium G3. Control diet: typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1700mg potassium, 165 mg magnesium, 450 mg calcium, 3,000mg sodium *Nutrient values presented for all diets are representative of the diets at the energy level of 2100 kcal **Duration** **Run-in:** 3 wks **Treatment:** 8 wks *(continued in next table)*	Adults ≥ 22 years of age not taking anti-hypertensive medication; SBP < 160 mmHg and a DBP of 80 to 95 mmHg **n:** G1: 151 G2: 154 G3: 154 **Mean years (SD):** G1: 44 (10) G2: 45 (11) G3: 44 (11) **Age ≤ 45:** G1: 83 G2: 78 G3: 82 **Age > 45:** G1: 68 G2: 76 G3: 72	**At 8 weeks** **Net SBP change, mmHg (95% CI):** G1 ≤ 45:-5.0 G1 > 45:-6.8 *p*=NR G2 ≤ 45:-3.1 G2 > 45:-2.5 *p*=NR **Net DBP change, mmHg (95% CI):** G1 ≤ 45:-3.5 G1 > 45:-2.6 *p*=NR G2 ≤ 45:-1.8 G2 > 45:-0.4 *p*= NR	NR	**Withdrawals:** NR by subgroup **Adherence:** NR by subgroup **Actual nutrient intake:** NR by subgroup

CQ1 Summary Table B–6. DASH Pattern Subgroup: Age (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis Svetkey et al. 1999 *(continued)*	*(continued from previous table)* **Intervention delivery:** Participants attended the clinic each weekday to be weighed and to consume one meal on site (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium, was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages (coffee, tea, and sugar-free, caffeine free soft drinks) and up to 2 servings of specific alcoholic beverages (beer, white wine, and spirits) were allowed. There were four calorie levels of 1600, 2100, 2600, or 3100 kcals for each diet. Weight was kept stable.				
DASH subgroup analysis Moore et al. 1999 RCT USA, Outpatient Medical Setting Good	**Treatment Groups:** G1. DASH diet G2. Fruits and vegetables diet G3. Control diet G1: DASH, Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9g fiber, and 300 mg/d of cholesterol Treatment: rich in fruits, vegetables, and low fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein. Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4700mg potassium, 500mg magnesium, 1240mg calcium, 3,000mg sodium G2: Fruits and Vegetables diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4770mg potassium, 500mg magnesium, 450mg calcium, 3,000mg sodium *(continued in next table)*	Adults ≥ 22 years of age not taking anti-hypertensive medication; SBP < 160 mmHg and a DBP of 80 to 95 mmHg **n's** G1: 115 G2: 121 G3: 118 **Mean years (SD):** G1: 44.9 (9.9) G2: 45.0 (10.5) G3: 45.4 (10.7)	**At 8 weeks** **Mean change in SBP, mmHg:** G1 Y vs. G3 Y:-4.8 (-6.8, -2.7) P = 0.0001 G1 O vs. G3 O:-4.5 (-7.5, -1.5) *p*=0.0036 **Mean change in DBP , mmHg:** G1 Y vs. G3:-2.9 (-4.5, -1.2) *p*=0.0007 G1 O vs. G3: -2.8(-4.9, -0.8) *p*=0.0063 Y=younger O= older	NR	**Withdrawals:** NR by subgroup **Adherence:** NR by subgroup **Actual nutrient intake:** NR by subgroup

CQ1 Summary Table B–6. DASH Pattern Subgroup: Age (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH subgroup analysis Moore et al. 1999 *(continued)*	*(continued from previous table)* G3. Control diet: typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1700mg potassium, 165 mg magnesium, 450 mg calcium, 3,000mg sodium *Nutrient values presented for all diets are representative of the diets at the energy level of 2100 kcal **Duration** **Run-in:** 3 wks **Treatment:** 8 wks **Intervention delivery:** Participants attended the clinic each weekday to be weighed and to consume one meal on site (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium, was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages (coffee, tea, and sugar-free, caffeine free soft drinks) and up to 2 servings of specific alcoholic beverages (beer, white wine, and spirits) were allowed. There were four calorie levels of 1600, 2100, 2600, or 3100 kcals for each diet. Weight was kept stable.				

CQ1 Summary Table B–6. DASH Pattern Subgroup: Age (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Vollmer et al. 2001 RCT: crossover USA, Outpatient Medical Setting Fair	**Treatment Groups:** G1. DASH diet G2. Typical American Diet Run-in: Control diet + high sodium level, 50 mmol/d G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol. Emphasis on fruits, vegetables, and low-fat dairy foods, includes whole grains, poultry, fish, and nuts, and is reduced in fats, red meat, sweets, and sugar-containing beverages. G2: Control diet : 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol. **Duration** **Run-in:** 2 wks **Treatment:** 90 days**,** 30 days per sodium condition **Intervention delivery** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were high (H; 150 mmol/d), intermediate (I; 100 mmol/d), and low (L; 50 mmol/d).All food was provided. Weight was kept stable	Adults ≥ 22 years; target of 50% enrollment of blacks and women **n:** G1: 208 G2: 204 **Age, mean years (SD)*:** G1: 47 (10) G2: 49 (10) * reported in Sacks, et al. 2001. **> 45 years/ Older, n (%):** G1:111 (53) G2:129 (63) **≤ 45 years/ Younger, n (%):** G1: 97 (47) G2: 75 (37)	**Mean Change in SBP, mmHg at higher sodium intake level (95% CI)*:** G1 Y vs. G2 Y: -7.1 P= NR G1 O vs. G2 O: -4.3 P = NR **Mean Change in DBP, mmHg at higher sodium intake level (95% CI)*:** G1 Y vs. G2 Y: -3.4 P= NR G1 O vs. G2 O: -2.2 P = NR *Analyses are unadjusted for other groups. All models included adjustment for baseline BP, study site, feeding cohort and carryover effects. Y= younger O= older	NR	**Withdrawals:** NR by subgroup **Adherence:** NR by subgroup **Actual Nutrient Intake:** NR

CQ1 Summary Table B–7. ***Glycemic Index/Load***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
Canadian Trial of Carbohydrates in Diabetes (CCD) Wolever et al. 2008(25) RCT Canada, multicenter Fair	**TREATMENT GROUPS:** G1: Low-CHO diet: Low CHO, high monounsaturated-fat G2: Low-GI diet: High-CHO, low glycemic index G3: High-GI diet: High CHO, high glycemic index Run-in for all groups: 55% of energy as CHO, 15% of energy as protein, and 30% of energy as fat and with ≤10% SFAs, ≤10% PUFA and the remainder as MUFA G1: Low-CHO Diet: 1,930 kcal of energy, 34.7 g of fat, 43.6 g of CHO, 19.7 g of protein,11.4 g of SF,14.1 g of MUFA, 6.3 g of PUFA, 22.4 g fiber, 302 mg/d of cholesterol, glycemic index of 59 G2: Low-GI Diet: 1,810 kcal of energy, 31.9 g of fat,45.9 g of CHO, 20.7 g of protein, 9.8 g of SF,12.9 g MUFA, 6.3 g PUFA, 22.5 g fiber, 268 mg/d of cholesterol, glycemic index of 55 Key foods were olive or canola oils or spreads, nuts, and other foods low in SFAs and high in MUFAs. G3: HI GI Diet: 1,930 kcal of energy, 34.0% of fat, and 43.1% of CHO, 20.2% of proteins, 11.3% of SF, 13.9% MUFA, 6.1% PUFA, 20.3 g fiber, and 323 mg/d of cholesterol; Glycemic index of 59. Key foods were starchy carbohydrates **DURATION:** **Treatment:** 1 year **INTERVENTION DELIVERY:** Participants given list of key foods to consume and specifications how much to consume. Participants were seen by dietician every 2 and 4 wks after randomization and then every 4 wks for weighing, review of key-food diaries, and pickup of supplies of key foods.	Adults 35–75, with T2DM ***N*:** G1: 54 G2: 56 G3: 52 **MEAN YEARS (SEM):** G1: 58.6 (1.2) G2: 60.6 (1.0) G3: 60.4 (1.1) **SEX, *N* (%) FEMALE:** G1: 54 (47) G2: 56 (66) G3: 52 (50) **RACE/ETHNICITY:** NR **WEIGHT, KG (SEM):** G1: 84.7 (2.6) G2: 81.1 (2.5) G3: 84.4 (2.5) **BMI:** G1: 31.1 (0.6) G2: 31.6 (0.6) G3: 30.1 (0.6) **MEAN SBP, MMHG (SEM):** G1: 127 (3) G2: 124 (4) G3: 129 (2) **MEAN DBP, MMHG**	**At 1 year** **SBP, MMHG (SEM):** G1: 128 (1) G2: 129 (1) G3: 127 (1) G1 vs. G3: *p*=NS G1 vs. G2: *p*=NS G2 vs. G3: *p*=NS **DBP, MMHG:** Data NR *p*=NS	**At 1 year** **MEAN CHANGE IN HDL-C, MMOL/L (SEM):** G1: 1.21 (0.03) G2: 1.16 (0.03) G3: 1.19 (0.03) G1 vs. G3: *p*=NS G1 vs. G2:–4%, *p*<0.05 G3 vs. G2: *p*=NS **MEAN CHANGE IN LDL-C, MMOL/L (SEM):** G1: 2.89 (0.05) G2: 2.92 (0.05) G3: 3.00 (0.08) G1 vs. G3: *p*=NS G1 vs. G2: *p*=NS G2 vs. G3: *p*=NS **MEAN CHANGE IN TC, MMOL/L (SEM):** G1: 4.99 (0.08) G2: 5.04 (0.08) G3: 5.04 (0.08) G1 vs. G3: *p*=NS G1 vs. G2: *p*=NS **MEAN CHANGE IN TG, MMHG (SEM):** G1: 1.93 (0.06) G2: 2.17 (0.07) G3: 2.00 (0.07) G1 vs. G3: *p*=NS G1 vs. G2: 12%, *p*<0.05 G2 vs. G3: *p*=NS **MEAN CHANGE IN APOA1, G/L (SEM):** G1: 1.59 (0.01) G2: 1.55 (0.02) G3: 1.60 (0.02)	**WITHDRAWALS, *N* (%):** G1: 10 (5.4) G2: 11 (6.16) G3: 11 (5.72) **ADHERENCE: REPORTED AS % CONSUMED (SD) OF AMOUNT PRESCRIBED:** G1: 106 (3) G2: 81 (3) G3: 85 (3) **ACTUAL NUTRIENT INTAKE:** **Mean SF, % energy (SEM):** G1: 10.8 (0.3) G2: 8.2 (0.4) G3: 10.2 (0.4) **MEAN CHO, % ENERGY (SEM):** G1: 39.3 (0.7) G2: 45.9 (0.9) G3: 46.5 (0.9) **MEAN ENERGY, KCAL (SEM):** G1: 2,020 (57) G2: 1,800 (50) G3: 1,890 (48) **MEAN FAT, % ENERGY (SEM):** G1: 40.1 (0.6) G2: 26.5 (0.8) G3: 30.8 (0.7) **MEAN MUFA, % ENERGY**

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
		(SEM): G1: 78 (2) G2: 77 (2) G3: 78 (1) 43% of subjects on at least 1 lipid-lowering medication		G1 vs. G2: *p*=NS G1 vs. G3: *p*=NS G2 vs. G3: *p*=NS *p*<0.05 *(continued in next table)*	**(SEM):** G1: 18.3 (0.3) G2: 10.7 (0.4) G3: 12.3 (0.3) **MEAN PUFA, % ENERGY (SEM):** G1: 8.2 (0.2) G2: 5.1 (0.2) G3: 5.5 (0.2) *(continued in next table)*

CQ1 Summary Table B–7. Glycemic Index/Load (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
Canadian Trial of Carbohydrates in Diabetes (CCD) Wolever et al. 2008(25) *(continued)*				*(continued from previous table)* **MEAN CHANGE IN APO B100, G/L (SEM):** G1: 1.01 (0.02) G2: 1.04 (0.02) G3: 1.03 (0.02) G1 vs. G3: NR, *p*=NS G2 vs. G3: NR, *p*=NS G1 vs. G2: NR, *p*=NS	*(continued from previous table)* **MEAN FIBER, % ENERGY (SEM):** G1: 23.0 (0.8) G2: 36.3 (1.3) G3: 21.0 (0.8) **MEAN PROTEIN, % ENERGY (SEM):** G1: 19.1 (0.4) G2: 20.6 (0.4) G3: 20.4 (0.4) **MEAN CHOLESTEROL, MG (SEM):** G1: 265 (12) G2: 223 (13)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
					G3: 286 (21)
Jenkins et al. 2008(34) RCT Canada, Hospital Good	**TREATMENT GROUPS:** G1: Low-glycemic index (GI) diet G2: High-cereal fiber diet G1: Participants were advised to eat low-glycemic index breads and breakfast cereals, pasta, parboiled rice, beans, peas, lentils, and nuts were also advised. Participants were instructed to eat temperate fruit (apples, pears, oranges, peaches, cherries, and berries). G1: 1,916 kcal of energy, 36.1% fat, 42.2% CHO, 20.3% protein, 11.2% SF, 14.6% MUFA, 7.4% PUFA, 13.9 g fiber, and 156.4 mg/d of cholesterol G2: Participants were advised to take the whole grain options. Tropical fruit (bananas, mangos, guavas, grapes, raisins, watermelon, cantaloupe) were prescribed. *(continued in next table)*	Men and postmenopausal women with T2DM who take oral medication 85% overweight or obese ***N*:** G1: 106 G2: 104 **AGE, MEAN YEARS, (SD):** G1: 60 (10) G2: 61 (9) **SEX *N*, (%):** Male G1: 65 (61.3) G2: 63 (60.6) Female G1: 41 (38.7) G2: 41 (39.4) *(continued in next table)*	**At 24 weeks** **SBP, MMHG:** G1: 124.7 G2: 125.8 *p*=NS **DBP, MMHG:** G1: 72.1 G2: 73.5 *p*=NS	**At 24 weeks** **MEAN TC, MG/DL:** G1: 168.4 G2: 162.6 *p*=NS **MEAN HDL-C, MG/DL:** G1: 42.8 G2: 43.6 *p*=0.005 **MEAN LDL-C, MG/DL:** G1: 101.3 G2: 95.3 *p*=NS **MEAN TG, MG/DL:** G1: 122.2 G2: 124.6 *p*=NS **MEAN TC: HDL-C, MG/DL:** G1: 4.06 G2: 3.94 *p*=NS *(continued in next table)*	**WITHDRAWALS, *N* (%):** G1: 19 (19) G2: 23 (23) **ADHERENCE:** NR **ACTUAL NUTRIENT INTAKE AT 24 WEEKS:** *N*=195 **KCAL:** G1: 1,706 G2: 1,690 **FAT,%:** G1: 33.3 G2: 30.5 **CHO, %:** G1: 44.0 G2: 47.5 **PROTEIN, %:** G1: 21.2 G2: 20.7 *(continued in next table)*

CQ1 Summary Table B–7. Glycemic Index/Load (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
Jenkins et al. 2008(34) *(continued)*	*(continued from previous table)* G2: 1,830 kcal of energy, 33.0% fat, 45.4% of CHO, 20.1% of protein,10.3% SF, 13.2% MUFA, 6.7% PUFA, 14.1 g fiber,150.2 mg/d of cholesterol. In both diets, the number of CHO servings prescribed covered 42% to 43% of total calories and 3 servings of fruit and 5 servings of vegetables were encouraged. Participants advised against eating foods recommended in the alternative treatment such as fruit options and starchy items. All participants were specifically advised to avoid foods such as pancakes, muffins, bagels, rolls, cookies, french fries, and chips. **DURATION:** **Treatment:** 24 weeks **INTERVENTION DELIVERY:** Participants received information on either low-glycemic index or high-cereal fiber food options from different categories (breakfast cereals, breads, vegetables, fruit) as approximately 15-g carbohydrate servings. Instruction was provided on evaluating portion size. Participants completed checklists on a daily basis and discussed their 7-day diet records with their dietician when visiting the clinical center at 2 weeks, 4 weeks, and monthly for 6 months.	*(continued from previous table)* **RACE/ETHNICITY *N*, (%):** European G1: 79 (74.5) G2: 65 (62.5) Indian G1: 14 (13.2) G2: 21 (20.2) Far Eastern G1: 6 (5.7) G2: 6 (5.8) African G1: 4 (3.8) G2: 9 (8.7) Hispanic G1: 3 (2.8) G2: 2 (1.9) Native American G1: 0 (0.0) G2: 1 (1.0) **MEAN WEIGHT, KG (SD):** G1: 87.0 (20.0) G2: 87.8 (19.4) **BMI:** NR **SBP, MMHG (SD):** G1: 127 (16) G2: 128 (14) **DBP, MMHG (SD):** G1: 74 (10) G2: 75 (9)		*(continued from previous table)* **MEAN LDL-C: HDL-C, MG/DL:** G1: 2.45 G2: 2.31 *p*=NS	*(continued from previous table)* **SF, %:** G1: 9.6 G2: 9.3 **MUFA, %:** G1: 13.3 G2: 12.2 **PUFA, %:** G1: 6.7 G2: 6.2 **FIBER, G:** G1: 1 8.7 G2: 15.7 **CHOLESTEROL, MG/D:** G1: 142.9 G2: 142.0

CQ1 Summary Table B–7. Glycemic Index/Load (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
Yusof et al. 2009(40) RCT Malaysia, outpatient clinic Good	**TREATMENT GROUPS:** G1: Low-glycemic index (GI) diet G2: Conventional carbohydrate exchange (CCE) diet G1: Participants instructed to eat at least one low-GI food from lists and advised to consume carbohydrate foods evenly throughout the day. G2: Participants also advised to spread carbohydrate consumption throughout the day and had a set number of carbohydrate exchanges for each meal Both diets designed to be high in CHO (50–60% of energy), low in fat (25–30% of energy) and rich in low- or high-GI foods depending on the treatment. **DURATION:** **Treatment:** 12 wks **INTERVENTION DELIVERY:** Dietary advice similar for both treatment groups. Dietician gave individual dietary advice to all subjects over 12 wks.	Overweight Asian adults with type 2 DM ***N*:** G1: 52 G2: 52 **AGE, MEAN YEARS:** NR **SEX:** NR **RACE/ETHNICITY:** NR **WEIGHT. MEAN KG (SD):** G1: 69.12 (13.33) G2: 66.83 (11.50) **BMI:** NR **MEAN SBP, MMHG (SD):** G1: 127.53 (15.39) G2: 139.19 (19.15) **MEAN DBP, MMHG (SD):** G1: 76.81 (9.95) G2: 79.31 (8.23)	**At 4 weeks** **DBP, MMHG (SE):** G1: 76.1 (1.1) G2: 77.3 (1.4) *p*=NR **SBP, MMHG (SE):** G1: 127.5 (2.2) G2: 139.2 (2.7) *p*=NR **At 12 weeks** **MEAN CHANGE IN SBP, MMHG (SE):** G1: 127.5 (2.0) G2: 137.0 (2.3) *p*=NR **MEAN CHANGE IN DBP, MMHG (SE):** G1: 75.2 (1.2) G2: 79.2 (1.3) *p*=NR	**At 12 weeks** **MEAN CHANGE IN HDL-C, MMOL/(SE):** G1: 1.14 (0.04) G2: 1.21 (0.05) *p*=NR **MEAN CHANGE IN LDL-C, MMOL/(SE):** G1: 2.67 (0.11) G2: 2.93 (0.14) *p*=NR **MEAN CHANGE IN TC, MMOL/L (SE):** G1: 4.54 (0.12) G2: 4.80 (0.16) *p*=NR **MEAN CHANGE IN TG, MMOL/L (SE):** G1: 1.59 (0.10) G2: 1.46 (0.08) *p*=NR **At 4 weeks** **MEAN CHANGE IN HDL-C, MMOL/L (SE):** G1: 1.12 (0.04) G2: 1.21 (0.05) *p*=NR **MEAN CHANGE IN LDL-C, MMOL/L (SE):** G1: 2.74 (0.09) G2: 2.77 (0.11) P= NR **MEAN CHANGE IN TC, MMOL/L (SE):** G1: 4.61 (0.12) G2: 4.57 (0.12) *p*=NR **MEAN CHANGE IN TG, MMOL/L (SE):**	**WITHDRAWALS, *N* (%):** G1: 1 (1.9) G2: 3 (5.8) **ADHERENCE:** NR **ACTUAL NUTRIENT INTAKE:** **At 12 weeks:** **KCAL:** G1: 1,512 G2: 1,526 **FAT, G:** G1: 51.0 G2: 51.0 **CHO, G:** G1: 200 G2: 207 **PROTEIN, G:** G1: 70 G2: 66 **FIBER, G:** G1: 24 G2: 11 **GLYCEMIC INDEX, G:** G1: 57 G2: 64 **GLYCEMIC LOAD:** G1: 108 G2: 131

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
				G1: 1.67 (0.13) G2: 1.29 (0.06) *p*=NR	

CQ1 Summary Table B–8. Dietary Fat and Cholesterol

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27); Obarzanek et al. 2001(28) RCT USA, outpatient medical setting **GOOD**	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet- Refer to the main DASH dietary pattern table G3: Control diet Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9 g fiber, and 300 mg/d of cholesterol G1: Diet rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein. Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, G3: Control diet typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was and was kept stable by changing calorie level. Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal. **DURATION:** **Run-in:** 3 wks **Treatment:** 8 wks	Adults ≥22 years; SBP <160 mmHg and a DBP of 80–95 mmHg ***N*:** G1: 151 G3: 154 **AGE, MEAN YEARS (SD):** G1: 44 (10) G3: 44 (11) **SEX, *N** (%):** Male G1: 74 (49.0) G3: 81 (52.6) Female G1: 77 (51.0) G3: 73 (47.4) **RACE/ETHNICITY, *N* (%):** Black G1: 93 (61.1) G3: 92 (59.7) Non-minority G1: 47 (31.1)		**At 8 weeks** *N*=436* **HDL-C MMOL/L, NET CHANGE (95% CI):** G1 vs. G3: –0.09 (–0.13, –0.06) *p*< 0.0001 **LDL-C MMOL/L, NET CHANGE (95% CI):** G1 vs. G3: –0.28 (–0.40, –0.16) *p*<0.0001 ***436 participants (95% of the 459) who provided fasting blood samples at baseline and end of the intervention**	**WITHDRAWALS, *N* (%):** G1: 2 (1.3) G3: 7 (4.5) **ADHERENCE:*** assessed by percent attendance at onsite meals **ONSITE MEAL ATTENDANCE, %:** G1: 96.1 G3: 95.8 Adherence was also assessed by percent of days per person with perfect adherence to study diets. Perfect adherence was defined as all study foods consumed and no nonstudy foods consumed. **MEAN % OF DAYS WITH PERFECT ADHERENCE PER PERSON:** G1: 93.2 G3: 94.6 ***Procedures for adherence to**

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
	INTERVENTION DELIVERY: Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages and up to 2 servings of specific alcoholic beverages were allowed.	G3: 54 (35.1) Other Minority G1: 11 (7.3) G3: 8 (5.2) **MEAN WEIGHT, KG:** G1: 83.4 G3: 81.5 **MEAN BMI, KG/M^2:** G1: 28.5 G3: 28.0			**the diets were revised after first participant groups completed the program. Data on adherence is for the 362 participants enrolled after the first participant group completed the program.**

CQ1 Summary Table B–8. Dietary Fat and Cholesterol (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Harsha et al. 2004(30) RCT, crossover design within each diet USA, outpatient medical setting GOOD	**TREATMENT GROUPS:** G1: DASH diet G2: Typical American Diet Run-in: Control diet + high sodium level, 50 mmol/d G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol. G2: Control diet: 37% fat, 16% SF13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION:** **Run-in:** 2 wks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were	Adults ≥22 years; target of 50% enrollment of Blacks and women ***N*:** G1: 208 G2: 204 **AGE, MEAN YEARS (SD):** G1: 47 (10) G2: 49 (10) **SEX, *N** (%)** Male G1: 85 (41) G2: 93 (46) Female G1: 123 (59)		**At 30 days** **MEAN CHANGE IN LDL-C MMOL/L, AT 30 DAYS BY NA LEVEL (95% CI)**:** G1 H vs. G2 H: –0.33 (–0.45, –0.21) *p*<0.0001 G1 I vs. G2 I: –0.30 (–0.45, –0.16) *p*<0.0001 G1 L vs. G2 L:–0.37 (–0.49, –0.24) *p*<0.0001 **MEAN CHANGE IN HDL-C MMOL/L, AT 30 DAYS BY NA LEVEL (95% CI)*:** G1 H vs. G2 H: –0.10 (0.14, –0.06) *p*<0.0001 G1 I vs. G2 I: –0.09 (–0.14, –0.05) *p*<0.0001 G1 L vs. G2 L: –0.08 (–0.11, –0.04)	**WITHDRAWALS, *N* (%):** G1: 10 (95) G2: 12 (94) **ADHERENCE:** NR **Actual nutrient intake:** **Energy kcal/day, mean (SD):** G1: 2576 (511) G2: 2576 (493) **TOTAL FAT, % OF ENERGY (SD):** G1: 27.4 (0.2) G2: 38.6 (4.2) **TOTAL CHO, % OF ENERGY**

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
	high (H; 150 mmol/d), intermediate (I; 100 mmol/d), and low (L; 50 mmol/d).All food was provided. Weight was kept stable.	G2: 111 (54) *_n_ from Vollmer WM, Sacks FM, Ard J et al. 2001(45) **RACE, _N_ (%)** Black G1: 118 (57) G2: 114 (56) Non-Hispanic White G1: 83 (40) G2: 81 (40) Asian or other G1: 6 (3) G2: 10 (5) **WEIGHT:** NR **MEAN BMI KG/M^2 (SD):** G1: 29 (5) G2: 30 (5)		_p_<0.0001 **MEAN CHANGE IN TG MMOL/L, AT 30 DAYS BY NA LEVEL (95% CI):**** G1 H vs. G2 H: 0.06 (–0.05, 0.18) _p_=0.3 G1 I vs. G2 I: –0.02 (–0.16, 0.11) _p_=0.7 G1 L vs.G2 L: 0.03 (–0.09, 0.15) _p_=0.6 *_n_=390 ****N*=379**	**(SD):** G1: 58.5 (0.3) G2: 49.2 (0.3) **PROTEIN, G:** NR **SF, % OF ENERGY (SD):** G1: 6.2 (0.1) G2: 15.0 (0.2) **MUFA, % OF ENERGY (SD):** G1: 11.2 (0.1) G2: 12.5 (0.3) **PUFA, % OF ENERGY (SD):** G1: 8.0 (0.2) G2: 7.4 (0.3) **FIBER, G/DAY, MEAN (SD):** G1: 35.0 (6.1) G2: 17.3 (18.0) **CHOLESTEROL, MG/DAY, MEAN (SD):** G1: 194 (48) G2: 324 (62.7)

CQ1 Summary Table B–8. Dietary Fat and Cholesterol (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
DELTA–1 Ginsberg1998 (32)	**TREATMENT GROUPS:** G1: National Cholesterol Education Program (NCEP)	Adults ages 22–65 years with normal lipid levels	NR	**At 8 weeks** **MEAN APO A–1, MG/DL:**	**WITHDRAWALS, _N_ (%):** G1: NR

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
RCT, crossover USA, University research centers Fair	Step 1 diet G2: Low-saturated fat diet (low-SFA) G3. Average American diet (AAD) G1: 30% of calories from fat and 9% SFA, 14% MUFA and 7% PUFA, 55% CHO and 15% protein G2: 26% of calories from fat and 5% SFA, 14% MUFA and 7% PUFA, 59% CHO and 15% protein G3: 37% of calories from fat,16% SFA, 14% MUFA, 7% PUFA , 48% CHO, 15% protein **DURATION:** **Treatment:** 8 wks **Washout:** 4–6 wks **INTERVENTION DELIVERY** Each diet period was consumed for 8 weeks, with a washout of 4 to 6 wks between each diet period. Food was provided and participants ate 2 meals each weekday onsite. All 3rd meals, snacks, and weekend food were provided (packaged) except for one weekend meal (optional "self-selected "Saturday meal to allow for personal choice). Participants were weighed 2/wk adjustments were made in kcals to maintain stable body weight. Compliance assessed by tray checks at meals eaten onsite and by self-report on standardized forms for offsite meals.	***N*:** G1: NR G2: NR Total: 103 **AGE, MEAN YEARS:** Men: 36.0 Women: 39.4 **SEX, *N* (%):** Men: 46 (45) Women: 57 (55) **RACE/ETHNICITY, *N* (%):** Blacks: 26 (25) Non-Blacks:77 **WEIGHT:** NR **BMI:** NR **SBP:** NR **DBP:** NR		G1: 135.4 (2.0) G2: 130.4 (1.9) G3: 142.2 (2.0) G1 vs. G3: *p*<0.01 G2 vs. G3: *p*<0.01 **MEAN APO B, MG/DL:** G1: 113.6 (2.6) G2: 111.6 (2.6) G3: 116 (2.4) G1 vs. G3: *p*=NR G2 vs. G3: p<0.01 **MEAN HDL-C, MG/DL:** G1: 48.5 (1.1) G2: 46.2 (1.0) G3: 52.2 (1.1) G1 vs. G3: *p*<0.01 G2 vs. G3: *p*<0.01 **MEAN LDL-C MG/DL:** G1: 122.2 (2.6) G2: 116.9 (2.6) G3: 131.4 (2.7) G1 vs. G3: p<0.01 G2 vs. G3: *p*<0.01 **MEAN LP (A), MG/DL:** G1: 17.0 (1.8) G2: 18.2 (1.9) G3: 15.5 (1.8): G1 vs. G3: *p*<0.01 G2 vs. G3: *p*<0.01 **MEAN TG (%), MG/DL** G1: 92.4 (3.7) G2: 93.0 (3.7) G3: 85.1 (3.4) G1 vs. G3: *p*<0.01 G2 vs. G3: *p*=NR	G2: NR Total: 15 (14.5%) **ADHERENCE:** NR **Actual nutrient intake:*** **MEAN FAT,% (SEM):** G1: 28.6 (0.2) G2: 25.3 (0.3) G3: 34.3 (0.5) **MEAN SFA, % (SEM):** G1: 9.0 (0.1) G2: 6.1 (0.5) G3: 15.0 (0.4) **MEAN MUFA, % (SEM):** G1: 12.9 (0.1) G2: 12.4 (0.1) G3: 12.8 (0.1) **MEAN PUFA % (SEM):** G1: 6.7 (0.1) G2: 6.7 (0.1) G3: 6.5 (0.1) **MEAN CHOLESTEROL, MG/D (SEM):** G1: 267 (7.6) G2: 275 (4.0) G3: 285 (3.9) *Mean ± SEM based on 24 complete menu cycles for AAD, 23 cycles for NCEP Step 1 diet, & 22 cycles for low-SFA diet

CQ1 Summary Table B–8. Dietary Fat and Cholesterol (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
Gardner et al. 2005(33) RCT USA, Clinical Research Center Fair	**TREATMENT GROUPS:** G1: Low-Fat Plus diet G2: Low-Fat diet G1: Low-Fat diet design with additions consistent with the 2000 American Heart Association revised guidelines. More plant-based, designed to include considerably more vegetables, legumes, whole grains, and fruits. Addition of butter, cheese, and eggs to increase the SF and cholesterol content to match the Low-Fat diet. G2: The Low-Fat diet was relatively typical of a low-fat U.S. diet consistent with former American Heart Association Step I guidelines. Designed to include many reduced-fat prepared-food items (for example, reduced-fat cheeses, low-fat frozen lasagna, and low-fat and low-sugar-rich snack foods). The Low-Fat diet and the Low-Fat Plus diet were designed to be identical in total fat, saturated fat, protein, carbohydrate, and cholesterol content, with ≤30% of energy from total fat and ≤10% of energy or less from SF. **DURATION** **Treatment:** 4 weeks **Followup:** mean 28 days **INTERVENTION DELIVERY:** Lunch or dinner eaten onsite, provided with meals, snacks, and beverages on an outpatient basis for 28 days. Weight was held constant.	Hypercholesterolemic adults 30 to 65 years of age ***n:*** G1: 59 G2: 61 **AGE, MEAN YEARS (SD):** G1: 49 (8) G2: 48 (10) **SEX, *N* (%):** Men: G1: 26 (43) G2: 34 (57) Women: G1: 33 (55) G2: 27 (45) **RACE/ETHNICITY, *N* (%):** Non-Hispanic White G1: 46 (76) G2: 45 (75) **WEIGHT:** NR **BMI, KG/M² (SD):** G1: 26 (3) G2: 27 (3) **SBP:** NR **DBP:** NR	NR	**At 4 weeks** **MEAN CHANGE IN TC, MG/DL (%):** G1: –17.6 (–7.9) G2: –9.2 (–4.1) **BETWEEN GROUP DIFFERENCE IN TC, MG/DL (95% CI):** G1 vs. G2: –9 (–2, –15) *p*=0.014 **MEAN CHANGE IN LDL-C, MG/DL (%):** G1: –13.8 (–9.3) G2: –7 (–4.6%) **BETWEEN GROUP DIFFERENCE IN LDL-C, MG/DL (95% CI):** G1: –7 (–2, –12) *p*=0.016 **MEAN CHANGE DIFFERENCE IN HDL-C, MG/DL:** G1: –3.8 (–7.7%) G2: –2.5 (–5.5) **BETWEEN GROUP DIFFERENCE IN HDL-C, MG/DL (95% CI):** G1 VS. G2: –2 (0.4, –3) *p*=NS **MEAN CHANGE DIFFERENCE IN TG, MG/DL:** G1: +0.1 (0.1) G2: +1.2 (0.9) **BETWEEN GROUP DIFFERENCE IN TG, MG/DL (95% CI):** G1 vs. G2: 0.9 (34, –39) *p*=NS	**WITHDRAWALS, *N* (%):** G1: 2 (3.3) G2: 3 (4.9) **ADHERENCE (%):** G1: ≥99 G2: ≥99 Adherence was measured by daily tracking of incomplete consumption of study foods or consumption of any non-study foods. **ACTUAL NUTRIENT INTAKE:** Average of 7 day menus determined by chemical analyses, once for each on-study menu at mean of 28 days **FAT, % OF ENERGY:** G1: 31.7 G2: 29.8 **SF, % OF ENERGY:** G1: 9.5 G2: 9.5 **CHO, % OF ENERGY:** G1: 54.1 G2: 55.6 **PROTEIN, % OF ENERGY:** G1: 14.1 G2: 14.6 **CHOLESTEROL, MG:** G1: 200 G2: 187

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
					MUFA, %: G1: 9.4 G2: 9.2 *(continued in next table)*

CQ1 Summary Table B–8. *Dietary Fat and Cholesterol (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
Gardner et al. 2005(33) *(continued)*					*(continued from previous table)* **PUFA, %:** G1: 9 G2: 6.4 **FIBER, G:** G1: 40.8 G2: 22.0
Women's Health Initiative Dietary Modification Trial Howard et al. 2006(38); Tinker et al. 2008(39) RCT USA, 40 clinical centers Fair	**TREATMENT GROUPS:** G1: Intervention group G2: Usual diet group G1: Low-fat diet with total fat as 20% of total energy, 5 fruits and vegetables and ≤6 grains (Intensive behavior modification to reduce total fat intake to 20% of calories and increase vegetables/fruit intake to 5 servings/d and grains to at least 6 servings/d) **DURATION:** **Treatment:** Mean of 8.1 years **INTERVENTION DELIVERY:** G1: Year 1 participated in 18 intensive nutritional and	Healthy postmenopausal women aged 50 to 79 years ***N*:** G1: 19,541 G2: 29,294 **AGE, MEAN YEARS, (SD):** G1: 62.3 (6.9) G2: 62.3 (6.9) **SEX, %:** Female: 100	**At 1 year** **MEAN SBP, MMHG (SD):** G1: 124.4 (17.1) G2: 125.4 (16.8) *p*=NR **MEAN DBP, MMHG (SD):** G1: 73.9 (9.2) G2: 74.7 (9.1) *p*=NR **At 3 years** **MEAN CHANGE IN SBP MMHG (SD):**	**AT 3 YEARS** **CHANGE IN LDL-C , MG/DL (SD):** G1: –9.7 (29.3) G2: –6.2 (29.1) G1 vs. G2 (95% CI): –3.55 (–6.58 to –0.52) *p*< 0.05 **CHANGE IN HDL-C, MG/DL (SD)** G1: –0.7 (9.4) G2: –0.3 (10.2) G1 vs. G2 (95% CI): –0.43 (–1.42 to 0.57) *p*=NS **CHANGE IN NON-HDL-C, MG/DL (SD):** G1: –9.7 (32.0)	**WITHDRAWALS, *N* (%):** G1: 1867 (9.5) G2: 2617 (8.9) **ADHERENCE:** NR **Actual nutrient intake:** **At 1 year** **ENERGY, KCAL:** G1: 1502 G2: 1594 **TOTAL FAT, %:** G1: 24.2

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
	behavioral modification trainings followed by quarterly sessions. Diet was not intended to promote reduced energy intake. G2: Given a copy of the Dietary Guidelines for Americans; not asked to make dietary changes and had no contact with nutritionist	**RACE/ETHNICITY, N (%):** AMERICAN INDIAN AND ALASKAN NATIVE G1: 80 (0.4) G2:105 (0.4) ASIAN/PACIFIC ISLANDER G1: 399 (2.2) G2: 618 (2.2) BLACK OR AFRICAN AMERICAN G1: 1,841 (10.0) G2: 2,726 (9.9) NATIVE HAWAIIAN/OTHER PACIFIC ISLANDER G1: 399 (2.2) G2: 618 (2.2) *(continued in next table)*	G1: –2.2 (16.3) G2: –2.1 (16.4) G1 vs. G2 (95% CI):–0.17 (–0.49, 0.15) *p*=NS **MEAN CHANGE IN DBP MMHG (SD):** G1: –2.6 (9.4) G2: –2.3 (9.4) G1 vs. G2 (95% CI):–0.31 (–0.50, 0.13) *p*<0.001 *(continued in next table)*	G2: –6.6 (32.6) G1 vs. G2 (95% CI): –3.08 (–6.37 to 0.22) *p*=NS **CHANGE IN TG, MG/DL (SD:)** G1: 1.0 (0.4) G2: 1.0 (0.3) G1 vs. G2 (95% CI): 0.00 (–0.03 to 0.04) *p*=NS	G2: 35.0 **SATURATED FAT, %:** G1: 8.0 G2:11.7 ***TRANS* FATTY ACIDS, %:** G1:1.6 G2: 2.5 **PUFA. %:** G1: 5.2 G2: 7.2 **CHO, %:** G1: 58.5 G2: 48.0 *(continued in next table)*

CQ1 Summary Table B–8. *Dietary Fat and Cholesterol (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
Women's Health Initiative Dietary Modification Trial Howard et al. 2006(38); Tinker et al. 2008(39)		*(continued from previous table)* **RACE/ETHNICITY, N (%):** WHITE G1: 1,586 (82.3)	*(continued from previous table)* **At 6 years** **MEAN SBP, MMHG (SD):** G1: 124.5 (16.5) G2: 124.6 (16.3)		*(continued from previous table)* **At 6 years** **ENERGY, KCAL:** G1: 1435 G2: 1548

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Lipid Outcomes	Attrition Adherence/Compliance Actual Nutrient Intake
(continued)		G2: 22,685 (82.5) HISPANIC OR LATINO G1: 689 (3.7) G2: 1016 (3.7) OTHER G1: 239 (1.3) G2: 361 (1.3) **WEIGHT, KG (SD):** G1: 76.8 (16.6) G2: 76.7 (16.5) **MEAN BMI (SD):** G1: 29.1 (5.9) G2: 29.1 (5.9) **MEAN SBP, MMHG (SD):** G1: 127.5 (17.2) G2: 127.9 (17.2) **MEAN DBP, MMHG (SD):** G1: 75.9 (9.1) G2: 76.0 (9.1)	*p*=NR **MEAN DBP, MMHG (SD):** G1: 71.7 (9.2) G2: 71.9 (9.2) *p*=NR		**TOTAL FAT, %:** G1: 28.6 G2: 35.0 **SATURATED FAT, %:** G1: 9.5 G2: 12.4 ***TRANS* FATTY ACIDS, %:** G1: 1.8 G2: 2.3 **PUFA, %:** G1: 6.0 G2: 7.5 **CHO, %:** G1: 54.1 G2: 45.9

CQ2 Summary Tables

A Note about the unit of measure presented for dietary and urinary sodium: Sodium is presented in studies in mmol, grams, and milligrams (mg). The Workgroup chose to convert the sodium results to milligrams for the evidence statements, recommendations, and rationales so that the data from different studies would be displayed in a consistent unit. Also, U.S. dietary recommendations and the Nutrition Facts Lanel display sodium in milligrams, and this unit (mg) will be clearer to health care providers. Urinary and dietary sodium are portrayed in the original units from each published study in the summary tables.

CQ2 Summary Table C–1. Overall Sodium and Blood Pressure Outcomes

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
Cappuccio et al. 2006(65) Community-based cluster RCT 12 villages (6 rural, 6 semi-urban) Ashanti region of Central Ghana Fair	**TREATMENT GROUPS:** G1: Specific salt-reduction education G2: Control: general health education **DURATION:** **Treatment:** 6 months **INTERVENTION DELIVERY:** Group intervention G1 & G2: Intensive health education program carried out by community health workers; educational and health promotion sessions open to all villagers, regardless of trial participation. Meetings held daily for 1st week of trial, then once a week. Sessions lasted ≈1 hour (both for intervention and control). No mention was made of any possible dietary prevention of hypertension. G1 only: In the intervention villages, additional advice was given not to add salt to food and in cooking, to limit the amount of salted fish, salted pigs' feet, and salted beef and to soak the items in water overnight before eating them.	Adult males and females, ≈40 to 75 years of age ***N:*** G1: 522 G2: 491 **AGE, MEAN YEARS (SD):** G1: 54 (11) G2: 55 (11) **SEX, *N* (%):** Female G1: 324 (62) G2: 304 (62) **RACE/ETHNICITY *N*, (%):** African: 100% **WEIGHT, KG (SD):** G1: 54 (11) G2: 54 (11) **BMI, KG/M^2 (SD):** G1: 21 (4) G2: 21 (4)	**At 3 months** ***N*:** G1: 444 G2: 450 **SBP, MMHG (SD):** G1: 124.6 (26.6) G2: 123.8 (26.0) **DBP, MMHG (SD)** G1: 74.2 (13.7) G2: 74.0 (14.1) **At 6 months** ***N*:** G1: 399 G2: 402 **SBP, MMHG (SD):** G1: 127.9 (27.7) G2: 127.4 (26.0) **DBP, MMHG (SD):** G1: 76.0 (14.2) G2: 78.7 (14.3)	**At 3 months** ***N:*** G1: 444 G2: 450 **URINARY NA, MMOL/24 H (SD):** G1: 94.0 (44.5) G2: 97.5 (42.3) **At 6 months** ***N*:** G1: 399 G2: 402 **URINARY NA, MMOL/24 H (SD):** G1: 91.8 (41.8) G2: 89.8 (39.1) **Effect of intervention (control—intervention) on reduction in urinary sodium excretion** **At 3 months** **URINARY NA, MMOL/24 H (95% CI):** –0.5 (–12.3, 11.3)	**Withdrawals, *n* (%):** **3 MONTHS** G1: 78 (14.9) G2: 41 (8.4) **6 MONTHS** G1: 123 (23.6) G2: 89 (18.1) **ADHERENCE:** NR **NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
		MEAN SBP, MMHG (SD): G1: 129 (25) G2: 127 (27) **MEAN DBP, MMHG (SD):** G1: 77 (13) G2: 76 (13) *(continued in next table)*	**Effect of intervention (control – intervention) on reduction in BP (adjusted for time of day)** *(continued in next table)*	**At 6 months** **URINARY NA, MMOL/24 H (95% CI):** 6.0 (–4.1, 16.1)	

CQ2 Summary Table C–1. ***Overall Sodium and Blood Pressure Outcomes (continued)***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
Cappuccio et al. 2006(65) *(continued)*		*(continued from previous table)* **HYPERTENSION, *N* (%):** G1: 154 (30) G2: 137 (28) **URINARY SODIUM, MMOL/DAY (SD)** G1: 99.9 (44.7) G2: 102.5 (45.3)	*(continued from previous table)* **At 3 months** **SBP, MMHG (95% CI):** –0.48 (–5.45, 4.50) **DBP, MMHG (95% CI):** –1.02 (–3.95, 1.91) **At 6 months** **SBP, MMHG (95% CI):** –2.54 (–6.54, 1.45) **DBP, MMHG (95% CI):** –3.95 (–7.11, –0.78) *p*=0.015		
DASH-Sodium Sacks, et al. 2001(29) RCT, crossover	**TREATMENT GROUPS:** G1: DASH diet G2: Control	Adults ≥22 years of age, SBP of 120–159 mmHg, DBP of 80–95 mmHg, target of 50% enrollment of	**After 30 days of intervention** **SBP MEAN CHANGE, MMHG (95% CI):**	**After 30 days of intervention** **URINARY NA, MMOL/DAY (SD):** G1 H: 144 (58)	**WITHDRAWALS, *N* (%):** G1: 10 (4.8) G2: 12 (5.9)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
USA, outpatient medical centers Good	G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION** **Run-in:** 2 weeks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were higher (H; 150 mmol/d), intermediate (I; 100 mmol/d), and lower (L; 50 mmol/d). All food was provided. Weight was kept stable.	Blacks and women ***N*:** G1: 208 G2: 204 **AGE, MEAN YEARS (SD):** G1: 47 (10) G2: 49 (10) **SEX, *N* (%)** Female G1: 123 (59) G2: 111 (54) **RACE/ETHNICITY, *N* (%)** Black G1: 118 (57) G2: 114 (56) *(continued in next table)*	G1 I vs. G1 H: –1.3 (–2.6, 0.0) *p*<0.05 G1 L vs. G1 I: –1.7 (–3.0, –0.4) *p*<0.01 G2 H vs. G2 L: –6.7 (–5.4, –8.0) *p*<0.001 G2 I vs. G2 H: –2.1 (–3.4, –0.8) *p*<0.001 G2 L vs. G2 I: –4.6 (–5.9, –3.2) *p*<0.001 G2 H vs. G2 L: –3.0 (–1.7, –4.3) *p*<0.001 G1 H vs. G2 H: –5.9 (–8.0, –3.7) *p*< 0.001 G1 I vs. G2 I: –5.0 (–7.6, –2.5) *p*< 0.001 G1 L vs. G2 L: –2.2 (–4.4, –0.1) *p*< 0.05 G1 L vs. G2 H: –8.9 (–6.7, –11.1); *p*<0.001 *(continued in next table)*	G1 I: 107 (52) G1 L: 67 (46) G2 H: 141 (55) G2 I: 106 (44) G2 L: 64 (37) **URINARY NA, G/DAY (SD):** G1 H: 303 (1.3) G1 I: 2.5 (1.2) G1 L: 1.5 (1.0) G2 H: 3.3 (1.3) G2 I: 2.4 (1.0) G2 L: 1.5 (0.8)	**ADHERENCE:** Reported as 24-hour urinary excretion: The levels of urinary potassium, phosphorus, and urea nitrogen (reflective of the intake of fruit and vegetables, dairy products, and protein, respectively) were higher in the DASH-diet group than in the control-diet group, and were nearly identical for all three sodium levels. **ACTUAL NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion.

CQ2 Summary Table C–1. ***Overall Sodium and Blood Pressure Outcomes (continued)***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
DASH-Sodium Sacks, et al. 2001(29) *(continued)*		*(continued from previous table)* **RACE/ETHNICITY, *N* (%)** Non-Hispanic White G1: 83 (40) G2: 81 (40) Asian or other	*(continued from previous table)* **DBP MEAN CHANGE, MMHG (95% CI):** G1 I vs. G1 H: –0.6 (–1.5, 0.2) *p*=NS G1 L vs. G1 I: –1.0 (–1.9, –0.1) *p*<0.01 G1 H vs. G1 L: –1.6 (–0.8, –2.5)		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
		G1: 6 (3) G2: 10 (5) **WEIGHT:** NR **MEAN BMI, KG/M^2 (SD):** G1: 29 (5) G2: 30 (5) **MEAN SBP, MMHG (SD):** G1: 134 (10) G2: 135 (10) **MEAN DBP, MMHG (SD):** G1: 86 (5) G2: 86 (4) **URINARY SODIUM, MMOL/DAY (SD):** G1: 158 (79) G2: 152 (72)	*p*<0.001 G2 I vs. G2 H: –1.1 (–1.9, –0.2) *p*<0.01 G2 L vs. G2 I: –2.4 (–3.3, –1.5) *p*<0.001 G2 H vs. G2 L: –3.5 (–2.6, –4.3) *p*<0.001 G1 H vs. G2 H: –2.9 (–4.3, –1.5) *p*< 0.001 G1 I vs. G2 I: –2.5 (–4.1, –0.8) *p*< 0.01 G1 L vs. G2 L: –1.0 (–2.5, 0.4) *p*=NS G1L vs. G2 H: –4.5 (–3.1, –5.9) *p*<0.001		

CQ2 Summary Table C–1. Overall Sodium and Blood Pressure Outcomes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
Ancillary DASH-Sodium followup at one center Ard et al. 2004(64) Longitudinal observational study USA, single clinical center Fair	**TREATMENT GROUPS:** G1: DASH diet G2: Control G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION:** **Run-in:** 2 weeks **Treatment:** 90 days, 30 days per sodium condition **Followup:** 12 months **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were higher (H; 150 mmol/d), intermediate (I; 100 mmol/d), and lower (L; 50 mmol/d). All food was provided. Weight was kept stable. Ancillary study: followup 12 months after completion of intervention.	Adults ≥22 years of age, SBP of 120–159 mmHg, DBP of 80–95 mmHg, target of 50% enrollment of Blacks and women ***N*:** G1: 29 G2: 27 **AGE, MEAN YEARS (SD):** G1: 46.62 (11.20) G2: 51.59 (9.75) **SEX, % FEMALE:** G1: 66 G2: 78 **RACE/ETHNICITY, % NON-WHITE:** G1: 31 G2: 48 **WEIGHT, KG (SD):** NR **BMI, KG/M^2 (SD):** G1: 27.79 (4.87) G2: 29.54 (4.30) **MEAN SBP, MMHG (SD):** G1: 132.17 (10.21) G2: 139.54 (9.70) **MEAN DBP, MMHG (SD):** G1: 84.08 (5.10) G2: 86.00 (4.53) **HYPERTENSION, *N* (%):**	Change from end of intervention treatment to 12-month followup, mean (95% CI) **SBP, MMHG:** G1: 4.46 (–0.22, 9.14) G2: 1.82 (–4.19, 7.82) *p*=0.48 G1 H: 0.09 (–11.15, 11.32) G2 H: 5.58 (–18.44, 13.55) *p*=0.37 G1 I: 4.90 (–2.25, 12.05) G2 I: 2.97 (–10.14, 16.09) *p*=0.76 G1 L: 8.83 (0.44, 17.21) G2 L: 3.25 (–10.54, 10.08) *p*=0.09 **DBP, MMHG:** G1: 0.11 (–3.32, 3.55) G2: 0.79 (–2.40, 3.98) *p*= 0.77 G1 H: –1.82 (–9.85, 6.20) G2 H: 2.50 (–0.94, 5.94) *p*=0.29 G1 I: 0.50 (–4.91, 5.91) G2 I: 1.51 (–6.15, 9.18) *p*=0.81 G1 L: 1.80 (–5.38, 8.98) G2 L: 1.73 (–8.35, 4.90) *p*=0.41	Change from end of intervention treatment to 12-month followup, mean (95% CI) **URINARY NA, MMOL/DAY:** G1: 7.12 (–11.89, 26.11) G2: 11.42 (–28.47, 51.31) *p*=0.84 G1 H: –10.91 (–40.44, 18.62) G2 H: –23.61 (–154.73, 107.51) *p*=0.82 G1 I: –4.92 (–37.37, 27.54) G2 I: 6.75 (–34.21, 47.70) *p*=0.61 G1 L: 43.91 (6.08, 81.73) G2 L: 51.70 (26.76, 76.63) *p*=0.69	**WITHDRAWALS:** Upon completion of trial, 56 of 113 entered 12 month observational followup study. 52 of 56 had 12-month followup visit **ADHERENCE:** NA **ACTUAL NUTRIENT INTAKE AT 12-MONTH FOLLOWUP:** Sodium, mg (SD) G1: 2599.68 (1110.06) G2: 2214.69 (735.98)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
		G1: 27.6 G2: 63.0			

CQ2 Summary Table C–1. Overall Sodium and Blood Pressure Outcomes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58); Cook et al. 2005(59) 2 X 2 factorial RCT USA, 9 academic medical centers Good	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual care **DURATION** **Treatment:** 36–48 months **Additional Follow-up after Treatment:** None **INTERVENTION DELIVERY:** Individual and group counseling through in-person, telephone, and mail contact **INTENSIVE PHASE:** Groups of 11 to 34, counseled weekly for 10 weeks; primary goal was to provide core knowledge and behavioral skills to make and maintain reductions in Na intake. **TRANSITIONAL PHASE:** 4 monthly sessions; designed to prevent relapse and	Adults 30–54 years, not taking antihypertensive drugs, SBP<140 mmHg, DBP 83 to 89 mmHg, BMI representing 110% to 165% of desirable body weight ***N*:** G1: 594 G2: 596 **AGE:** G1: 44.2 (6.1) G2: 43.2 (6.1) **SEX, % MALE:** G1: 64.8 G2: 68.3 **Race/ethnicity:** White, %	**6 months** **SBP MEAN CHANGE, MMHG (SD):** G1: –5.1 (8.6) G2: –2.2 (8.1) **SBP NET CHANGE, MMHG (SE):** G1 vs. G2: –2.9 (0.5) *p*<0.001 **DBP MEAN CHANGE, MMHG (SD):** G1: –4.4 (6.7) G2: –2.8 (6.1) **DBP NET CHANGE, MMHG (SDE):** G1 vs. G2: –1.6 (0.4)	**6 months** ***N*:** G1: 147 G2: 126 **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –75.5 (81.5) G2: –24.5 (10.38) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D 95% CI):** G1 vs. G2: –51.0 (28.9, 73.0) **18 months** ***N*:** G1: 450 G2: 467 **24-HOUR URINARY NA MEAN CHANGE,**	**WITHDRAWALS:** Proportion of participants with BP readings at all 3 scheduled visits at or after 36 months ranged from 88.9% to 91.6% Completion of sodium excretion data at 36 months ranged from 79.1% to 80.9% **ADHERENCE:** Adherence measures such as food diaries and overnight urine samples were not used as study outcome data. **ACTUAL NUTRIENT INTAKE:** 24-hour dietary recall and 3-day food record information was obtained at 18- and 36-months for randomly selected

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
	ease transition to less frequent contact **FINAL EXTENDED PHASE:** 1 or 2 monthly contacts; 3 to 6 refresher sessions were offered; goal: maintain participants' behavior changes **GOAL FOR G1:** Reduction in sodium intake of 80 mmol per day, or less.	G1: 81.1 G2: 79.5 Black, % G1: 16.8 G2: 17.3 **WEIGHT, KG (SD):** G1: 94.0 (14.3) G2: 93.6 (13.5) **BMI:** NR **MEAN SBP, MMHG (SD):** G1: 127.7 (6.6) G2: 127.3 (6.4) **MEAN DBP, MMHG (SD):** G1: 86.1 (1.9) G2: 85.8 (1.9) *(continued in next table)*	*p*<0.001 **18 months** **SBP MEAN CHANGE, MMHG (SD):** G1: –3.8 (8.2) G2: –1.8 (7.0) **SBP NET CHANGE, MMHG (SE):** G1 vs. G2: –2.0 (0.5) *p*<0.001 **DBP MEAN CHANGE, MMHG (SD):** G1: –4.4 (6.5) G2: –3.2 (5.8) **DBP NET CHANGE, MMHG (SE):** G1 vs. G2: –1.2 (0.4) *p*=0.002 *(continued in next table)*	**MMOL/D (SD):** G1: –59.5 (91.7) G2: –16.8 (94.8) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D 95% CI):** G1 vs. G2: –42.7 (30.6, 54.8) **36 months** ***N*:** G1: 470 G2: 482 **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –50.9 (86.3) G2: –10.5 (88.5) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D 95% CI):** G1 vs. G2: –40.4 (29.3, 51.5)	samples.

CQ2 Summary Table C–1. ***Overall Sodium and Blood Pressure Outcomes (continued)***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group,		*(continued from previous table)* **URINARY SODIUM, MMOL/D (SD):** G1: 186.1 (80.7) G2: 188.0 (80.9)	*(continued from previous table)* **36 months** **SBP MEAN CHANGE, MMHG (SD):** G1: –0.7 (9.0)		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
1997(54); Kumanyika et al. 2005(58); Cook et al. 2005(59) *(continued)*			G2: +0.6 (8.5) **SBP NET CHANGE, MMHG (SE):** G1 vs. G2: –1.2 (0.5) *p*=0.02 **DBP MEAN CHANGE, MMHG (SD):** G1: –3.0 (6.5) G2: –2.4 (7.0) **DBP NET CHANGE, MMHG (SDE):** G1 vs. G2: –0.7 (0.4) *p*=0.10		
TONE Whelton et al. 1998(53); Appel et al. 2001(55); Espeland et al. 2002(56) RCT USA, 4 academic health centers Good	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual care **DURATION:** Mean of 27.8 months (range 15.6 to 35.9 months) after randomization **INTERVENTION DELIVERY:** In the reduced sodium group, each person had an introductory individual session. The TONE interventions consisted of a 4-month "intensive" phase with weekly meetings, a 4-month "extended" phase with biweekly meetings, and a maintenance phase. The interventionist typically was a registered dietitian. The meetings were conducted as group sessions (9–12 participants) with individual sessions at every fourth contact. *(continued in next table)*	Adults 60 to 80 years; had baseline BP <145/85 mmHg while on a single antihypertensive medication ***N*:** G1: 340 G2: 341 **Age, mean years (SD):** 65.8 (4.6) **SEX, FEMALE %:** 47 **RACE/ETHNICITY, %:** African American: 23 **OVERWEIGHT, %:** 43 **BMI:** NR *(continued in next table)*	**Mean interval, 3.5 months (baseline to visit prior to medication withdrawal)** **SBP CHANGE, MEAN MMHG (SD):** G1: –4.6 (11.3) G2: –0.4 (10.5) **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –4.3 (–6.0, –2.5) *p*<0.001 **DBP CHANGE, MEAN MMHG (SD):** G1: –2.2 (8.0) G2: –0.2 (7.0) *(continued in next table)*	**30 months** **24-HOUR URINARY NA CHANGE, MEAN MMOL (SD):** G1: –45 (55.8) G2: –5 (50.0) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL (95% CI):** –40 (–48, –32) *p*<0.001	**WITHDRAWALS:** Attended final study visit (15–37 months) G1: 91% G2: 92% **ADHERENCE:** NR **DAILY NUTRIENT INTAKE:** Mean between-group difference (95% CI) **TOTAL ENERGY, KCAL:** –119 (–197, –41) **TOTAL FAT, G:** –5.8 (–10.1, –1.5) **MONOUNSATURATED FAT, G:** –2.2 (–4.0, –0.4) *(continued in next table)*

CQ2 Summary Table C–1. Overall Sodium and Blood Pressure Outcomes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
TONE Whelton et al. 1998(53); Appel et al. 2001(55); Espeland et al. 2002(56) *(continued)*	*(continued from previous table)* **GOAL FOR SODIUM REDUCTION:** Achieving and maintaining a 24-hour dietary sodium intake of 80 mmol (1,800 mg) or less G2 received no study-related counseling in lifestyle change; were invited to meetings on topics unrelated to trial goals.	*(continued from previous table)* **SBP ON MEDICATION, MEAN MMHG (SD):** 128.0 (9.4) **DBP ON MEDICATION, MEAN MMHG (SD):** 71.3 (7.3) **URINARY SODIUM, MEAN MMOL/DAY (SD):** G1: 144 (53) G2: 145 (55)	*(continued from previous table)* **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –2.0 (–3.2, –0.8) *p*=0.001 **30 months** **PROPORTION WITHOUT AN ENDPOINT, %:** G1: 36 G2: 21 **RELATIVE HR (95% CI) FOR ENDPOINTS ASSOCIATED WITH ASSIGNMENT G1 VS. G2:** 0.68 (0.56, 0.82) *p*<0.001		*(continued from previous table)* **POLYUNSATURATED FAT, G:** –1.1 (–2.3, 0.1) **PROTEIN, G:** –1.3 (–5.0, 2.4) **CHO, G:** –0.2 (–11.6, 11.2) **POTASSIUM, MG:** 160 (25, 295)

CQ2 Summary Table C–2. Different Levels of Sodium

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Svetkey et al. 2004(57); Bray et al. 2004(44); Vollmer et al. 2001(45) RCT, crossover USA, outpatient medical centers Good	**TREATMENT GROUPS:** G1: DASH diet G2: Control G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION:** **Run-in:** 2 weeks **Treatment:** 90 days, 30 days per sodium condition *(continued in next table)*	Adults ≥22 years of age, SBP of 120–159 mmHg, DBP of 80–95 mmHg, target of 50% enrollment of Blacks and women ***N*:** G1: 208 G2: 204 **AGE, MEAN YEARS (SD):** G1: 47 (10) G2: 49 (10) *(continued in next table)*	**After 30 days of treatment** **SBP MEAN CHANGE, MMHG (95% CI):** G1 I vs. G1 H: –1.3 (–2.6, 0.0) $p<0.05$ G1 L vs. G1 I: –1.7 (–3.0, –0.4) $p<0.01$ G2 H vs. G2 L: –6.7 (–5.4, –8.0) $p<0.001$ G2 I vs. G2 H: –2.1 (–3.4, –0.8) $p<0.001$ *(continued in next table)*	**After 30 days of treatment** **URINARY NA, MMOL/DAY (SD):** G1 H: 144 (58) G1 I: 107 (52) G1 L: 67 (46) G2 H: 141 (55) G2 I: 106 (44) G2 L: 64 (37) *(continued in next table)*	**WITHDRAWALS, *N* (%):** G1: 10 (4.8) G2: 12 (5.9) *(continued in next table)*

CQ2 Summary Table C–2. Different Levels of Sodium (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Svetkey et al. 2004(57); Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*	*(continued from previous table)* **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were higher (H; 150 mmol/d), intermediate (I; 100 mmol/d), and lower (L; 50 mmol/d). All food was provided. Weight was kept stable.	*(continued from previous table)* **SEX, *N* (%):** Female G1: 123 (59) G2: 111 (54) **RACE/ETHNICITY, *N** (%):** Black G1: 118 (57) G2: 114 (56) Non-Hispanic White	*(continued from previous table)* **SBP MEAN CHANGE, MMHG (95% CI):** G2 L vs. G2 I: –4.6 (–5.9, –3.2) $p<0.001$ G2 H vs. G2 L: –3.0 (–1.7, –4.3) $p<0.001$ G1 H vs. G2 H: –5.9 (–8.0, –3.7) P < 0.001 G1 I vs. G2 I: –5.0 (–7.6, –2.5) $p< 0.001$ G1 L vs. G2 L: –2.2 (–4.4, –0.1)	*(continued from previous table)* **URINARY NA, G/DAY (SD):** G1 H: 303 (1.3) G1 I: 2.5 (1.2) G1 L 1.5 (1.0) G2 H: 3.3 (1.3) G2 I: 2.4 (1.0) G2 L: 1.5 (0.8)	*(continued from previous table)* **ADHERENCE:** Reported as 24-hour urinary excretion: The levels of urinary potassium, phosphorus, and urea nitrogen (reflective of the intake of fruit and vegetables, dairy products, and protein, respectively) were higher in the DASH-diet group than in the control-diet group, and were nearly identical for all three

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		G1: 83 (40) G2: 81 (40) Asian or other G1: 6 (3) G2: 10 (5) **WEIGHT:** NR **MEAN BMI, KG/M^2 (SD):** G1: 29 (5) G2: 30 (5) **MEAN SBP, MMHG (SD):** G1: 134 (10) G2: 135 (10) **MEAN DBP, MMHG (SD):** G1: 86 (5) G2: 86 (4) **URINARY SODIUM MMOL/DAY (SD):** G1: 158 (79) G2: 152 (72)	*p*< 0.05 G1 L vs. G2 H: –8.9 (–6.7, –11.1) *p*<0.001 **DBP MEAN CHANGE, MMHG (95% CI):** G1 I vs. G1 H: –0.6 (–1.5, 0.2) *p*=NS G1 L vs. G1 I: –1.0 (–1.9, –0.1) *p*<0.01 G1 H vs. G1 L: –1.6 (–0.8, –2.5) *p*<0.001 G2 I vs. G2 H: –1.1 (–1.9, –0.2) *p*<0.01 G2 L vs. G2 I: –2.4 (–3.3, –1.5) *p*<0.001 G2 H vs. G2 L: –3.5 (–2.6, –4.3) *p*<0.001 G1 H vs. G2 H: –2.9 (–4.3, –1.5) *p*< 0.001 G1 I vs. G2 I: –2.5 (–4.1, –0.8) *p*< 0.01 G1 L vs. G2 L: –1.0 (–2.5, 0.4) *p*=NS *(continued in next table)*		sodium levels. **NUTRIENT INTAKE:** Actual nutrient intake for sodium is reported as urinary sodium excretion.

CQ2 Summary Table C–2. Different Levels of Sodium (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Svetkey et al.			*(continued from previous table)* **DBP MEAN CHANGE, MMHG (95% CI):**		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
2004(57); Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*			G1L vs. G2 H: –4.5 (–3.1, –5.9) *p*<0.001 For changes in subgroups, see Summary Tables on subpopulations (i.e., race, sex, hypertension status)		

CQ2 Summary Table C–3. Sodium and Other Dietary Changes

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
Charlton et al. 2008(62) RCT South Africa, Cape Town township Good	**TREATMENT GROUPS:** G1: Food-based intervention G2: Control G1: Intervention comprised 5 commonly consumed food items (brown bread, margarine, stock cubes, soup mixes, and Aromat) modified in Na, K, Mg and Ca content plus a salt replacement and 500 ml of maas (fermented milk) G2: Control diet provided the same foods but of standard commercial composition, as well as artificially sweetened cold drink instead of maas. Based on laboratory-determined chemical food analyses, compared to control foods, the intervention foods were planned to provide 41% less Na (100.3 vs. 170.3 mmol/d), 826% more K (70.9 vs. 8.6 mmol/d), 388% more Ca (857 vs. 221 mg/d) and 368% more Mg (13.8 v. 3.7 mmol/d) *(continued in next table)*	Black residents of a Cape Town township, 50 to 75 years of age, with drug-treated mild-to-moderate hypertension (SBP≤160 mmHg, DBP≤95 mmHg) ***N*:** G1: 47 G2: 45 **AGE, MEAN YEARS (SD):** G1: 61.8 (6.6) G2: 60.4 (7.4) **SEX, MALE, *N*:** G1: 7 G2: 6 **SEX, FEMALE, *N*:** G1: 33 G2: 34 *(continued in next table)*	**MEAN NET DIFFERENCE (G1–G2), MMHG (95% CI)** **SBP, OFFICE:** –6.194 (–11.442, –0.945) *p*=0.021 **DBP, OFFICE:** –0.595 (–3.019, 1.829) **24-HOUR ABPM, AVG SBP:** –4.527 (–9.047, –0.006) *p*=0.050 **24-HOUR ABPM, AVG DBP:** –2.494 (–5.160, 0.173) *p*=0.066	**Mean within group change from baseline** **URINARY NA, MMOL/24H (SD):** G1: –14.6 (54.4) G2: –5.9 (54.3) **URINARY K, MMOL/24H (SD):** G1: 20.0 (22.7) G2: –4.6 (14.8) **URINARY MG, MMOL/24H (SD):** G1: +0.88 (1.20) G2: +0.19 (0.81) **URINARY CA, MMOL/24H (SD):** G1: +0.27 (1.00) G2: +0.32 (1.11) *(continued in next table)*	**WITHDRAWALS, *N* (%):** G1: 7 (14.9) G2: 5 (11.1) **ADHERENCE:** Dietary compliance was monitored using data from 24-hour recalls and 24-hour urinary electrolyte concentrations; returned salt and Aromat shakers were weighed weekly. *(continued in next table)*

CQ2 Summary Table C–3. Sodium and Other Dietary Changes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
Charlton et al. 2008(62) *(continued)*	*(continued from previous table)* **DURATION:** **Run-in:** 3 weeks **Treatment:** 8 weeks **Intervention delivery:** Subjects were instructed to consume their usual amounts of food and sufficient food was provided for the whole family. A single dietitian was responsible for food-packing and all food was locked and sealed in large shopping bags, labeled only with participants' names and contact details. A driver delivered the food three times a week.	*(continued from previous table)* **RACE, % BLACK:** G1: 100 G2: 100 **WEIGHT, MEAN KG (SD):** G1: 83.3 (13.7) G2: 88.8 (15.5) **BMI, KG/M² (SD):** G1: 32.9 (5.8) G2: 35.3 (6.0) **MEAN SBP, MMHG (SD):** G1: 133.9 (14.6) G2: 135.4 (16.7) **MEAN DBP, MMHG (SD):** G1: 79.8 (8.6) G2: 82.3 (7.5)		*(continued from previous table)* **Mean between group difference (G1–G2)** **URINARY NA, MMOL/24H (SD):** –8.7 (46.9) **URINARY K, MMOL/24H (SD):** +24.6 (16.5) *p*<0.001 **URINARY MG, MMOL/24H (SD):** +0.68 (0.88) *p*<0.05 **URINARY CA, MMOL/24H (SD):** –0.05 (0.91)	*(continued from previous table)* **Reported daily dietary intake: mean difference (G1–G2)** **NA, MG (SD):** –1167 (1532) *p*<0.01 **K, MG (SD):** 867 (890) *p*<0.0001 **MG, (SD):** 71 (89) *p*<0.001 **CA, MG (SD):** 310 (392) *p*<0.001
China Salt Substitute Study China Salt Study Collaborative Group, 2007(61) RCT China, 39 sites distributed between 6 regional coordinating centers Good	**TREATMENT GROUPS:** G1: Salt substitute G2: Normal salt G1: Salt substitute was 65% Na Cl, 25% K Cl and 10% Mg sulphate G2: normal salt was 100% Na Cl **DURATION** **Run-in:** 4 week run-in on salt substitute Treatment: 12 months **Additional followup time after treatment:** none *(continued in next table)*	Adult males and females, living in rural China, at elevated risk of future vascular disease ***N*:** G1: 306 G2: 302 **AGE, MEAN YEARS (SD):** G1: 59 (10.0) G2: 61 (9.7) **SEX, FEMALE, *N* (%):** G1:166 (52) G2:174 (58)	**SBP:** SBP lower in G1 vs. G2 at 6, 9 and 12 month visits; (data reported in figure) *p*<0.002) Maximum net reduction achieved at 12 months: 5.4 (2.3, 8.5) **Over 12 months:** **SBP MEAN DIFFERENCE, MMHG (95% CI):** G1 vs. G2: 3.7 (1.6, 5.9) *p*<0.001	No significant differences between groups in first morning urine sodium concentrations at 6 months or 12 months G1 had significantly higher first morning urine concentrations of potassium at 6 months and 12 months **AT 6 MONTHS:** G1 vs. G2: 8.6 mmol/l 95% CI: (-1.1, 18.2) **At 12 months:** G1 vs. G2: 8.0 mmol/l 95% CI: (-3.3, 19.2)	**WITHDRAWALS, *N* (%):** G1: 14 (4.6) G2: 9 (3) **NUTRIENT INTAKE:** Concentrations of sodium and potassium were measured.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
		RACE/ETHNICITY: All were “rural Chinese” *(continued in next table)*	**DBP:** No differences between groups at any time (p>0.20)		

CQ2 Summary Table C–3. Sodium and Other Dietary Changes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
China Salt Substitute Study China Salt Study Collaborative Group, 2007(61) *(continued)*	*(continued from previous table)* **CHARACTERISTICS OF TREATMENT DELIVERY:** Participants were instructed to use study salt for all food preparation throughout the study duration; existing salt and foods previously pickled in salt were not removed from participants’ households. Salt (substitute & normal) was delivered in identical 1 kg bags; up to 3 kg/month available to each randomized participant to cover all household uses.	*(continued from previous table)* **WEIGHT:** NR **BMI, MEAN KG/M² (SD):** G1: 26 (3.6) G2: 25 (3.9) **MEAN SBP, MMHG (SD):** G1: 159 (25) G2: 159 (26) **MEAN DBP, MMHG (SD):** G1: 93 (14) G2: 93 (14) **URINARY SODIUM, MEAN MMOL/DAY (IQR):** G1: 151 (92–201) G2: 154 (94–200)			

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
China Salt Substitute Study Subgroup Analysis Hu et al. 2009(60) Subgroup analysis of RCT China, 2 sites (overall RCT conducted in 39 sites distributed among 6 regional coordinating centers) Fair	**TREATMENT GROUPS:** G1: Salt substitute G2: Normal salt G1: Salt substitute was 65% Na Cl, 25% K Cl and 10% Mg sulphate G2: normal salt was 100% Na Cl **DURATION:** **Run-in:** 4 week run-in on salt substitute **Treatment:** 12 months **Additional followup time after treatment:** none **CHARACTERISTICS OF TREATMENT DELIVERY:** Participants were instructed to use study salt for all food preparation throughout the study duration; existing salt and foods previously pickled in salt were not removed from participants' households	Adult males and females, living in rural China, at elevated risk of future vascular disease ***N*:** G1: 95 G2: 97 **AGE, MEAN YEARS (SD):** G1: 59 (10.0) G2: 59 (9.1) **SEX, MALE, *N* (%):** G1: 43 (46) G2: 33 (35) **RACE/ETHNICITY:** All were "rural Chinese" *(continued in next table)*	**At 12 months** **CHANGE IN PERIPHERAL SBP, MMHG (SD):** G1: –0.2 (18.1) G2: 6.9 (23.0) *p*=0.23 **CHANGE IN PERIPHERAL DBP, MMHG (SD):** G1: 0.1 (10.6) G2: 2.1 (11.4) *p*=0.227 **CHANGE IN CENTRAL SBP, MMHG (SD):** G1: 1.1 (17.4) G2: 7.4 (21.9) *p*=0.032 *(continued in next table)*	NR	**WITHDRAWALS, *N* (%):** G1: 2 (2.1) G2: 3 (31) **ADHERENCE:** NR **NUTRIENT INTAKE:** Concentrations of sodium and potassium were measured.

CQ2 Summary Table C–3. Sodium and Other Dietary Changes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
China Salt Substitute Study Subgroup Analysis Hu et al. 2009(60) *(continued)*		*(continued from previous table)* **WEIGHT:** NR **BMI, MEAN KG/M² (SD):** G1: 27 (3.9) G2: 26 (3.8)	*(continued from previous table)* **CHANGE IN CENTRAL DBP, MMHG (SD):** G1: 0.2 (10.8) G2: 2.3 (11.8) *p*=0.210		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
		MEAN SBP, MMHG (SD): G1: 149.4 (22.3) G2: 150 24.2) **MEAN DBP, MMHG (SD):** G1: 91.0 (12.8) G2: 91.8 (13.3) **URINARY SODIUM, MEAN MMOL/DAY:** NR			
DASH-Sodium Sacks et al. 2001(29) RCT, crossover USA, outpatient medical centers Good	**TREATMENT GROUPS:** G1: DASH diet G2: Control G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION** **Run-in:** 2 weeks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were higher (H; 150 mmol/d), intermediate (I; 100 mmol/d), and lower (L; 50 mmol/d). All food was provided. Weight was kept stable.	Adults ≥22 years of age, SBP of 120–159 mmHg, DBP of 80–95 mmHg, target of 50% enrollment of Blacks and women ***N*:** G1: 208 G2: 204 **AGE, MEAN YEARS (SD):** G1: 47 (10) G2: 49 (10) **SEX, *N* (%)** Female G1: 123 (59) G2: 111 (54) *(continued in next table)*	**After 30 days of intervention** **SBP MEAN CHANGE, MMHG (95% CI):** G1 I vs. G1 H: –1.3 (–2.6, 0.0) *p*<0.05 G1 L vs. G1 I: –1.7 (–3.0, –0.4) *p*<0.01 G2 H vs. G2 L: –6.7 (–5.4, –8.0) *p*<0.001 G2 I vs. G2 H: –2.1 (–3.4, –0.8) *p*<0.001 G2 L vs. G2 I: –4.6 (–5.9, –3.2) *p*<0.001 G2 H vs. G2 L: –3.0 (–1.7, –4.3) *p*<0.001 G1 H vs. G2 H: –5.9 (–8.0, –3.7) *p*< 0.001 *(continued in next table)*	**After 30 days of intervention** **URINARY NA, G/DAY (SD):** G1 H: 303 (1.3) G1 I: 2.5 (1.2) G1 L 1.5 (1.0) G2 H: 3.3 (1.3) G2 I: 2.4 (1.0) G2 L: 1.5 (0.8)	**WITHDRAWALS, *N* (%):** G1: 10 (4.8) G2: 12 (5.9) **ADHERENCE:** Reported as 24-hour urinary excretion: The levels of urinary potassium, phosphorus, and urea nitrogen (reflective of the intake of fruit and vegetables, dairy products, and protein, respectively) were higher in the DASH-diet group than in the control-diet group, and were nearly identical for all three sodium levels. **NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion.

CQ2 Summary Table C–3. Sodium and Other Dietary Changes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29) *(continued)*		*(continued from previous table)* **RACE/ETHNICITY, *N* (%)** Black G1: 118 (57) G2: 114 (56) Non-Hispanic White G1: 83 (40) G2: 81 (40) Asian or other G1: 6 (3) G2: 10 (5) **WEIGHT:** NR **MEAN BMI, KG/M^2 (SD):** G1: 29 (5) G2: 30 (5) **MEAN SBP, MMHG (SD):** G1: 134 (10) G2: 135 (10) **MEAN DBP, MMHG (SD):** G1: 86 (5) G2: 86 (4) **URINARY SODIUM MMOL/DAY (SD):** G1: 158 (79) G2: 152 (72)	*(continued from previous table)* **SBP MEAN CHANGE, MMHG (95% CI):** G1 I vs. G2 I: –5.0 (–7.6, –2.5) *p*< 0.001 G1 L vs. G2 L: –2.2 (–4.4, –0.1) *p*< 0.05 G1 L vs. G2 H: –8.9 (–6.7, –11.1) *p*<0.001 **DBP MEAN CHANGE, MMHG (95% CI):** G1 I vs. G1 H: –0.6 (–1.5, 0.2) *p*=NS G1 L vs. G1 I: –1.0 (–1.9, –0.1) *p*<0.01 G1 H vs. G1 L: –1.6 (–0.8, –2.5) *p*<0.001 G2 I vs. G2 H: –1.1 (–1.9, –0.2) *p*<0.01 G2 L vs. G2 I: –2.4 (–3.3, –1.5) *p*<0.001 G2 H vs. G2 L: –3.5 (–2.6, –4.3) *p*<0.001 G1 H vs. G2 H: –2.9 (–4.3, –1.5) *p*< 0.001 G1 I vs. G2 I: –2.5 (–4.1, –0.8) *p*< 0.01 G1 L vs. G2 L: –1.0 (–2.5, 0.4) *p*=NS G1L vs. G2 H: –4.5 (–3.1, –5.9) *p*<0.001		

CQ2 Summary Table C–3. Sodium and Other Dietary Changes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Actual Nutrient Intake
TONE Whelton et al. 1998(53); Appel et al. 2001(55); Espeland et al. 2002(56) RCT USA, 4 academic health centers Good	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual care **DURATION** Mean of 27.8 months (range 15.6 to 35.9 months) after randomization **INTERVENTION DELIVERY:** In the reduced sodium group, each person had an introductory individual session. The TONE interventions consisted of a 4-month "intensive" phase with weekly meetings, a 4-month "extended" phase with biweekly meetings, and a maintenance phase. The interventionist typically was a registered dietitian. The meetings were conducted as group sessions (9–12 participants) with individual sessions at every fourth contact. Goal for sodium reduction: achieving and maintaining a 24-hour dietary sodium intake of 80 mmol (1,800 mg) or less G2 received no study-related counseling in lifestyle change; were invited to meetings on topics unrelated to trial goals	Adults 60 to 80 years; had baseline BP <145/85 mmHg while on a single antihypertensive medication. ***N*:** G1: 340 G2: 341 **AGE, MEAN YEARS (SD):** 65.8 (4.6) **SEX, FEMALE %:** 47 **RACE/ETHNICITY, %:** African American: 23 **OVERWEIGHT, %:** 43 **BMI:** NR **SBP ON MEDICATION, MEAN MMHG (SD):** 128.0 (9.4) **DBP ON MEDICATION, MEAN MMHG (SD):** 71.3 (7.3) **URINARY SODIUM, MEAN MMOL/DAY (SD):** G1: 144 (53) G2: 145 (55)	**Mean interval, 3.5 months (baseline to visit prior to medication withdrawal)** **SBP CHANGE, MEAN MMHG (SD):** G1: –4.6 (11.3) G2: –0.4 (10.5) **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –4.3 (–6.0, –2.5) *p*<0.001 **DBP CHANGE, MEAN MMHG (SD):** G1: –2.2 (8.0) G2: –0.2 (7.0) **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –2.0 (–3.2, –0.8) *p*=0.001 **30 months** **PROPORTION WITHOUT AN ENDPOINT, %:** G1: 36 G2: 21 **RELATIVE HR (95% CI) FOR ENDPOINTS ASSOCIATED WITH ASSIGNMENT G1 VS. G2:** 0.68 (0.56, 0.82) *p*<0.001	**30 months** **24-HOUR URINARY NA CHANGE, MEAN MMOL (SD):** G1: –45 (55.8) G2: –5 (50.0) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL (95% CI):** –40 (–48, –32) *p*<0.001	**WITHDRAWALS:** Attended final study visit (15–37 months) G1: 91% G2: 92% **DAILY NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion.

CQ2 Summary Table C–4a. ***Sodium and Subpopulation: Sex***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-SODIUM Subgroup analysis Sacks et al. 2001(29); Bray et al. 2004(44); Vollmer et al. 2001(45) RCT, crossover USA, outpatient medical centers Fair	**TREATMENT GROUPS:** G1: DASH diet G2: Control G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION** **Run-in:** 2 weeks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were higher (H; 150 mmol/d), intermediate (I; 100 mmol/d), and lower (L; 50 mmol/d). All food was provided. Weight was kept stable.	Adults ≥22 years of age, SBP of 120–159 mmHg, DBP of 80–95 mmHg, target of 50% enrollment of Blacks and women ***N*:** Men G1: 85 G2: 93 Women G1: 123 G2: 111 **MEAN SBP, MMHG (SD):** Men G1 H: 125 (11) G1 I: 124 (11) G1 L: 123 (10) G2 H: 131 (11) G2 I: 127 (10) G2 L: 125 (9) Women G1 H: 128 (11) G1 I: 127 (13) G1 L: 124 (11) G2 H: 135 (12) G2 I: 133 (13) G2 L: 127 (11) **MEAN DBP, MMHG (SD):** Men G1 H: 81 (7) G1 I: 81 (7) G1 L: 80 (6) G2 H: 84 (7) G2 I: 82 (6) G2 L: 81 (6)	**Men** **MEAN CHANGE (95% CI)* IN SBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –1.7 (–3.4, 0.0) *p*<0.10 G1 L vs. G1 I: –0.7 *p*=NR (NS) G1 I vs. G1 H: –0.9 *p*=NR (NS) G2 L vs. G2 H: –5.7 (–7.3, –4.1) *p*<0.01 G2 L vs. G2 I: –3.1 *p*<0.01 G2 I vs. G2 H: –2.6 *p*<0.01 G1 H vs. G2 H: –5.1 (–7.7, –2.6) G1 L vs. G2 H: –6.8 (–9.3, –4.3) **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –1.6 *p*<0.01 G1 L vs. G1 I: –0.7 *p*=NR (NS) G1 I vs. G1 H: –0.5 *p*=NR (NS) G2 L vs. G2 H: –3.2 *p*<0.01 G2 L vs. G2 I: –1.9 *p*<0.01 G2 I vs. G2 H: –1.4 *p*<0.05 G1 H vs. G2 H: –2.7 (–4.4, –1.0) G1 L vs. G2 H: –4.2 (–5.9, –2.6) *(continued in next table)*	Not reported by subgroup **Overall:** **After 30 days of intervention** **URINARY NA, MMOL/DAY (SD):** G1 H: 144 (58) G1 I: 107 (52) G1 L: 67 (46) G2 H: 141 (55) G2 I: 106 (44) G2 L: 64 (37) **URINARY NA, G/DAY (SD):** G1 H: 303 (1.3) G1 I: 2.5 (1.2) G1 L: 1.5 (1.0) G2 H: 3.3 (1.3) G2 I: 2.4 (1.0) G2 L: 1.5 (0.8)	**WITHDRAWALS, *N* (%):** Not reported by subgroup Overall: G1: 10 (4.8) G2: 12 (5.9) **ADHERENCE:** Reported as 24-hour urinary excretion: The levels of urinary potassium, phosphorus, and urea nitrogen (reflective of the intake of fruit and vegetables, dairy products, and protein, respectively) were higher in the DASH-diet group than in the control-diet group, and were nearly identical for all three sodium levels. **NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion, which was not reported by subgroup.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		(continued in next table)			

CQ2 Summary Table C–4a. Sodium and Subpopulation: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-SODIUM Subgroup analysis Sacks et al. 2001(29); Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*		*(continued from previous table)* **MEAN DBP, MMHG (SD):** Women G1 H: 81 (7) G1 I: 80 (7) G1 L: 79 (7) G2 H: 83 (7) G2 I: 82 (7) G2 L: 80 (6) **Other baseline characteristics not reported by males or females separately.** **OVERALL SAMPLE CHARACTERISTICS:** Age, mean years (SD): G1: 47 (10) G2: 49 (10) **SEX, *N* (%):** Female G1: 123 G2: 111	*(continued from previous table)* **Women** **MEAN CHANGE (95% CI)* IN SBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –4.0 (–5.4, –2.5) *p*<0.05 G1 L vs. G1 I: –2.4 *p*<0.01 G1 I vs. G1 H: –1.6 *p*<0.05 G2 L vs. G2 H: –7.5 (–9.0, –6.0) *p*<0.01 G2 L vs. G2 I: –5.8 *p*<0.01 G2 I vs. G2 H: –1.7 *p*<0.05 G1 H vs. G2 H: –6.6 (–8.8, –4.3) G1 L vs. G2 H: –10.5 (–12.8, –8.2) *p*<0.05 **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:**		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		RACE/ETHNICITY, *N* (%): Black G1: 118 (57) G2: 114 (56) **NON-HISPANIC WHITE** G1: 83 (40) G2: 81 (40) **ASIAN OR OTHER** G1: 6 (3) G2: 10 (5) *(continued in next table)*	G1 L vs. G1 H: –1.7 (–2.6, –0.8) *p*<0.01 G1 L vs. G1 I: –1.2 *p*<0.05 G1 I vs. G1 H: –0.5 *p*=NR (NS) G2 L vs. G2 H: –3.7 (–4.7, –2.7) *p*<0.01 G2 L vs. G2 I: –2.8 *p*<0.01 *(continued in next table)*		

CQ2 Summary Table C–4a. *Sodium and Subpopulation: Sex (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-SODIUM Subgroup analysis Sacks et al. 2001(29); Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*		*(continued from previous table)* **MEAN BMI KG/M^2 (SD):** G1: 29 (5) G2: 30 (5) **URINARY SODIUM MMOL/DAY (SD):** G1: 158 (79) G2: 152 (72)	*(continued from previous table)* **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G2 I vs. G2 H: –0.8 *p*<0.10 G1 H vs. G2 H: –3.0 (–4.5, –1.5) G1 L vs. G2 H: –4.7 (–6.2, –3.2) 95% CI not reported for all comparisons		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58) 2 X 2 factorial RCT USA, 9 academic medical centers Good	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual care **DURATION:** **Treatment:** 36–48 months **Additional Followup after Treatment:** none **INTERVENTION DELIVERY:** Individual and group counseling through in-person, telephone, and mail contact **INTENSIVE PHASE:** Groups of 11 to 34, counseled weekly for 10 weeks; primary goal was to provide core knowledge and behavioral skills to make and maintain reductions in Na intake. **TRANSITIONAL PHASE:** 4 monthly sessions; designed to prevent relapse and ease transition to less frequent contact **FINAL EXTENDED PHASE:** 1 or 2 monthly contacts; 3 to 6 refresher sessions were offered; goal: maintain participants' behavior changes Goal for G1: reduction in sodium intake of 80 mmol per day or less	Adults 30–54 years, not taking antihypertensive drugs, SBP<140 mmHg, DBP 83 to 89 mmHg, BMI representing 110% to 165% of desirable body weight **URINARY SODIUM, MMOL/D (SD):** Men G1: 203.8 (84.2) G2: 201.7 (84.1) Women G1: 153.4 (61.9) G2: 158.0 (64.1) Other baseline characteristics not reported by intervention group + males or females separately. **OVERALL SAMPLE CHARACTERISTICS:** ***N*:** G1: 594 G2: 596 *(continued in next table)*	**6 Months** **BLACK MEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –4.3 (9.1) G2: 0.5 (7.8) **SBP DIFFERENCE, MMHG (95% CI):** –4.8 (–8.6, –1.0) **DBP MEAN CHANGE, MMHG (SD):** G1: –3.4 (7.0) G2: –1.3 (7.2) **DBP DIFFERENCE, MMHG (95% CI):** –2.1 (–5.3, 1.1) **WHITE MEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –4.6 (8.5) G2: –2.4 (7.8) **SBP DIFFERENCE, MMHG (95% CI):** –2.2 (–3.5, –0.9) *(continued in next table)*	**6 Months** **MEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –82.1 (85.0) G2: –26.3 (116.5) **24-hour urinary Na net difference, mmol/d (95% CI):** G1 vs. G2: 55.8 (26.3, 85.2) **WOMEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –62.5 (73.5) G2: –20.4 (–68.6) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 42.0 (11.8, 72.4) **18 Months** **MEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –68.7 (99.7) G2: –15.0 (102.6) *(continued in next table)*	**WITHDRAWALS:** Proportion of participants with BP readings at all 3 scheduled visits at or after 36 months ranged from 88.9% to 91.6% Completion of sodium excretion data at 36 months ranged from 79.1% to 80.9% **ADHERENCE:** Adherence measures such as food diaries and overnight urine samples were not used as study outcome data. **NUTRIENT INTAKE:** 24-hour dietary recall and 3-day food record information was obtained at 18- and 36-months for randomly selected samples.

CQ2 Summary Table C–4a. Sodium and Subpopulation: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58) *(continued)*		*(continued from previous table)* **OVERALL SAMPLE CHARACTERISTICS:** **AGE:** G1: 44.2 (6.1) G2: 43.2 (6.1) **SEX, % MALE:** G1: 64.8 G2: 68.3 **RACE/ETHNICITY:** White, % G1: 81.1 G2: 79.5 Black, % G1: 16.8 G2: 17.3 **WEIGHT, KG (SD):** G1: 94.0 (14.3) G2: 93.6 (13.5) **BMI:** NR **MEAN SBP, MMHG (SD):** G1: 127.7 (6.6) G2: 127.3 (6.4) **MEAN DBP, MMHG (SD):** G1: 86.1 (1.9) G2: 85.8 (1.9)	*(continued from previous table)* **DBP MEAN CHANGE, MMHG (SD):** G1: –4.0 (6.6) G2: –3.2 (6.0) **DBP DIFFERENCE, MMHG (95% CI):** –0.9 (–1.9, 0.1) **BLACK WOMEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –5.9 (7.6) G2: –1.3 (9.5) **SBP DIFFERENCE, MMHG (95% CI):** –4.6 (–8.1, –1.1) **DBP MEAN CHANGE, MMHG (SD):** G1: –5.4 (6.5) G2: –2.8 (7.2) **DBP DIFFERENCE, MMHG (95% CI):** –2.5 (–5.3, 0.2) **WHITE WOMEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –6.3 (9.2) G2: –3.3 (8.3) **SBP DIFFERENCE, MMHG**	*(continued from previous table)* **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 53.6 (37.7, 69.6) **WOMEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –41.8 (70.8) G2: –20.8 (74.4) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 21.0 (4.4, 37.6) **36 months** **MEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –60.1 (91.3) G2: –8.8 (95.2) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 51.3 (36.8, 65.8) **WOMEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –34.4 (73.8) G2: –14.6 (70.4) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 19.8 (3.6, 35.9)	

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			(95% CI): –3.0 (–5.2, –0.8) *(continued in next table)*		

CQ2 Summary Table C–4a. *Sodium and Subpopulation: Sex (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58) *(continued)*			*(continued from previous table)* **DBP MEAN CHANGE, MMHG (SD):** G1: –5.1 (6.9) G2: –2.7 (5.6) **DBP DIFFERENCE, MMHG (95% CI):** –2.3 (–3.9, –0.7) **18 Months** **BLACK MEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –2.7 (11.1) G2: –1.3 (7.5) **SBP DIFFERENCE, MMHG (95% CI):** –1.4 (–5.9, 3.1) **DBP MEAN CHANGE, MMHG (SD):** G1: –4.5 (8.3)		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			G2: –3.4 (6.4) **DBP DIFFERENCE, MMHG (95% CI):** –1.1 (–4.5, 2.4) **WHITE MEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –3.7 (7.9) G2: –2.2 (6.5) **SBP DIFFERENCE, MMHG (95% CI):** –1.5 (–2.7, –0.4) *(continued in next table)*		

CQ2 Summary Table C–4a. ***Sodium and Subpopulation: Sex (continued)***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58) *(continued)*			*(continued from previous table)* **DBP MEAN CHANGE, MMHG (SD):** G1: –4.0 (6.3) G2: –3.4 (5.8) **DBP DIFFERENCE, MMHG (95% CI):** –0.6 (–1.6, 0.4) **BLACK WOMEN** **SBP MEAN CHANGE, MMHG**		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			(SD): G1: –5.0 (8.6) G2: 0.2 (8.4) **SBP DIFFERENCE, MMHG (95% CI):** –5.2 (–8.7, –1.7) **DBP MEAN CHANGE, MMHG (SD):** G1: –5.6 (6.7) G2: –1.3 (7.1) **DBP DIFFERENCE, MMHG (95% CI):** –4.2 (–7.0, –1.4) **WHITE WOMEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –4.1 (8.1) G2: –2.4 (7.4) **SBP DIFFERENCE, MMHG (95% CI):** –1.8 (–3.8, 0.2) **DBP MEAN CHANGE, MMHG (SD):** G1: –4.9 (6.1) G2: –3.3 (5.3) *(continued in next table)*		

CQ2 Summary Table C–4a. Sodium and Subpopulation: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58) *(continued)*			*(continued from previous table)* **DBP DIFFERENCE, MMHG (95% CI):** –1.6 (–3.1, –0.1) **36 Months** **BLACK MEN** **SBP MEAN CHANGE, MMHG (SD):** G1: 2.2 (10.3) G2: 1.7 (7.4) **SBP DIFFERENCE, MMHG (95% CI):** 0.5 (–3.8, 4.9) **DBP MEAN CHANGE, MMHG (SD):** G1: –0.6 (8.1) G2: –1.9 (7.0) **DBP DIFFERENCE, MMHG (95% CI):** 1.4 (–2.2, 4.9) **WHITE MEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –1.3 (8.5) G2: –0.3 (7.8) **SBP DIFFERENCE, MMHG (95% CI):** –1.1 (–2.4, 0.2) **DBP MEAN CHANGE, MMHG (SD):**		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			G1: –3.0 (6.2) G2: –2.7 (7.1) *(continued in next table)*		

CQ2 Summary Table C–4a. Sodium and Subpopulation: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58) *(continued)*			*(continued from previous table)* **DBP DIFFERENCE, MMHG (95% CI):** –0.3 (–1.4, 0.8) **BLACK WOMEN** **SBP MEAN CHANGE, MMHG (SD):** G1: –1.0 (11.1) G2: 2.0 (9.2) **SBP DIFFERENCE, MMHG (95% CI):** –3.0 (–7.2 (1.3) **DBP MEAN CHANGE, MMHG (SD):** G1: –4.0 (8.2) G2: –1.6 (7.5) **DBP DIFFERENCE, MMHG (95% CI):** –2.4 (–5.7, 0.8) **WHITE WOMEN**		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			SBP MEAN CHANGE, MMHG (SD): G1: 0.5 (8.9) G2: 2.1 (10.4) **SBP DIFFERENCE, MMHG (95% CI):** –1.5 (–4.0, 0.9) **DBP MEAN CHANGE, MMHG (SD):** G1: –3.4 (5.8) G2: –1.9 (6.8) **DBP DIFFERENCE, MMHG (95% CI):** –1.4 (–3.1, 0.2)		

CQ2 Summary Table C–4a. Sodium and Subpopulation: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TONE Whelton et al. 1998(53); Appel et al. 2001(55); Espeland et al. 2002(56) RCT USA, 4 academic health centers Good	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual care **DURATION:** **Treatment:** Average of 27.6 months (range 15.6 to 35.9 months) after randomization **Followup:** NR **INTERVENTION DELIVERY:** In the reduced sodium group, each person had an introductory individual session. The TONE	Adults 60 to 80 years; had baseline BP <145/85 mmHg while on a single antihypertensive medication ***N*:** G1: 340 G2: 341 **MEAN SBP, MMHG (SD):** Men G1: 129.0 (9.0)	**Mean interval, 3.5 months** **Men** **SBP CHANGE, MEAN MMHG (SD):** G1: –5.6 (11.3) G2: –0.4 (9.5) **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –5.2 (–7.5, –2.9)	**30 months** **Men** **24-HOUR URINARY NA CHANGE, MEAN MMOL/L (SD):** G1: –59 (53.0) G2: –7 (53.6) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL/L (95% CI):** –53 (–64, –41)	**WITHDRAWALS, %:** Not reported by subgroup **OVERALL:** Attended final study visit (15–37 months) G1: 91% G2: 92% **ADHERENCE:** Not reported by subgroup

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
	interventions consisted of a 4-month “intensive” phase with weekly meetings, a 3-month “extended” phase with biweekly meetings, and a maintenance phase. The interventionist typically was a registered dietitian. The meetings were conducted as group sessions (9–12 participants) with individual sessions at every fourth contact. Goal for sodium reduction: achieving and maintaining a 24-hour dietary sodium intake of 80 mmol (1,800 mg) or less	G2: 126.9 (9.7) Women G1: 127.7 (9.5) G2: 127.7 (8.9) **MEAN DBP, MMHG (SD):** Men G1: 72.7 (6.6) G2: 72.2 (7.0) Women G1: 70.0 (8.1) G2: 70.4 (7.2) **URINARY SODIUM, MEAN MMOL/DAY (SD):** Men G1: 162 (53) G2: 159 (55) Women G1: 125 (45) G2: 128 (48) Other baseline characteristics not reported by sex grouping. *(continued in next table)*	*p*<0.001 **DBP CHANGE, MEAN MMHG (SD):** G1: –2.7 (7.7) G2: –0.1 (7.0) **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –2.6 (–4.2, –1.0) *p*=0.002 **Women** **SBP CHANGE, MEAN MMHG (SD):** G1: –3.7 G2: –0.4 **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –3.4 (–6.0, –0.6) *p*=0.02 **DBP CHANGE, MEAN MMHG (SD):** G1: –1.6 (8.2) G2: –0.3 (7.0) *(continued in next table)*	*p*<0.001 **Women** **24-HOUR URINARY NA CHANGE, MEAN MMOL/L (SD):** G1: –30 (55) G2: –3 (45) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL/L (95% CI):** –27 (–39, –16) *p*<0.001	**DAILY NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion.

CQ2 Summary Table C–4a. Sodium and Subpopulation: Sex (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TONE Whelton et al. 1998(53); Appel et al. 2001(55); Espeland et al. 2002(56) *(continued)*		*(continued from previous table)* **Overall sample characteristics:** **AGE, MEAN YEARS (SD):** 65.8 (4.6) **SEX, FEMALE %:** 47 **RACE/ETHNICITY, %:** African American: 23 **OVERWEIGHT, %:** 43 **BMI:** NR	*(continued from previous table)* **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –1.3 (–3.1, 0.4) *p*=0.14		

CQ2 Summary Table C–4b. Sodium and Subpopulation: Race/Ethnicity

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Vollmer, et al. 2001(45); Bray et al. 2004(44) RCT, crossover USA, outpatient	**TREATMENT GROUPS:** G1: DASH diet G2: Control G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol	Adults ≥22 years of age, SBP of 120–159 mmHg, DBP of 80–95 mmHg, target of 50% enrollment of Blacks and women ***N*:** African American G1: 119	**African American** **MEAN CHANGE (95% CI)* IN SBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –3.6 (–5.1, –2.2) *p*<0.01 G1 L vs. G1 I: –2.1 *p*<0.01	Not reported by subgroup **OVERALL:** **After 30 days of intervention** **URINARY NA, MMOL/DAY (SD):** G1 H: 144 (58) G1 I: 107 (52) G1 L: 67 (46)	**WITHDRAWALS, *N* (%):** Not reported by subgroup **OVERALL:** G1: 10 (4.8) G2: 12 (5.9) *(continued in next table)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
medical centers Fair	**DURATION:** **Run-in:** 2 weeks **Treatment:** 90 days, 30 days per sodium condition *(continued in next table)*	G2: 115 Non-African American G1: 89 G2: 89 *(continued in next table)*	G1 I vs. G1 H: –1.5 *p*<0.05 G2 L vs. G2 H: –8.0 (–9.4, –6.5) *p*<0.01 *(continued in next table)*	G2 H: 141 (55) G2 I: 106 (44) G2 L: 64 (37) *(continued in next table)*	

CQ2 Summary Table C–4b. Sodium and Subpopulation: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Vollmer, et al. 2001(45); Bray et al. 2004(44) *(continued)*	*(continued from previous table)* **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were higher (H; 150 mmol/d), intermediate (I; 100 mmol/d), and lower (L; 50 mmol/d). All food was provided. Weight was kept stable.	*(continued from previous table)* **MEAN SBP, MMHG (SD):** African American G1 H: 128 (11) G1 I: 127 (12) G1 L: 125 (11) G2 H: 134 (12) G2 I: 131 (12) G2 L: 126 (10) Non-African American G1 H: 125 (11) G1 I: 124 (11) G1 L: 123 (10) G2 H: 131 (11) G2 I: 129 (12) G2 L: 127 (10) **MEAN DBP, MMHG (SD):** African American G1 H: 82 (7) G1 I: 81 (8)	*(continued from previous table)* G2 L vs. G2 I: –5.7 *p*<0.01 G2 I vs. G2 H: –2.2 *p*<0.01 G1 H vs. G2 H: –59. (–8.2, –3.6) G1 L vs. G2 H: –9.6 (–11.8, –7.3) *p*=NR (NS) **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –1.9 (–2.9, –1.0) *p*<0.01 G1 L vs. G1 I: –1.0 *p*<0.05 G1 I vs. G1 H: –0.9 *p*<0.10 G2 L vs. G2 H: –4.5 (–5.5, –3.6) *p*<0.01 G2 L vs. G2 I: –3.0	*(continued from previous table)* **URINARY NA, G/DAY (SD):** G1 H: 303 (1.3) G1 I: 2.5 (1.2) G1 L 1.5 (1.0) G2 H: 3.3 (1.3) G2 I: 2.4 (1.0) G2 L: 1.5 (0.8)	*(continued from previous table)* **ADHERENCE:** Reported as 24-hour urinary excretion: The levels of urinary potassium, phosphorus, and urea nitrogen (reflective of the intake of fruit and vegetables, dairy products, and protein, respectively) were higher in the DASH-diet group than in the control-diet group, and were nearly identical for all three sodium levels. **NUTRIENT INTAKE:** Nutrient intake for sodium is reflected as urinary sodium excretion, which was not reported by subgroup.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		G1 L: 80 (6) G2 H: 84 (7) G2 I: 82 (6) G2 L: 80 (6) Non-African American G1 H: 80 (7) G1 I: 80 (7) G1 L: 79 (6) G2 H: 83 (7) G2 I: 82 (6) G2 L: 81 (6) *(continued in next table)*	*p*<0.01 G2 I vs. G2 H: –1.5 *p*<0.01 G1 H vs. G2 H: –3.1 (–4.6, –1.6) G1 L vs. G2 H: –5.0 (–6.5, –3.6) *p*=NR (NS) **Non-African American** **MEAN CHANGE (95% CI)* IN SBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –2.2 (–3.8, –0.5) *p*<0.01 G1 L vs. G1 I: –1.3 *p*=NR (NS) *(continued in next table)*		

CQ2 Summary Table C–4b. *Sodium and Subpopulation: Race/Ethnicity (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Sacks et al. 2001(29); Vollmer, et al. 2001(45); Bray et al. 2004(44) *(continued)*		*(continued from previous table)* **Other baseline characteristics not reported by race/ethnicity subgroup.** **Overall sample characteristics:** **AGE, MEAN YEARS (SD):** G1: 47 (10) G2: 49 (10)	*(continued from previous table)* **Non-African American** **MEAN CHANGE (95% CI)* IN SBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 I vs. G1 H: –0.9 *p*=NR (NS) G2 L vs. G2 H: –5.1 (–6.7, –3.4) *p*<0.01 G2 L vs. G2 I: –3.0 *p*<0.01 G2 I vs. G2 H: –2.1		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		SEX, *N* (%) Female G1: 123 (59) G2: 111 (54) **RACE/ETHNICITY, *N** (%)** Black G1: 118 (57) G2: 114 (56) Non-Hispanic white G1: 83 (40) G2: 81 (40) Asian or other G1: 6 (3) G2: 10 (5) **WEIGHT:** NR **MEAN BMI, KG/M^2 (SD):** G1: 29 (5) G2: 30 (5) **URINARY SODIUM MMOL/DAY (SD):** G1: 158 (79) G2: 152 (72)	*p*<0.05 G1 H vs. G2 H: –5.6 (–8.1, –3.0) G1 L vs. G2 H: –7.8 (–10.3, –5.2) *p*=NR (NS) **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –1.3 (–2.4, –0.2) *p*<0.05 G1 L vs. G1 I: –1.0 *p*<0.10 G1 I vs. G1 H: –0.3 *p*=NR (NS) G2 L vs. G2 H: –2.2 (–3.2, –1.1) *p*<0.01 G2 L vs. G2 I: –1.6 *p*<0.01 G2 I vs. G2 H: –0.6 *p*=NR (NS) G1 H vs. G2 H: –2.4 (–4.1, –0.8) G1 L vs. G2 H: –3.7 (–5.4, –2.0) *p*=NR (NS)		

CQ2 Summary Table C–4b. Sodium and Subpopulation: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II Kumanyika et al.	**TREATMENT GROUPS:**	Adults 30–54 years, not taking antihypertensive	**6 Months**	**6 Months**	**WITHDRAWALS:**

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
2005(58) RCT, 2 X 2 factorial USA, 9 academic medical centers Fair	G1: Sodium reduction G2: Usual care **DURATION:** **Treatment:** 36–48 months **Additional Followup after Treatment:** none **INTERVENTION DELIVERY:** Individual and group counseling through in-person, telephone, and mail contact. **INTENSIVE PHASE:** Groups of 11 to 34, counseled weekly for 10 weeks; primary goal was to provide core knowledge and behavioral skills to make and maintain reductions in Na intake. **TRANSITIONAL PHASE:** 4 monthly sessions; designed to prevent relapse and ease transition to less frequent contact **FINAL EXTENDED PHASE:** 1 or 2 monthly contacts; 3 to 6 refresher sessions were offered; goal: maintain participants' behavior changes **GOAL FOR G1:** Reduction in sodium intake of 80 mmol per day or less	drugs, SBP<140 mmHg, DBP 83 to 89 mmHg, BMI representing 110% to 165% of desirable body weight **Baseline characteristics not reported by intervention group + race/ethnicity separately.** **Overall sample characteristics:** ***N*:** G1: 594 G2: 596 **AGE:** G1: 44.2 (6.1) G2: 43.2 (6.1) **SEX, % MALE:** G1: 64.8 G2: 68.3 **RACE/ETHNICITY:** White, % G1: 81.1 G2: 79.5 Black, % G1: 16.8 G2: 17.3 **WEIGHT, KG (SD):** G1: 94.0 (14.3) G2: 93.6 (13.5) **BMI:** NR *(continued in next table)*	**Black Men** **SBP MEAN CHANGE, MMHG (SD):** G1: –4.3 (9.1) G2: 0.5 (7.8) **SBP DIFFERENCE, MMHG (95% CI):** –4.8 (–8.6, –1.0) **DBP MEAN CHANGE, MMHG (SD):** G1: –3.4 (7.0) G2: –1.3 (7.2) **DBP DIFFERENCE, MMHG (95% CI):** –2.1 (–5.3, 1.1) **White Men** **SBP MEAN CHANGE, MMHG (SD):** G1: –4.6 (8.5) G2: –2.4 (7.8) **SBP DIFFERENCE, MMHG (95% CI):** –2.2 (–3.5, –0.9) **DBP MEAN CHANGE, MMHG (SD):** G1: –4.0 (6.6) G2: –3.2 (6.0) **DBP DIFFERENCE, MMHG (95% CI):** –0.9 (–1.9, 0.1) *(continued in next table)*	**Black Men** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –82.8 (101.8) G2: –50.9 (198.2) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 31.9 (–117.4, 181.3) **White Men** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –82.0 (84.6) G2: –21.1 (96.9) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 60.9 (32.1, 89.7) **Black Women** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –29.4 (67.5) G2: –7.0 (82.5) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 22.4 (–43.4, 88.3) **White Women** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –71.9 (73.9) G2: –27.9 (60.1) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 44.0 (8.7, 79.3)	Proportion of participants with BP readings at all 3 scheduled visits at or after 36 months ranged from 88.9% to 91.6% Completion of sodium excretion data at 36 months ranged from 79.1% to 80.9% **ADHERENCE:** Adherence measures such as food diaries were not used as study outcome data. **NUTRIENT INTAKE:** The primary measure of sodium intake was sodium excretion in 24-hour urine samples.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
				(continued in next table)	

CQ2 Summary Table C–4b. Sodium and Subpopulation: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II Kumanyika et al. 2005(58) *(continued)*		*(continued from previous table)* **MEAN SBP, MMHG (SD):** G1: 127.7 (6.6) G2: 127.3 (6.4) **MEAN DBP, MMHG (SD):** G1: 86.1 (1.9) G2: 85.8 (1.9) **URINARY SODIUM:** G1: 186.1 (80.7) G2: 188.0 (80.9)	*(continued from previous table)* **Black Women** **SBP MEAN CHANGE, MMHG (SD):** G1: –5.9 (7.6) G2: –1.3 (9.5) **SBP DIFFERENCE, MMHG (95% CI):** –4.6 (–8.1, –1.1) **DBP MEAN CHANGE, MMHG (SD):** G1: –5.4 (6.5) G2: –2.8 (7.2) **DBP DIFFERENCE, MMHG (95% CI):** –2.5 (–5.3, 0.2) **White Women** **SBP MEAN CHANGE, MMHG (SD):** G1: –6.3 (9.2) G2: –3.3 (8.3) **SBP DIFFERENCE, MMHG (95% CI):**	*(continued from previous table)* **18 Months** **Black Men** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –58.1 (72.9) G2: –8.2 (145.5) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 49.9 (–11.4, 111.2) **White Men** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –71.1 (101.9) G2: –14.9 (97.1) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 56.1 (39.2, 73.0) **Black Women** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –35.9 (74.2)	

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			–3.0 (–5.2, –0.8) **DBP MEAN CHANGE, MMHG (SD):** G1: –5.1 (6.9) G2: –2.7 (5.6) **DBP DIFFERENCE, MMHG (95% CI):** –2.3 (–3.9, –0.7) *(continued in next table)*	G2: –20.9 (51.3) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 15.0 (–14.6, 44.6) **White Women** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –43.2 (69.5) G2: –22.8 (80.8) *(continued in next table)*	

CQ2 Summary Table C–4b. ***Sodium and Subpopulation: Race/Ethnicity (continued)***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II Kumanyika et al. 2005(58) *(continued)*			*(continued from previous table)* **18 Months** **Black Men** **SBP MEAN CHANGE, MMHG (SD):** G1: –2.7 (11.1) G2: –1.3 (7.5) **SBP DIFFERENCE, MMHG (95% CI):** –1.4 (–5.9, 3.1) **DBP MEAN CHANGE, MMHG (SD):** G1: –4.5 (8.3)	*(continued from previous table)* **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 20.4 (0.2, 40.7) **36 Months** **BLACK MEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –49.4 (92.1) G2: 25.2 (76.3) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 74.6 (–37.0, 69.0)	

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			G2: –3.4 (6.4) **DBP DIFFERENCE, MMHG (95% CI):** –1.1 (–4.5, 2.4) **White Men** **SBP MEAN CHANGE, MMHG (SD):** G1: –3.7 (7.9) G2: –2.2 (6.5) **SBP DIFFERENCE, MMHG (95% CI):** –1.5 (–2.7, –0.4) **DBP MEAN CHANGE, MMHG (SD):** G1: –4.0 (6.3) G2: –3.4 (5.8) **DBP DIFFERENCE, MMHG (95% CI):** –0.6 (–1.6, 0.4) *(continued in next table)*	**WHITE MEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –61.5 (91.8) G2: –13.4 (97.2) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 48.0 (32.4, 64.0) **BLACK WOMEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –26.7 (86.0) G2: –5.5 (73.9) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 21.3 (–14.0, 56.5) **WHITE WOMEN** **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –37.0 (69.0) G2: –18.6 (70.0) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D (95% CI):** G1 vs. G2: 18.4 (0.0, 36.8)	

CQ2 Summary Table C–4b. Sodium and Subpopulation: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II			*(continued from previous table)*		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
Kumanyika et al. 2005(58) *(continued)*			**Black Women** **SBP MEAN CHANGE, MMHG (SD):** G1: –5.0 (8.6) G2: 0.2 (8.4) **SBP DIFFERENCE, MMHG (95% CI):** –5.2 (–8.7, –1.7) **DBP MEAN CHANGE, MMHG (SD):** G1: –5.6 (6.7) G2: –1.3 (7.1) **DBP DIFFERENCE, MMHG (95% CI):** –4.2 (–7.0, –1.4) **White Women** **SBP MEAN CHANGE, MMHG (SD):** G1: –4.1 (8.1) G2: –2.4 (7.4) **SBP DIFFERENCE, MMHG (95% CI):** –1.8 (–3.8, 0.2) **DBP MEAN CHANGE, MMHG (SD):** G1: –4.9 (6.1) G2: –3.3 (5.3) **DBP DIFFERENCE, MMHG (95% CI):** –1.6 (–3.1, –0.1) *(continued in next table)*		

CQ2 Summary Table C–4b. Sodium and Subpopulation: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II Kumanyika et al. 2005(58) *(continued)*			*(continued from previous table)* **36 Months** **Black Men** **SBP MEAN CHANGE, MMHG (SD):** G1: 2.2 (10.3) G2: 1.7 (7.4) **SBP DIFFERENCE, MMHG (95% CI):** 0.5 (–3.8, 4.9) **DBP MEAN CHANGE, MMHG (SD):** G1: –0.6 (8.1) G2: –1.9 (7.0) **DBP DIFFERENCE, MMHG (95% CI):** 1.4 (–2.2, 4.9) **White Men** **SBP MEAN CHANGE, MMHG (SD):** G1: –1.3 (8.5) G2: –0.3 (7.8) **SBP DIFFERENCE, MMHG (95% CI):** –1.1 (–2.4, 0.2) **DBP MEAN CHANGE, MMHG (SD):** G1: –3.0 (6.2) G2: –2.7 (7.1) **DBP DIFFERENCE, MMHG**		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			(95% CI): –0.3 (–1.4, 0.8) *(continued in next table)*		

CQ2 Summary Table C–4b. Sodium and Subpopulation: Race/Ethnicity (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II Kumanyika et al. 2005(58) *(continued)*			*(continued from previous table)* **Black Women** **SBP MEAN CHANGE, MMHG (SD):** G1: –1.0 (11.1) G2: 2.0 (9.2) **SBP DIFFERENCE, MMHG (95% CI):** –3.0 (–7.2 (1.3) **DBP MEAN CHANGE, MMHG (SD):** G1: –4.0 (8.2) G2: –1.6 (7.5) **DBP DIFFERENCE, MMHG (95% CI):** –2.4 (–5.7, 0.8) **White Women** **SBP MEAN CHANGE, MMHG (SD):** G1: 0.5 (8.9)		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
			G2: 2.1 (10.4) **SBP DIFFERENCE, MMHG (95% CI):** –1.5 (–4.0, 0.9) **DBP MEAN CHANGE, MMHG (SD):** G1: –3.4 (5.8) G2: –1.9 (6.8) **DBP DIFFERENCE, MMHG (95% CI):** –1.4 (–3.1, 0.2)		

CQ2 Summary Table C–4b. ***Sodium and Subpopulation: Race/Ethnicity (continued)***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TONE Whelton et al. 1998(53); Appel et al. 2001(55) RCT USA, 4 clinical centers Fair	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual care **DURATION:** **Treatment:** Average of 27.6 months (range 15.6 to 35.9 months) after randomization **Followup:** NR **INTERVENTION DELIVERY:** In the reduced sodium group, each person had an introductory individual session. The TONE interventions consisted of a 4-month "intensive" phase with weekly meetings, a 3-month "extended" phase with biweekly meetings, and a maintenance phase. The interventionist typically was a registered dietitian. The	Adults 60 to 80 years; had baseline BP<145/85 mmHg while on a single antihypertensive medication ***N*:** G1: 340 G2: 341 **MEAN SBP, MMHG (SD):** African American G1: 125.6 (7.6) G2: 127.3 (8.4) Non-African American G1: 129.2 (9.5)	**Mean interval, 3.5 months** African American **SBP CHANGE, MEAN MMHG (SD):** G1: –3.8 (10.1) G2: 1.1 (10.7) **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –5.0 (–8.4, –1.6) *p*=0.005 **DBP CHANGE, MEAN MMHG (SD):**	Not reported by race/ethnicity grouping alone **30 months** **African American Men** **24-HOUR URINARY NA CHANGE, MEAN MMOL/L (SD):** G1: –55 (44) G2: –14 (48) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL/L (95% CI):** –41 (–69, –13) *p*=0.007 **Non-African American Men**	**WITHDRAWALS, %:** Not reported by subgroup Overall: Attended final study visit (15–37 months) G1: 91% G2: 92% **ADHERENCE:** Not reported by subgroup **DAILY NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
	meetings were conducted as group sessions (9–12 participants) with individual sessions at every fourth contact. **GOAL FOR SODIUM REDUCTION:** Achieving and maintaining a 24-hour dietary sodium intake of 80 mmol (1,800 mg) or less	G2: 127.2 (9.7) **MEAN DBP, MMHG (SD):** African American G1: 71.6 (6.7) G2: 70.2 (7.5) Non-African American G1: 71.3 (7.7) G2: 71.8 (7.0) **URINARY SODIUM, MEAN MMOL/DAY (SD):** Other baseline characteristics not reported by race/ethnicity grouping. **Overall sample characteristics:** **AGE, MEAN YEARS (SD):** 65.8 (4.6) **SEX, FEMALE %:** 47 *(continued in next table)*	G1: –2.7 (7.1) G2: 0.3 (7.4) **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –2.9 (–5.3, –0.5) *p*=0.02 **Non-African American** **SBP CHANGE, MEAN MMHG (SD):** G1: –4.9 (11.6) G2: –0.9 (10.4) **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –4.0 (–5.9, –2.0) *p*<0.001 **DBP CHANGE, MEAN MMHG (SD):** G1: –2.0 (8.2) G2: –0.4 (6.8) *(continued in next table)*	**24-HOUR URINARY NA CHANGE, MEAN MMOL/L (SD):** G1: –60 (54) G2: –6 (54) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL/L (95% CI):** –54 (–67, –42) *p*<0.001 **African American Women** **24-HOUR URINARY NA CHANGE, MEAN MMOL/L (SD):** G1: –26 (64) G2: –1 (48) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL/L (95% CI):** –25 (–47, –3) *p*=0.03 *(continued in next table)*	

CQ2 Summary Table C–4b. *Sodium and Subpopulation: Race/Ethnicity (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TONE Whelton et al. 1998(53); Appel et al.		*(continued from previous table)* **RACE/ETHNICITY, %:**	*(continued from previous table)* **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG**	*(continued from previous table)* **Non-African American Women** **24-HOUR URINARY NA CHANGE, MEAN**	

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
2001(55) *(continued)*		African American: 23 **OVERWEIGHT, %:** 43 **BMI:** NR **SBP ON MEDICATION, MEAN MMHG (SD):** 128.0 (9.4) **DBP ON MEDICATION, MEAN MMHG (SD):** 71.3 (7.3) **URINARY SODIUM, MEAN MMOL/DAY (SD):** G1: 144 (53) G2: 145 (55)	**(95% CI):** –1.7 (–3.0, –0.3) *p*=0.01	**MMOL/L (SD):** G1: –32 (51) G2: –4 (43) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL/L (95% CI):** –25 (–41, –15) *p*<0.001	

CQ2 Summary Table C–4c. Sodium and Subpopulation: Age

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
DASH-Sodium Subgroup analysis Bray et al. 2004(44); Vollmer et al. 2001(45) RCT, crossover USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Control G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol **DURATION:** **Run-in:** 2 weeks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were higher (H; 150 mmol/d), intermediate (I; 100 mmol/d), and lower (L; 50 mmol/d). All food was provided. Weight was kept stable.	Adults ≥22 years of age, SBP of 120–159 mmHg, DBP of 80–95 mmHg, target of 50% enrollment of Blacks and women ***N*:** ≤45 years G1: 97 G2: 75 >45 years G1: 111 G2: 129 **MEAN SBP, MMHG (SD):** Age ≤45 years G1 H: 125 (11) G1 I: 124 (11) G1 L: 124 (10) G2 H: 128 (10) G2 I: 126 (9) G2 L: 123 (7) Age >45 years G1 H: 129 (12) G1 I: 127 (12) G1 L: 124 (11) G2 H: 136 (12) G2 I: 133 (13) G2 L: 128 (11) **MEAN DBP, MMHG (SD):** Age ≤45 years G1 H: 81 (7) G1 I: 81 (7) G1 L: 81 (7) G2 H: 83 (7)	**Age ≤45 years** **MEAN CHANGE (95% CI)* IN SBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –1.4 (–2.9, 0.2) *p*<0.10 (NS) G1 L vs. G1 I: –0.1 *p*=NR (NS) G1 I vs. G1 H: –1.3 *p*=NR (NS) G2 L vs. G2 H: –5.3 (–7.0, –3.5) *p*<0.01 G2 L vs. G2 I: –3.9 *p*<0.01 G2 I vs. G2 H: –1.4 *p*=NR (NS) G1 H vs. G2 H: –4.3 (–6.9, –1.7) G1 L vs. G2 H: –5.6 (–8.2, –3.1) **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –1.1 (–2.1, 0.0) *p*<0.05 G1 L vs. G1 I: –0.6 *p*=NR (NS) G1 I vs. G1 H: –0.5 *p*=NR (NS) G2 L vs. G2 H: –2.8 (–4.0, –1.7) *p*<0.01 G2 L vs. G2 I: –2.6 *p*<0.01 G2 I vs. G2 H: –0.2 P=NR (NS) G1 H vs. G2 H: –2.2 (–3.9, –0.6) G1 L vs. G2 H: –3.3 (–5.0, –1.6)	Not reported by age subgroup **Overall:** **After 30 days of intervention** **URINARY NA, MMOL/DAY (SD):** G1 H: 144 (58) G1 I: 107 (52) G1 L: 67 (46) G2 H: 141 (55) G2 I: 106 (44) G2 L: 64 (37) **URINARY NA, G/DAY (SD):** G1 H: 303 (1.3) G1 I: 2.5 (1.2) G1 L 1.5 (1.0) G2 H: 3.3 (1.3) G2 I: 2.4 (1.0) G2 L: 1.5 (0.8)	**WITHDRAWALS, *N* (%):** Not reported by age subgroup **OVERALL:** G1: 10 (4.8) G2: 12 (5.9) **ADHERENCE:** Reported as 24-hour urinary excretion: The levels of urinary potassium, phosphorus, and urea nitrogen (reflective of the intake of fruit and vegetables, dairy products, and protein, respectively) were higher in the DASH-diet group than in the control-diet group, and were nearly identical for all three sodium levels. **NUTRIENT INTAKE:** Actual nutrient Intake for sodium is reflected as urinary sodium excretion, which was not reported by age subgroup

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
		G2 I: 83 (6) G2 L: 80 (6) *(continued in next table)*	*(continued in next table)*		

CQ2 Summary Table C–4c. Sodium and Subpopulation: Age (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
DASH-Sodium Subgroup analysis Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*		*(continued from previous table)* **MEAN DBP, MMHG (SD):** Age >45 years G1 H: 80 (7) G1 I: 80 (7) G1 L: 79 (6) G2 H: 84 (7) G2 I: 82 (7) G2 L: 80 (6) **Other baseline characteristics not reported by age grouping.** **Overall sample characteristics:** **AGE, MEAN YEARS (SD):** G1: 47 (10) G2: 49 (10) **SEX, *N* (%):** Female G1: 123 G2: 111 **RACE/ETHNICITY, *N* (%):** Black G1: 118 (57) G2: 114 (56) Non-Hispanic white G1: 83 (40) G2: 81 (40) Asian or other	*(continued from previous table)* **Age >45 years** **MEAN CHANGE (95% CI)* IN SBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –4.5 (–6.0, –3.0) *p*<0.01 G1 L vs. G1 I: –3.2 *p*<0.01 G1 I vs. G1 H: –1.3 *p*<0.10 (NS) G2 L vs. G2 H: –7.5 (–8.9, –6.1) *p*<0.01 G2 L vs. G2 I: –5.0 *p*<0.01 G2 I vs. G2 H: –1.3 *p*<0.10 (NS) G1 H vs. G2 H: –7.1 (–9.4, –4.9) G1 L vs. G2 H: –11.6 (–13.9, –9.4) *p*<0.01 **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –2.2 (–3.1, –1.2) *p*<0.01 G1 L vs. G1 I: –1.3 *p*<0.01 G1 I vs. G1 H: –0.8 *p*<0.10 (NS) G2 L vs. G2 H: –3.8 (–4.8, –2.9) *p*<0.01 G2 L vs. G2 I: –2.3 *p*<0.01		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
		G1: 6 (3) G2: 10 (5) *(continued in next table)*	*(continued in next table)*		

CQ2 Summary Table C–4c. Sodium and Subpopulation: Age (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
DASH-Sodium Subgroup analysis Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*		*(continued from previous table)* **MEAN BMI KG/M^2 (SD):** G1: 29 (5) G2: 30 (5) **URINARY SODIUM, MMOL/DAY (SD):** G1: 158 (79) G2: 152 (72)	*(continued from previous table)* **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G2 I vs. G2 H: –1.6 P<0.01 G1 H vs. G2 H: –3.4 (–4.8, –1.9) G1 L vs. G2 H: –5.5 (–7.0, –4.0) *p*<0.05 **95% CI not reported for all comparisons**		
TONE Whelton et al. 1998(53); Appel et al. 2001(55); Espeland et al. 2002(56) RCT USA, 4 academic health centers Good	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual care **DURATION:** **Treatment:** Average of 27.8 months (range 15.6 to 35.9 months) after randomization **INTERVENTION DELIVERY:** In the reduced sodium group, each person had an introductory individual session. The TONE interventions consisted of a 4-month "intensive" phase with weekly meetings, a 3-month "extended" phase with biweekly meetings, and a maintenance phase. The interventionist typically was a registered dietitian. The meetings were conducted as group sessions (9–12 participants) with individual sessions at every fourth contact. **GOAL FOR SODIUM REDUCTION:** Achieving and maintaining a 24-hour dietary sodium intake of 80 mmol (1,800 mg) or less G2 received no study-related counseling in lifestyle	Adults 60 to 80 years; had baseline BP <145/85 mmHg while on a single antihypertensive medication ***N*:** G1: 340 G2: 341 **MEAN SBP, MMHG (SD):** 60–69 year age group G1: 128.2 (9.2) G2: 126.8 (9.6) 70–80 year age group G1: 129.2 (9.4) G2: 128.7 (8.6) **MEAN DBP, MMHG (SD):** 60–69 year age group G1: 72.1 (7.4) G2: 72.3 (6.4) 70–80 year age group	**Mean interval, 3.5 months** **60–69 year age group** **SBP CHANGE, MEAN MMHG (SD):** G1: –5.2 (11.1) G2: –0.2 (10.3) **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –5.0 (–6.9, –3.1) *p*<0.001 **DBP CHANGE, MEAN MMHG (SD):** G1: –2.3 (8.1) G2: –0.2 (7.0) **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –2.1 (–3.5, –0.8)	**60–69 year age group** **24-HOUR URINARY NA CHANGE, MEAN MMOL/L (SD):** G1: –46 (57) G2: –8 (52) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL/L (95% CI):** –38 (–48, –29) *p*<0.001 **70–80 year age group** **24-HOUR URINARY NA CHANGE, MEAN MMOL/L (SD):** G1: –41 (52) G2: 5 (42) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL/L (95% CI):** –46 (–62, –30) *p*<0.001	**WITHDRAWALS, %:** Not reported by age group **OVERALL:** Attended final study visit (15–37 months) G1: 91% G2: 92% **ADHERENCE:** Not reported by age group **DAILY NUTRIENT INTAKE** Actual nutrient intake for sodium is reflected as urinary sodium excretion.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
	change; were invited to meetings on topics unrelated to trial goals	G1: 68.8 (7.2) G2: 68.2 (8.8) *(continued in next table)*	*p*=0.002 *(continued in next table)*		

CQ2 Summary Table C–4c. Sodium and Subpopulation: Age (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Nutrient Intake
TONE Whelton et al. 1998(53); Appel et al. 2001(55); Espeland et al. 2002(56) *(continued)*		*(continued from previous table)* **URINARY SODIUM, MEAN MMOL/DAY (SD):** 60–69 year age group G1: 144 (54) G2: 151 (66) 70–80 year age group G1: 142 (48) G2: 124 (39) **Other baseline characteristics not reported by age grouping.** **Overall sample characteristics:** **AGE, MEAN YEARS (SD):** 65.8 (4.6) **SEX, FEMALE %:** 47 **RACE/ETHNICITY, %:** African American: 23 **OVERWEIGHT, %:** 43 **BMI:** NR	*(continued from previous table)* **70–80 year age group** **SBP CHANGE, MEAN MMHG (SD):** G1: –2.6 (11.8) G2: –1.1 (11.2) **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –1.5 (–5.4, 2.4) *p*=0.46 **DBP CHANGE, MEAN MMHG (SD):** G1: –1.6 (7.5) G2: –0.2 (6.8) **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –1.4 (–3.9, 1.0) *p*=0.25		

CQ2 Summary Table C–4d. Sodium and Subpopulation: Hypertension Status

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Svetkey et al. 2004(57); Bray et al. 2004(44); Vollmer et al. 2001(45) RCT, crossover USA, outpatient medical settings Fair	**TREATMENT GROUPS:** G1: DASH diet G2: Typical American diet Run-in: Control diet + high sodium level, 50 mmol/d G1: 27% of calories from total fat; 6% from SF, 13% MUFA, and 8% PUFA and 151 mg/d of cholesterol. Emphasis on fruits, vegetables, and low-fat dairy foods, includes whole grains, poultry, fish, and nuts, and is reduced in fats, red meat, sweets, and sugar-sweetened beverages. G2: Control diet: 37% fat, 16% SF, 13% MUFA, 8% PUFA, 300 mg/d cholesterol. **DURATION:** **Run-in:** 2 wks **Treatment:** 90 days, 30 days per sodium condition **INTERVENTION DELIVERY:** There were three 30-day feeding periods, 1 at each of the 3 sodium levels (randomly assigned). Levels were higher (H; 150 mmol/d), intermediate (I; 100 mmol/d), and lower (L; 50 mmol/d). All food was provided. Weight was kept stable.	Adults ≥22 years of age, SBP of 120–159 mmHg, DBP of 80–95 mmHg, target of 50% enrollment of Blacks and women **HYPERTENSIVE, *N* (%):** G1: 85 (40.9) G2: 83 (40.7) **NONHYPERTENSIVE, *N* (%):** G1: 123 (59.1) G2: 121 (59.3) **HYPERTENSIVE** **MEAN SBP, MMHG (SD):** G1 H: 134 (11) G1 I: 133 (12) G1 L: 129 (11) G2 H: 141 (11) G2 I: 139 (12) G2 L: 133 (11) **MEAN DBP, MMHG (SD):** G1 H: 84 (7) G1 I: 84 (7) G1 L: 82 (6) G2 H: 86 (7) G2 I: 85 (6) G2 L: 82 (6) **NONHYPERTENSIVE** **MEAN SBP, MMHG (SD):** G1 H: 122 (9) G1 I: 121 (9) G1 L: 120 (9) G2 H: 122 (9)	**Hypertensive** **MEAN CHANGE (95% CI)* IN SBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: 4.9 (–6.6, –3.3) *p*<0.01 G1 L vs. G1 I: –3.3 *p*<0.01 G1 I vs. G1 H: –1.6 *p*<0.10 G2 L vs. G2 H: –-8.3 (–10.0, –6.6) *p*<0.01 G2 L vs. G2 I: –6.2 *p*<0.01 G2 I vs. G2 H: –2.1 *p*<.0.5 G1 H vs. G2 H: –6.6 (–9.1, –4.0) G1 L vs. G2 H: –11.5 (–14.1, –8.9) *p*<0.01 **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H:–2.5 (–3.6, –1.4) *p*<0.05 G1 L vs. G1 I: –2.0 *p*<0.01 G1 I vs. G1 H: –0.5 *p*=NR (NS) G1 H vs. G2 H: –3.2 (–4.8, –1.5) G1 L vs. G2 H: –5.7 (–7.4, –4.0) *(continued in next table)*	Not reported by hypertensive & nonhypertensive subgroups **Overall:** **After 30 days of intervention** **URINARY NA, G/DAY (SD):** G1 H: 303 (1.3) G1 I: 2.5 (1.2) G1 L: 1.5 (1.0) G2 H: 3.3 (1.3) G2 I: 2.4 (1.0) G2 L: 1.5 (0.8)	**WITHDRAWALS, N (%):** Not reported by subgroup **OVERALL:** G1: 10 (4.8) G2: 12 (5.9) **ADHERENCE:** Reported as 24-hour urinary excretion: The levels of urinary potassium, phosphorus, and urea nitrogen (reflective of the intake of fruit and vegetables, dairy products, and protein, respectively) were higher in the DASH-diet group than in the control-diet group, and were nearly identical for all three sodium levels. **NUTRIENT INTAKE:** Nutrient intake for sodium is reflected as urinary sodium excretion.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		G2 I: 125 (7) G2 L: 122 (6) *(continued in next table)*			

CQ2 Summary Table C–4d. *Sodium and Subpopulation: Hypertension Status (continued)*

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Svetkey et al. 2004(57); Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*		*(continued from previous table)* **MEAN DBP, MMHG (SD):** G1 H: 79 (6) G1 I: 78 (7) G1 L: 78 (6) G2 H: 81 (6) G2 I: 81 (6) G2 L: 79 (6) Subgroup analyses from Svetkey et al. 2004(57) **Stage I Hypertensives** ***N*:** G1: 79 G2: 76 **AGE, YEARS (SD):** G1: 49.4 (10.8) G2: 52.0 (10.3) **SEX, WOMEN:** G1: 63.3%	*(continued from previous table)* **Nonhypertensive** **Mean change (95% CI)* in SBP by diet group + sodium reduction level:** G1 L vs. G H: –1.7 (–3.1, –0.3) *p*<0.05 G1 L vs. G1 I: –0.6 *p*=NR (NS) G1 I vs. G1 H: –1.1 *p*=NR (NS) G2 L vs. G2 H: –5.6 (–7.0, –4.1) *p*<0.01 G2 L vs. G2 I: –3.4 *p*<0.01 G2 I vs. G2 H: –2.2 *p*<0.01 G1 H vs. G2 H: –5.4 (–7.7, –3.2) G1 L vs. G2 H: –7.1 (–9.4, –4.9) **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** G1 L vs. G1 H: –1.1 (–2.0, –0.1) *p*<0.05		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		G2: 60.5% **RACE/ETHNICITY, %** Non-Hispanic white G1: 38.0 G2: 35.5 African American G1: 60.8 G2: 59.2 Other G1: 1.3 G2: 5.3 **SBP, MMHG:** G1: 142.0 (8.0) G2: 144.1 (7.2) *(continued in next table)*	G1 L vs. G1 I: –0.3 *p*=NR (NS) G1 I vs. G1 H: –0.8 *p*=NR (NS) G2 L vs. G2 H: –2.8 (–3.8, –1.9) *p*<0.01 G2 L vs. G2 I: –2.0 *p*<0.01 G2 I vs. G2 H: –0.8 *p*<0.10 G1 H vs. G2 H: –2.7 (–4.1, –1.2) G1 L vs. G2 H: –3.7 (–5.2, –2.3) *(continued in next table)*		

CQ2 Summary Table C–4d. ***Sodium and Subpopulation: Hypertension Status (continued)***

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Svetkey et al. 2004(57); Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*		*(continued from previous table)* **DBP, MMHG:** G1: 88.6 (4.9) G2: 88.1 (4.1) **BMI:** G1: 28.3 (5.0) G2: 29.5 (5.0) **URINARY SODIUM,**	*(continued from previous table)* **MEAN CHANGE (95% CI)* IN DBP BY DIET GROUP + SODIUM REDUCTION LEVEL:** *CI not reported for all comparisons Subgroup analyses from Svetkey et al. 2004(57) **Hypertensive** **END-OF-FEEDING BP**		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		MMOL/24-H: G1: 157.5 (79.7) G2: 153.4 (73.1) **Isolated Systolic Hypertension (ISH):** ***N*:** G1: 37 G2: 40 **AGE, YEARS (SD):** G1: 54.8 (10.9) G2: 53.7 (11.1) **SEX, WOMEN:** G1: 73.0% G2: 60.0% **RACE/ETHNICITY, %:** Non-Hispanic White G1: 37.8 G2: 40.0 African American G1: 59.5 G2: 57.5 Other G1: 2.7 G2: 2.5 *(continued in next table)*	**CONTROL RATES, %:** G1 H: 63 G2 H: 32 G1 I: 65 G2 I: 51 G1 L: 84 G2 L: 74 G1 H vs. G2 H: *p*<0.01 G2 I vs. G2 H: *p*<0.01 G1 I vs. G2 H: *p*<0.01 G2 L vs. G2 H: *p*<0.01 G1 L vs. G2 H: *p*<0.01 G1 L vs. G1 H: *p*<0.05 **ISH** **END-OF-FEEDING BP CONTROL RATES, %:** G1 H: 57 G2 H: 43 G1 I: 62 G2 I: 53 G1 L: 78 G2 L: 75 G1 H vs. G2 H: *p*=NS G2 I vs. G2 H: *p*=NS G1 I vs. G2 H: *p*=NS G2 L vs. G2 H: *p*<0.01 G1 L vs. G2 H: *p*<0.01 G1 L vs. G1 H: *p*<0.05		

CQ2 Summary Table C–4d. Sodium and Subpopulation: Hypertension Status (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Svetkey et al. 2004(57); Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*		*(continued from previous table)* **SBP, MMHG:** G1: 146.6 (5.0) G2: 145.7 (4.7) **DBP, MMHG:** G1: 84.2 (3.4) G2: 84.9 (2.9) **BMI:** G1: 28.6 (5.5) G2: 30.0 (4.6) **URINARY SODIUM, MMOL/24-H:** G1: 150.1 (72.5) G2: 154.3 (68.5) **High-normal BP:** ***N*:** G1: 63 G2: 68 **AGE, YEARS (SD):** G1: 48.1 (8.6) G2: 48.1 (10.3) **SEX, WOMEN:** G1: 57.1% G2: 55.8% **RACE/ETHNICITY, %:** Non-Hispanic White G1: 38.1 G2: 35.3 African American G1: 58.7			

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
		G2: 60.3 *(continued in next table)*			

CQ2 Summary Table C–4d. Sodium and Subpopulation: Hypertension Status (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
DASH-Sodium Svetkey et al. 2004(57); Bray et al. 2004(44); Vollmer et al. 2001(45) *(continued)*		*(continued from previous table)* **RACE/ETHNICITY, %:** Other G1: 3.2 G2: 4.4 **SBP, MMHG:** G1: 132.0 (4.2) G2: 132.4 (4.5) **DBP, MMHG:** G1: 84.9 (3.2) G2: 85.3 (2.9) **BMI:** G1: 29.9 (4.8) G2: 29.6 (5.3) **URINARY SODIUM, MMOL/24-H:** G1: 155.3 (78.5) G2: 149.6 (75.6)			
TOHP II The Trials of Hypertension	**TREATMENT GROUPS:** G1: Sodium reduction	Adults 30–54 years, not taking antihypertensive drugs, SBP<140 mmHg,	**6 months** **SBP MEAN CHANGE, MMHG**	**6 months** ***N*:**	**WITHDRAWALS:** Proportion of participants with BP readings at all 3 scheduled

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58); Cook et al. 2005(59) RCT, 2 X 2 factorial USA, 9 academic medical centers Good	G2: Usual care **DURATION:** **Treatment:** 36–48 months **Additional followup after treatment:** none **INTERVENTION DELIVERY:** Individual and group counseling through in-person, telephone, and mail contact. **INTENSIVE PHASE:** Groups of 11 to 34, counseled weekly for 10 weeks; primary goal was to provide core knowledge and behavioral skills to make and maintain reductions in Na intake. *(continued in next table)*	DBP 83 to 89 mmHg, BMI representing 110% to 165% of desirable body weight ***N*:** G1: 594 G2: 596 **AGE:** G1: 44.2 (6.1) G2: 43.2 (6.1) *(continued in next table)*	**(SD):** G1: –5.1 (8.6) G2: –2.2 (8.1) **SBP NET CHANGE, MMHG (SE):** G1 vs. G2: –2.9 (0.5) *p*<0.001 **DBP MEAN CHANGE, MMHG (SD):** G1: –4.4 (6.7) G2: –2.8 (6.1) **DBP NET CHANGE, MMHG (SDE):** G1 vs. G2: –1.6 (0.4) *p*<0.001 *(continued in next table)*	G1: 147 G2: 126 **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –75.5 (81.5) G2: –24.5 (10.38) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D 95% CI):** G1 vs. G2: –51.0 (28.9, 73.0) **18 months** ***N*:** G1: 450 G2: 467 *(continued in next table)*	visits at or after 36 months ranged from 88.9% to 91.6% Completion of sodium excretion data at 36 months ranged from 79.1% to 80.9% **ADHERENCE:** Adherence measures such as food diaries and overnight urine samples were not used as study outcome data. *(continued in next table)*

CQ2 Summary Table C–4d. Sodium and Subpopulation: Hypertension Status (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP II The Trials of Hypertension Prevention Collaborative Research Group, 1997(54); Kumanyika et al. 2005(58); Cook et al. 2005(59) *(continued)*	*(continued from previous table)* **TRANSITIONAL PHASE:** 4 monthly sessions; designed to prevent relapse and ease transition to less frequent contact **FINAL EXTENDED PHASE:** 1 or 2 monthly contacts; 3 to 6 refresher sessions were offered; goal: maintain participants' behavior changes Goal for G1: reduction in sodium intake of 80 mmol per	*(continued from previous table)* **SEX, % MALE:** G1: 64.8 G2: 68.3 **RACE/ETHNICITY:** White, % G1: 81.1	*(continued from previous table)* **18 months** **SBP MEAN CHANGE, MMHG (SD):** G1: –3.8 (8.2) G2: –1.8 (7.0) **SBP NET CHANGE, MMHG (SE):**	*(continued from previous table)* **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –59.5 (91.7) G2: –16.8 (94.8) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D 95% CI):** G1 vs. G2: –42.7 (30.6, 54.8)	*(continued from previous table)* **NUTRIENT INTAKE:** 24-hour dietary recall and 3-day food record information was obtained at 18- and 36-months for randomly selected samples.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
	day or less.	G2: 79.5 Black, % G1: 16.8 G2: 17.3 **WEIGHT, KG (SD):** G1: 94.0 (14.3) G2: 93.6 (13.5) **BMI:** NR **MEAN SBP, MMHG (SD):** G1: 127.7 (6.6) G2: 127.3 (6.4) **MEAN DBP, MMHG (SD):** G1: 86.1 (1.9) G2: 85.8 (1.9) **URINARY SODIUM, MMOL/D (SD):** G1: 186.1 (80.7) G2: 188.0 (80.9)	G1 vs. G2: –2.0 (0.5) *p*<0.001 **DBP MEAN CHANGE, MMHG (SD):** G1: –4.4 (6.5) G2: –3.2 (5.8) **DBP NET CHANGE, MMHG (SE):** G1 vs. G2: –1.2 (0.4) *p*=0.002 **36 months** **SBP MEAN CHANGE, MMHG (SD):** G1: –0.7 (9.0) G2: +0.6 (8.5) **SBP NET CHANGE, MMHG (SE):** G1 vs. G2: –1.2 (0.5) *p*=0.02 **DBP MEAN CHANGE, MMHG (SD):** G1: –3.0 (6.5) G2: –2.4 (7.0) **DBP NET CHANGE, MMHG (SDE):** G1 vs. G2: –0.7 (0.4) *p*=0.10	**36 months** ***N*:** G1: 470 G2: 482 **24-HOUR URINARY NA MEAN CHANGE, MMOL/D (SD):** G1: –50.9 (86.3) G2: –10.5 (88.5) **24-HOUR URINARY NA NET DIFFERENCE, MMOL/D 95% CI):** G1 vs. G2: –40.4 (29.3, 51.5)	

CQ2 Summary Table C–4d. Sodium and Subpopulation: Hypertension Status (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Na	Attrition Adherence/Compliance Actual Nutrient Intake
TONE Whelton et al. 1998(53); Appel et al. 2001(55) RCT USA, 4 academic health centers Good	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual care **DURATION** Mean of 27.8 months (range 15.6 to 35.9 months) after randomization **INTERVENTION DELIVERY:** In the reduced sodium group, each person had an introductory individual session. The TONE interventions consisted of a 4-month "intensive" phase with weekly meetings, a 4-month "extended" phase with biweekly meetings, and a maintenance phase. The interventionist typically was a registered dietitian. The meetings were conducted as group sessions (9–12 participants) with individual sessions at every fourth contact. **GOAL FOR SODIUM REDUCTION:** Achieving and maintaining a 24-hour dietary sodium intake of 80 mmol (1,800 mg) or less G2 received no study-related counseling in lifestyle change; were invited to meetings on topics unrelated to trial goals	Adults 60 to 80 years; had baseline BP <145/85 mmHg while on a single antihypertensive medication. ***N*:** G1: 340 G2: 341 **AGE, MEAN YEARS (SD):** 65.8 (4.6) **SEX, FEMALE %:** 47 **RACE/ETHNICITY, %:** African American: 23 **OVERWEIGHT, %:** 43 **BMI:** NR **SBP ON MEDICATION, MEAN MMHG (SD):** 128.0 (9.4) **DBP ON MEDICATION, MEAN MMHG (SD):** 71.3 (7.3) **URINARY SODIUM, MEAN MMOL/DAY (SD):** G1: 144 (53) G2: 145 (55)	**Mean interval, 3.5 months (baseline to visit prior to medication withdrawal)** **SBP CHANGE, MEAN MMHG (SD):** G1: –4.6 (11.3) G2: –0.4 (10.5) **SBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –4.3 (–6.0, –2.5) *p*<0.001 **DBP CHANGE, MEAN MMHG (SD):** G1: –2.2 (8.0) G2: –0.2 (7.0) **DBP BETWEEN-GROUP DIFFERENCE, MEAN MMHG (95% CI):** –2.0 (–3.2, –0.8) *p*=0.001 **30 months** **PROPORTION WITHOUT AN ENDPOINT, %:** G1: 36 G2: 21 **RELATIVE HR (95% CI) FOR ENDPOINTS ASSOCIATED WITH ASSIGNMENT G1 VS. G2:** 0.68 (0.56, 0.82) *p*<0.001	**30 months** **24-HOUR URINARY NA CHANGE, MEAN MMOL (SD):** G1: –45 (55.8) G2: –5 (50.0) **24-HOUR URINARY NA CHANGE BETWEEN-GROUP DIFFERENCE, MEAN MMOL (95% CI):** –40 (–48, –32) *p*<0.001	**WITHDRAWALS:** Attended final study visit (15–37 months) G1: 91% G2: 92% **DAILY NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion.

CQ2 Summary Table C–5. Sodium and CVD Outcomes: Trials or Observational Followup of Trials

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP I and II long-term followup for CVD Cook 2007(66), 2009(68) Observational followup study Fair	**TREATMENT GROUPS:** G1: Sodium reduction intervention G2: Control **DURATION OF TREATMENT IN THE TRIALS:** TOHP I 18 months TOHP II 36 months **FOLLOWUP STUDY FOR CVD*** TOHP I Began ≈ 10 years after end of trial TOHP II Began ≈ 5 years after end of trial *In this analysis, the weight loss arms of TOHP II were included. Followup began 5 years after the end of the randomized trial.	Adults 30–54 years, DBP 80 to 89 mmHg without antihypertensive drugs **Baseline characteristics, at the start of the randomized trials:** ***N*:** TOHP I G1: 327 G2: 417 TOHP II G1: 1191 G2: 1191 **AGE:** TOHP I G1: 43.4 (6.6) G2: 42.6 (6.5) TOHP II G1: 43.9 (6.2) G2: 43.3 (6.1) **SEX, % MALE:** TOHP I G1: 232 (71.0) G2: 299 (71.7) TOHP II G1: 784 (65.8) G2: 782 (65.7) **RACE/ETHNICITY, N (%):** White TOHP I G1: 255 (78.0) G2: 319 (76.5) TOHP II G1: 950 (79.8) G2: 938 (78.8) *(continued in next table)*	**Cardiovascular disease,* Hazard ratio (95% CI)** **OVERALL:** 0.75 (0.57, 0.99) *p*=0.044 **CARDIOVASCULAR DISEASE,* HAZARD RATIO† (95% CI)** **OVERALL:** 0.70 (0.53, 0.94) *p*–0.018 TOHP I: 0.48 (0.25, 0.92) *p*=0.027 TOHP II: 0.79 (0.57, 1.09) *p*=0.16 **CARDIOVASCULAR DISEASE,* CRUDE RATE, %** **OVERALL:** G1: 7.5 G2: 9.0 *p*=0.19 *p* stratified by trial=0.21 TOHP I G1: 7.4 G2: 10.3 *p*=0.24 TOHP II G1: 7.6 G2:8.6 P=0.43 *MI, stroke, revascularization, or death due to cardiovascular cause † HR additionally adjusted for baseline weight and sodium excretion	**Followup response:** **OVERALL** G1: 77% G2: 77.5% **OR‡ (95% CI):** 0.93 (0.78, 1.11) *p*=0.42 ‡ Adjusted for trial, clinic, age, race, sex, and weight loss intervention **ADHERENCE:** Not applicable for CVD followup study

CQ2 Summary Table C–5. Sodium and CVD Outcomes: Trials or Observational Followup of Trials (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP I and II long-term followup for CVD Cook 2007(66), 2009(68) *(continued)*		*(continued from previous table)* Black TOHP I G1: 64 (19.6) G2: 87 (20.9) TOHP II G1: 212 (17.8) G2: 209 (17.6) Other TOHP I G1: 8 (2.4) G2: 11 (2.6) TOHP II G1: 29 (2.4) G2: 44 (3.7) **WEIGHT, KG (SD):** TOHP I G1: 82.7 (14.3) G2: 82.8 (13.9) TOHP II G1: 93.8 (14.3) G2:93.5 (13.8) **BMI, KG/M^2 (SD):** TOHP I G1: 27.1 (3.8) G2: 27.1 (3.6) TOHP II G1: 30.9 (3.1) G2: 30.9 (3.1) **MEAN SBP, MMHG (SD):** TOHP I G1: 124.8 (8.5) G2: 125.1 (8.1) TOHP II G1: 127.5 (6.6)		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
		G2: 127.4 (6.2) *(continued in next table)*		

CQ2 Summary Table C–5. Sodium and CVD Outcomes: Trials or Observational Followup of Trials (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
TOHP I and II long-term followup for CVD Cook 2007(66), 2009(68) *(continued)*		*(continued from previous table)* **MEAN DBP, MMHG (SD):** TOHP I G1: 83.7 (2.7) G2: 83.9 (2.8) TOHP II G1: 86.0 (1.9) G2:85.9 (1.9) **SODIUM EXCRETION, MMOL/24 H (SD):** TOHP I G1: 154.6 (59.9) G2: 156.4 (60.5) TOHP II G1: 182.9 (78.4) G2: 184.5 (76.8) **Change to end of randomized trials:** **WEIGHT CHANGE, KG (SD):** TOHP I G1: –0.2 (3.8) G2: 0.2 (3.9) TOHP II G1: 0.7 (5.5) G2: 0.8 (5.7) **SODIUM EXCRETION CHANGE, MMOL/24 H (SD):**		

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
		TOHP I G1: –55.2 (76.9) G2: –11.3 (77.7) TOHP II G1: –42.5 (89.0) G2: –9.8 (87.7)		

CQ2 Summary Table C–5. Sodium and CVD Outcomes: Trials or Observational Followup of Trials (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
Chang et al. 2006(67) RCT (randomized 5 kitchens) Taiwan, Veteran's retirement home Fair	**TREATMENT GROUPS:** G1: Potassium-enriched salt G2: Regular salt G1: Composition of potassium-enriched salt: 49% sodium chloride, 49% potassium chloride, 2% other additives G2: Composition of regular salt: 99.6% sodium chloride, 0.4% other additives. **DURATION:** **Average followup period:** ≈31 months **INTERVENTION DELIVERY:** G1: Potassium-enriched salt gradually replaced regular salt in the kitchens in a gradual manner; it was mixed with regular salt in a 1 to 3 ratio for 1st week, ratio increased to 1:1 in 2nd week, 3:1 in 3rd week; at 4th week the cooks used only potassium-enriched salt. G2: The kitchens used regular salt at all times.	Male veterans ***N*:** G1: 768 (Kitchens 2 & 3) G2: 1213 (Kitchens 1, 4 & 5) **AGE, MEAN YEARS (SD):** G1 Kitchen 2: 75.6 (7.7) Kitchen 3: 74.8 (7.0) G2 Kitchen 1: 74.8 (7.3) Kitchen 4: 74.6 (6.7) Kitchen 5: 74.6 (6.1) **SEX, MALE %:** 100 **RACE/ETHNICITY, %:** All Taiwanese **WEIGHT, KG (SD):** G1: 60.7 (10.8) 60.3 (9.8)	**Cause-specific incidence of death per 100,000 person years in G1 and G2** **Absolute risk reduction (95% CI)** CVD: –828.7 (–1424, –232.9) G1 vs. G2: $p<0.05$ **ISCHEMIC HEART DISEASE:** –256.3 (–600.3, 87.7) G1 vs. G2: p=NR (NS) **HYPERTENSIVE DISEASE:** 64.8 (164.5, 294.1) G1 vs. G2: p=NR (NS) **HEART FAILURE:** –227.3 (–389.5, –65.1) G1 vs. G2: $p<0.05$ **CEREBROVASCULAR DISEASE:** –389.8 (–741.1, –65.5) G1 vs. G2: $p<0.05$ **Relative risk reduction***	**WITHDRAWALS:** All were included in survival analysis **NUTRIENT INTAKE:** G1: Avg. amount of potassium-enriched salt used per day per kitchen: ≈1–2 kg: 1.41 (0.22) Each kitchen served ≈400 persons per meal. Salt was the major source of sodium added in the cooking process, whereas other sauces accounted for ≈30% of total sodium.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
		BMI, KG/M^2 (SD): G1: 23.3 (3.5) G2: 23.0 (3.3) **SBP, MEAN MMHG (SD):** G1: 131.3 (19.7) G2: 130.7 (20.4) **DBP ON MEDICATION, MEAN MMHG (SD):** G1: 71.2 (10.8) G2: 71.4 (10.8) **URINARY SODIUM, MEAN MMOL/DAY (SD):** NR	CVD: –38.8% **ISCHEMIC HEART DISEASE:** –32.5% **HYPERTENSIVE DISEASE:** 49.9% **HEART FAILURE:** –70.0% **CEREBROVASCULAR DISEASE:** –50.0% *Calculated as (rate of experimental – rate of control)/ (rate of control) X 100	

CQ2 Summary Table C–5. Sodium and CVD Outcomes: Trials or Observational Followup of Trials (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
TONE Appel et al. 2001(55) RCT USA, 4 academic health centers Good	**TREATMENT GROUPS:** G1: Sodium reduction G2: Usual :care **DURATION:** **Treatment:** Average of 27.6 months (range 15.6 to 35.9 months) after randomization Intervention delivery: In the reduced sodium group, each person had an introductory individual session. The TONE interventions consisted of a 4-month "intensive" phase with weekly meetings, a 3-month "extended" phase with biweekly meetings, and a maintenance phase. The interventionist typically was a	Adults 60 to 80 years; had baseline BP <145/85 mmHg while on a single antihypertensive medication. ***N*:** G1: 340 G2: 341 **AGE, MEAN YEARS (SD):** 65.8 (4.6) **SEX, FEMALE %:** 47 **RACE/ETHNICITY, %:**	**Reported Cardiovascular events, *n* of individuals (n of events)** **ANY CARDIOVASCULAR EVENT:** G1: 36 (44) G2: 46 (57) *p*=0.24 **STROKE:** G1: 1 (1) G2: 2 (2) *p*>0.99 **TRANSIENT ISCHEMIC ATTACK:**	**WITHDRAWALS:** Attended final study visit (15–37 months) G1: 91% G2: 92% **DAILY NUTRIENT INTAKE:** Actual nutrient intake for sodium is reflected as urinary sodium excretion.

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	CVD Events	Attrition Adherence/Compliance Actual Nutrient Intake
	registered dietitian. The meetings were conducted as group sessions (9–12 participants) with individual sessions at every fourth contact. **GOAL FOR SODIUM REDUCTION:** Achieving and maintaining a 24-hour dietary sodium intake of 80 mmol (1,800 mg) or less G2 received no study-related counseling in lifestyle change; were invited to meetings on topics unrelated to trial goals	African American: 23 **OVERWEIGHT, %:** 43 **BMI:** NR **SBP ON MEDICATION, MEAN MMHG (SD):** 128.0 (9.4) **DBP ON MEDICATION, MEAN MMHG (SD):** 71.3 (7.3) **URINARY SODIUM, MEAN MMOL/DAY (SD):** G1: 144 (53) G2: 145 (55)	G1: 7 (8) G2: 7 (8) *p*>0.99 **MI:** G1: 2 (2) G2: 4 (4) *p*=0.69 **ARRHYTHMIA:** G1: 6 (6) G2: 3 (4) *p*=0.34 **CONGESTIVE HEART FAILURE:** G1: 2 (4) G2: 1 (1) *p*>0.99 **ANGINA:** G1: 9 (10) G2: 17 (19) *p*=0.16 **OTHER:** G1: 12 (13) G2: 19 (19) *p*=0.27	

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
Ekinci et al. 2011(83) Prospective cohort	**STUDY GROUPS** Determined by level of 24-hour urinary sodium	Type 2 diabetics, in long-term followup	**Cardiovascular mortality by baseline parameter, sub-HR (95% CI)**	**LOSS TO FOLLOWUP:**

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
study Melbourne, Australia; University diabetes clinic Good	excretion G1: <150 mmol G2: 150–208 mmol G3: >208 mmol **DURATION:** Followup time: 9.9 years (median) **Other study characteristics:** Patients were given general dietary advice as part of their routine care at an initial assessment by a dietitian. However, detailed assessment of dietary salt intake was not performed. During followup, all patients continued to have standard medical care including antihypertensive, lipid-lowering, and anti-diabetic medications according to recommended guidelines.	***N*:** NR by group Total *N*=638 *N*=638 **AGE, MEAN YEARS (SD):** G1: 67 (12) G2: 64 (11) G3: 61 (12) **SEX, MALE %:** G1: 42 G2: 56 G3: 70 **RACE/ETHNICITY, %:** NR **OVERWEIGHT, %:** NR **OBESE (BMI >30KG/M^2), %:** G1: 41 G2: 45 G3: 55 **SBP, MEAN MMHG (SD):** G1: 141 (17) G2: 140 (17) G3: 140 (16) **DBP, MEAN MMHG (SD):** G1: 77 (10) G2: 80 (9) G3: 78 (10)	**24-H URINARY SODIUM EXCRETION:** 0.65 (0.44, 0.95) *p*=0.017 **SBP:** 0.97 (0.96–0.99) *p*<0.001 **PREEXISTING CVD:** 1.88 (1.14, 3.11) *p*=0.014	Overall *N* (%): 18 (2.8) **OTHER METHODOLOGICAL DETAILS:** High participation rate (96% of eligible sample) Long-term followup Small % LTF Multiple 24-h urine collections to estimate Na intake

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
Gardener et al. 2012(82) Population-based cohort study (using the Northern Manhattan Study cohort) USA, Manhattan Fair	**STUDY GROUPS** Determined by sodium intake (based on self-reported food consumption) G1: ≤1,500 mg/d G2+G3: 1,501–3,999 mg/d G4: ≥4,000 mg/d **DURATION:** Mean followup: 10 years **Other study characteristics:** Participants completed modified Block National Cancer Institute food frequency questionnaire at baseline. Questionnaire was modified to include items commonly eaten among Hispanics. Sodium intake calculated based on self-reported food consumption using DIETSYS software.	Adults >40 years of age, stroke free, residing in northern Manhattan for ≥3 months ***N*:** G1: 320 G2: 1,779 G3: 558 **AGE, MEAN (SD):** G1: 70 (10) G2: 69 (10) G3: 68 (9) **SEX, MALE *N* (%):** G1: 68 (21) G2: 622 (35) G3: 275 (49) **RACE/ETHNICITY, *N*:** Black or African American G1: 104 G2: 418 G3: 115 White G1: 49 G2: 397 G3: 106 Hispanic or Latino G1: 160 G2: 952 G3: 322 **BMI MEAN KG/M^2 (SD):** G1: 28 (5) G2: 28 (5) G3: 29 (6) **WEIGHT, MEAN KG (SD):**	**STROKE RISK PER DAILY DIETARY SODIUM AT 10 YR FOLLOWUP, HR* (95% CI)** Per 500 mg/d sodium increase 1.17 (1.07, 1.27) 1,501–2,300 mg/d dietary sodium 1.38 (0.84–2.27) 2,301–3,999 mg/d dietary sodium 1.32 (0.78, 2.23) 4,000–10,000 mg/d dietary sodium 2.59 (1.27, 5.28) *Adjusted for demographics + behavioral risk factors + vascular risk factors **STROKE, MI OR VASCULAR DEATH PER DAILY DIETARY SODIUM AT 10 YEAR FOLLOWUP, HR† (95% CI)** Per 500 mg/d sodium increase 1.05 (0.99, 1.11) 1,501–2,300 mg/d dietary sodium 1.35 (1.00, 1.82) 2,301–3,999 mg/d dietary sodium 1.21 (0.87, 1.67) 4,000–10,000 mg/d dietary sodium (1.06, 2.67) *Adjusted for demographics + behavioral risk factors + vascular risk factors	**LOSS TO FOLLOW-UP:** NR Person-time of followup accrued from baseline to end of followup (March 2011), the time of outcome event, time of death, or loss to followup. **OTHER METHODOLOGICAL DETAILS:** Sodium intake (exposure) assessed by self-report of food consumption Significant baseline differences *N*s included in models not clearly reported

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
		NR *(continued in next table)*		

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
Gardener et al. 2012(82) (continued)		*(continued from previous table)* **SBP, MEAN MMHG (SD):** G1: 144 (20) G2: 143 (21) G3: 144 (21) **DBP, MEAN MMHG (SD):** G1: 83 (11) G2: 83 (11) G3: 84 (11)		
Liang et al. 2011(81) Retrospective case-control study Guangdong Province, China Fair	**STUDY GROUPS** G1: Hospital inpatients w/ ischemic stroke (cases) G2: Hospital-based control patients **DURATION** N/A (45 minute interview) **Other study characteristics:** Information on typical food consumption collected using structured questionnaire developed for southern Chinese population.	Inpatients from Chinese hospitals with first ever ischemic stroke and outpatient controls with no history of stroke ***N*:** G1: 374 G2: 464 G1 Men: 226 G1 Women: 148 G2 Men: 248 G2 Women: 216 **AGE, MEAN YEARS (SD):** G1 Men: 69.6 (8.0) G1 Women: 69.1 (9.2) G2 Men: 68.7 (7.0)	**ISCHEMIC STROKE RISK BY WEEKLY DIETARY SODIUM INTAKE, ADJUSTED* OR (95% CI)** ≤3,726 mg/wk: 1.0 [Reference] 3,727, 5,565 mg/wk: 1.34 (0.83, 2.18) 5,566, 8,073 mg/wk: 1.82 (1.09, 3.06) ≥8,074mg/wk: 1.30 (0.73, 2.32) *Adjusted for weekly intake of iron, sodium, potassium, calcium, and magnesium; weekly energy intake; sex, age, BMI, education level, lifelong physical activity involvement, smoking status, cumulative smoking, alcohol drinking status, and presence of hypertension, hyperlipidemia, or diabetes **RISK OF ISCHEMIC STROKE RISK BY SODIUM INTAKE, ADJUSTED* OR (95% CI)**	**LOSS TO FOLLOWUP:** 6 (0.01%) **OTHER METHODOLOGICAL DETAILS:** Sodium intake based on questionnaire; reference recall period set at 1 yr before interview Sodium consumption from salt and soy sauce added to foods was difficult to quantify so excluded in calculation of Na intake

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
		G2 Women: 69.0 (9.0) **SEX, FEMALE %:** G1: 39.6 G2: 46.6 **RACE/ETHNICITY, %:** NR **OVERWEIGHT, %:** NR *(continued in next table)*	Low: 1 [Reference] Normal: 2.47 (1.47, 4.19) High: 2.33 (1.34, 4.09) *Adjusted for weekly energy intake, sex, age, BMI, education level, lifelong physical activity involvement, smoking status, cumulative smoking, alcohol drinking status, and presence of hypertension, hyperlipidemia, or diabetes	

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
Liang et al. 2011(81) *(continued)*		*(continued from previous table)* **BMI MEAN KG/M^2 (SD):** G1 Men: 22.9 (2.7) G1 Women: 21.5 (3.6) G2 Men: 23.1 (3.0) G2 Women: 22.8 (3.6) **SBP, MEAN MMHG (SD):** NR **DBP, MEAN MMHG (SD):** NR **HYPERTENSION, *N* (%):** G1 Men: 119 (52.7) G1 Women: 76 (51.4) G2 Men: 71 (28.6)		

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
		G2 Women: 60 (27.8) **URINARY SODIUM, MEAN MMOL/DAY (SD):** NR **MEAN SODIUM INTAKE, MG/WK (SD):** G1 Men: 7319 (5540) G1 Women: 5973 (5303) G2 Men: 7270 (5271) G2 Women: 6055 (3910)		

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
Marniemi et al. 2005(79) Case-control study Finland, population-based health survey Fair	**STUDY GROUPS** G1: AMI cases G2: AMI controls G3: Stroke cases G4: Stroke controls **DURATION:** Followup for up to 10 years **Other study characteristics:** Food consumption information obtained from dietary history interview	Elderly men and women, 65 to 99 years of age ***N*:** G1: 130 G2: 559 G3: 70 G4: 590 **AGE, MEAN YEARS (SD):** NR **SEX, FEMALE %:** NR **RACE/ETHNICITY, %:** NR **OVERWEIGHT, %:** NR **BMI:** NR **SBP, MEAN MMHG (SD):** NR **DBP, MEAN MMHG (SD):** NR **URINARY SODIUM, MEAN MMOL/DAY (SD):** NR	**DAILY SODIUM, MEAN MG (SD):** G1: 2,190 (953) G2: 2,280 (1210) G3: 2,350 (1250) G4: 2,330 (1770) **SERUM CONCENTRATION OF SODIUM, MEAN MMOL/L (SD):** G1: 142 (3) G2: 142 (3) G3: 141 (3) G4: 142 (3) **ADJUSTED* RR (95% CI) OF AMI AND STROKE BETWEEN TERTILES OF SODIUM INTAKE:** Middle tertile vs. lowest tertile AMI: 0.862 (0.55, 1.36) Stroke: 0.617 (0.33, 1.15) Highest tertile vs. lowest tertile AMI: 1.42 (0.81, 2.47) Stroke: 0.617 (0.33, 1.15) *Adjusted in Cox proportional hazards model for age, gender, smoking, functional capacity and weight adjusted energy intake **ADJUSTED* RR (95% CI) OF AMI AND STROKE BETWEEN TERTILES OF SERUM CONCENTRATION OF SODIUM:** Middle tertile vs. lowest tertile AMI: 1.02 (0.38, 1.55) Stroke: 1.01 (0.54, 1.88) Highest tertile vs. lowest tertile AMI: 0.866 (0.52, 1.44) Stroke: 0.968 (0.54, 1.72) *Adjusted for age, gender, smoking, and functional capacity	**LOSS TO FOLLOWUP:** 484 subjects died during 10-yr followup **OTHER METHODOLOGICAL DETAILS:** Sodium intake based on questionnaire LTF unclearly reported

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
NHANES I Alderman et al. 1998(72) Prospective cohort study Fair	**STUDY GROUPS** Full model involved three dietary measures of sodium intake, total calorie intake, and sodium/calorie ratio. S1–S8 represent sodium intake quartiles for men and women SC1–SC8 represent sodium/calorie ratio quartiles for men and women S1: First (lowest) quartile of sodium intake for men S2: Second quartile of sodium intake for men S3: Third quartile of sodium intake for men S4: Fourth (highest) quartile of sodium intake for men S5: First (lowest) quartile of sodium intake for women S6: Second quartile of sodium intake for women S7: Third quartile of sodium intake for women S8: Fourth (highest) quartile of sodium intake for women SC1: First (lowest) quartile of sodium/calorie ratio for men SC2: Second quartile of sodium/calorie ratio for men SC3: Third quartile of sodium/calorie ratio for men SC4: Fourth (highest) quartile of sodium/calorie ratio for men SC5: First (lowest) quartile of sodium/calorie ratio for women SC6: Second quartile of sodium/calorie ratio for women SC7: Third quartile of sodium/calorie ratio for women SC8: Fourth (highest) quartile of sodium/calorie ratio for women	Individuals 25–75 years of age at time of NHANES I survey **AGE, MEAN YEARS, (SD):** S1: 56.9 (14.3) S2: 54.4 (15.5) S3: 51.7 (15.5) S4: 48.6 (15.1) S5: 49.8 (16.0) S6: 49.2 (16.0) S7: 47.8 (15.9) S8: 43.9 (14.9) SC1: 50.3 (15.9) SC2: 52.9 (15.3) SC3: 54.0 (15.2) SC4: 54.5 (15.0) SC5: 46.1 (15.5) SC6: 48.1 (16.0) SC7: 48.7 (16.0) SC8: 47.9 (15.9) **SEX, %:** S1, SC1: Male: 100 S2, SC2: Male: 100 S3, SC3: Male: 100 S4, SC4: Male: 100 S5, SC5: Female: 100 S6, SC6: Female: 100 S7, SC7: Female: 100 S8, SC8: Female: 100 *(continued in next table)*	**Risk of CVD mortality: Associated variables based on full model, HR (95% CI)** **SODIUM (PER 1313 MG):** 0.89 (0.77, 1.02) *p*=0.0864 **CALORIES (PER 849 KCAL):** 0.98 (0.87, 1.11) *p*=0.7394 **SODIUM/CALORIES (PER 0.5787 MG/KCAL):** 1.13 (1.04, 1.24) *p*=0.0056 **MALE:** 1.89 (1.71, 2.09) *p*<0.0001 **BLACK RACE:** 1.05 (0.93, 1.18) *p*=0.4347 **HISTORY OF CVD:** 1.63 (1.46, 1.80) *p*<0.0001 **HISTORY OF HYPERTENSION:** 1.09 (0.97, 1.22) *p*=0.1668 **AGE (PER 15.9 YEARS)** 4.33 (3.98, 4.71) p<0.0001 **BMI (PER 5.15 KG/M2)** 1.04 (0.99, 1.10) *p*=0.1000 *(continued in next table)*	**LOSS TO FOLLOWUP:** Data on sodium intake missing for 2 participants who were therefore excluded **OTHER METHODOLOGICAL DETAILS:** This study was not included in Strazzullo et al.(85) SR/MA because authors determined that it focuses on the same cohort as He et al. 1999(75) which used more stringent criteria Included participants with existing CVD Sodium intake based on 24-hour dietary recall

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
NHANES I Alderman et al. 1998(72) *(continued)*		*(continued from previous table)* **RACE/ETHNICITY, BLACK, %:** S1: 24.4 S2: 17.0 S3: 13.3 S4: 8.8 S5: 26.0 S6: 18.3 S7: 15.4 S8: 11.5 SC1: 20.1 SC2: 14.8 SC3: 17.0 SC4: 11.6 SC5: 23.2 SC6: 17.4 SC7: 16.8 SC8: 13.8 **WEIGHT, MEAN KG, (SD):** S1: 76.0 (14.5) S2: 76.4 (13.4) S3: 76.4 (14.2) S4: 77.7 (13.7) S5: 68.4 (16.3) S6: 66.3 (15.2) S7: 65.6 (14.3) S8: 64.3 (14.9) SC1: 77.7 (14.3) SC2: 76.4 (13.7) SC3: 76.0 (14.1) SC4: 76.2 (13.7) SC5: 66.4 (15.9) SC6: 66.2 (14.9) SC7: 65.7 (15.5) SC8: 66.1 (14.7) *(continued in next table)*	*(continued from previous table)* **SBP (PER 24.98 MMHG)** 1.29 (1.23, 1.36) *p*<0.0001 **TABLE SALT USE (ALWAYS)** 0.99 (0.86, 1.13) *p*=0.8510 **TABLE SALT USE (NEVER)** 1.00 (0.89, 1.12) *p*=0.9825	

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
NHANES I Alderman et al. 1998(72) *(continued)*		*(continued from previous table)* **BMI, MEAN KG/M² (SD):** S1: 25.7 (4.3) S2: 25.4 (4.0) S3: 25.2 (4.2) S4: 25.5 (4.1) S5: 26.6 (6.0) S6: 25.6 (5.7) S7: 25.3 (5.5) S8: 24.6 (5.5) SC1: 25.7 (4.2) SC2: 25.4 (4.1) SC3: 25.2 (4.2) SC4: 25.4 (4.1) SC5: 25.6 (5.9) SC6: 25.5 (5.5) SC7: 25.4 (5.9) SC8: 25.6 (5.6) **SBP MEAN MMHG (SD):** S1: 142.4 (24.9) S2: 138.8 (33.2) S3: 136.0 (22.3) S4: 134.4 (20.6) S5: 136.7 (26.8) S6: 134.9 (26.1) S7: 133.7 (26.2) S8: 129.5 (24.5) SC1: 137.0 (22.8) SC2: 137.0 (22.9) SC3: 138.8 (22.6) SC4: 138.8 (23.7) SC5: 131.6 (25.5) SC6: 133.7 (25.8) SC7: 134.9 (26.4) SC8: 134.5 (26.4) *(continued in next table)*		

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
NHANES I Alderman et al. 1998(72) *(continued)*		*(continued from previous table)* **DBP, MEAN MMHG (SD):** S1: 87.3 (14.0) S2: 85.8 (13.0) S3: 84.5 (12.1) S4: 84.6 (11.8) S5: 83.5 (13.7) S6: 82.6 (13.8) S7: 81.8 (13.1) S8: 80.2 (12.8) SC1: 85.7 (12.8) SC2: 85.1 (12.8) SC3: 85.9 (12.8) SC4: 85.6 (12.9) SC1: 81.7 (13.7) SC2: 82.1 (13.3) SC3: 82.3 (13.1) SC4: 82.0 (13.4)		

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
NHANES Epidemiologic followup study He et al. 2002(76) Prospective cohort study Fair	**STUDY GROUPS** G1: Overweight participants G2: Nonoverweight participants Dietary sodium and other nutrient intake estimates obtained by 24-hour dietary recall baseline exam conducted from 1971 to 1975; incidence of CHF assessed using medical records and death certificates obtained in 1982 to 1984, 1986, 1987, and 1992 **DURATION:** **Average followup:** 19 years **Other study characteristics:** Dietary sodium and other nutrient intake estimates obtained by 24-hour dietary recall; incidence of CHF assessed using medical records and death certificates	Men and women, 25 to 74 years of age, without a history of CHF ***N*:** G1: 5,129 G2: 5,233 **AGE, MEAN YEARS (SD):** G1: 52.2 (15.2) G2: 48.2 (16.1) **SEX, MALE %:** G1: 44 G2: 36 **RACE/ETHNICITY, %:** African American G1: 19 G2: 13 **HYPERTENSION, %:** G1: 38 G2: 20 **SBP ON MEDICATION, MEAN MMHG (SD):** G1: 141.0 (24.7) G2: 129.2 (23.4) **DBP ON MEDICATION, MEAN MMHG (SD):** NR **SODIUM INTAKE, MEAN MMOL/DAY (SD):** G1: 86.8 (58.2) G2: 91.1 (56.2)	**NUMBER OF CASES OF CHF BY QUARTILE OF DIETARY SODIUM INTAKE (MMOL/D)** Quartile 0–50.2 G1: 208 G2: 110 Quartile >50.2–76.2 G1: 177 G2: 125 Quartile >76.2–113.6 G1: 146 G2: 91 Quartile >113.6 G1: 148 G2: 87 **RR* (95% CI) OF CHF BY QUARTILE OF DIETARY SODIUM INTAKE (MMOL/D):** Quartile 0–50.2 G1: 1.00 G2: 1.00 Quartile >50.2–76.2 G1: 1.04 (0.87, 1.24) G2: 0.88 (0.71, 1.09) Quartile >76.2–113.6 G1: 1.00 (0.79, 1.26) G2: 0.79 (0.63, 1.01) Quartile >113.6 G1: 1.40 (1.08, 1.81) G2: 0.84 (0.59, 1.20) **MULTIVARIATE RELATIVE RISK* (95% CI) OF CHF ASSOCIATED WITH A 100-MMOL INCREASE IN DIETARY SODIUM INTAKE:** G1: 1.25 (1.02, –1.54) G2: 0.97 (0.73, 1.30) *p*=0.15	**LOSS TO FOLLOWUP:** 4% of eligible participants were lost to followup **OTHER METHODOLOGICAL DETAILS:** Sodium intake based on 24-h dietary recall Low % LTF This study was not included in Strazzullo et al.(85), meta-analysis because CHF was not an outcome of interest

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
			*adjusted for baseline age, sex, race, and total calorie (energy intake)	

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
NHANES III Yang et al. 2011(77) Prospective cohort study Fair	**Study groups** **MEAN USUAL SODIUM INTAKE MG/D (SE):** Men: 4,323 (21) Women: 2,918 (17) **DURATION:** **Mean followup:** 14.8 years **Other study characteristics:** Dietary information obtained from in person 24-hour dietary recall; method developed at NCI to estimate usual intakes of sodium, potassium and total energy (since only 7% of participants provided a reliable second sample)	Nationally representative sample of U.S. adults ≥20 years of age **AGE YEARS, *N* (%):** <60 Men: 4,444 (85.2) Women: 4,904 (85.1) ≥60 Men: 1,455 (14.8) Women: 1,464 (18.5) **SEX, FEMALE *N* (%):** 6368 (52) **RACE/ETHNICITY, %:** Non-Hispanic White Men: 76.1 Women: 76.6 Non-Hispanic Black Men: 9.8 Women: 10.6 Mexican American Men: 6.1 Women: 4.7 **WEIGHT:** NR **BMI, %:** <25 Men: 43.3 Women:54.4 25–30 Men: 40.2 Women: 24.7 >30 Men: 16.6	**CVD MORTALITY BY ESTIMATED USUAL SODIUM INTAKE, MG (RANGE 839–8555), HR* (95% CI):** Q1: 1.00 [reference] Q2: 0.95 (0.71, 1.27) Q3: 0.90 (0.51, 1.60) Q4: 0.83 (0.31, 2.28) Total: 0.94 (0.67, 1.32) **IHD MORTALITY BY ESTIMATED USUAL SODIUM INTAKE, MG (RANGE 839–8555), HR* (95% CI):** Q1: 1.0 Q2: 1.17 (0.84, 1.62) Q3: 1.36 (0.71, 2.58) Q4: 1.70 (0.55, 5.27) Total: 1.20 (0.81, 1.77) **CVD MORTALITY BY SODIUM-POTASSIUM RATIO, (RANGE 0.46–2.98), HR* (95% CI):** Q1: 1.0 Q2: 1.13 (1.03, 1.23) Q3: 1.25 (1.07, 1.47) Q4: 1.46 (1.11, 1.92) Total: 1.90 (1.20, 3.03) * Adjusted for sex, race/ethnicity, educational attainment, BMI, smoking status, alcohol intake, total cholesterol, high-density lipoprotein cholesterol, physical activity, family history of CVD, and total calorie intake	**LOSS TO FOLLOWUP:** All MEC participants provided 24-hour dietary recall; among 12,267 NHANES III participants who were eligible for this analysis, 912 (7.4%) provided reliable second 24-hour dietary recalls. **Other methodological details:** Sodium intake based on a single 24-hour dietary recall Repeated exposure measurement only performed on 7% of participants

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
		Women: 20.9 *(continued in next table)*		

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
NHANES III Yang et al. 2011(77) *(continued)*		*(continued from previous table)* **HYPERTENSION, %:** Men: 20.6 Women: 18.6 **G2:** **SBP, %:** <125 mmHg Men: 62.6 Women: 74.6 ≥125 mmHg Men: 37.4 Women:25.4 **DBP, %:** <85 mmHg Men: 83.1 Women:93.1 ≥85 Men: 16.9 Women: 6.9		
O'Donnell et al. 2011(78) Retrospective cohort study [retrospective observational analysis combining populations of 2 RCTs] Fair	**STUDY GROUPS** Defined by sodium excretion, g/d G1: <2 G2: 2–2.99 G3: 3–3.99 G4: 4–5.99 G5: 6–6.99 G6: 7–8 G7: >8 **DURATION** Median followup: 58 months *(continued in next table)*	High-risk patients with coronary, peripheral, or cerebrovascular disease or diabetes with end-organ damage ***N*:** G1: 818 G2 + G3: 8,353 G4: 14,156 G5 + G6: 4,706 G7: 847 **AGE, MEAN YEARS (SD):** G1: 67.61 (7.62) G2 + G3: 67.04 (7.42)	**Association between estimated 24-hour urinary Na excretion and CV events and mortality multivariate analysis, HR (95% CI):** Composite Outcome: CV mortality, MI, Stroke, and Hospitalization for CHF: G1: 1.21 (1.03, 1.43) G2: 1.16 (1.04, 1.28) G3: 1.06 (0.98, 1.14) G4: 1 [reference] G5: 1.09 (0.99, 1.20) G6: 1.15 (1.00, 1.32) G7: 1.49 (1.28, 1.75) *(continued in next table)*	**LOSS TO FOLLOWUP:** 0.2% **OTHER METHODOLOGICAL DETAILS:** Used 1st morning void rather than 24-hour Equation used to estimate total sodium excretion was developed for an Asian population Key potential confounders not addressed adequately

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
		G4: 66.46 (7.15) G5 + G6: 65.79 (6.95) G7: 65.37 (6.75) *(continued in next table)*		Numerous significant differences between groups at baseline High participation rate (91.6% of those enrolled in the RCTs) Low % LTF

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
O'Donnell et al. 2011(78) *(continued)*	*(continued from previous table)* **Other study characteristics:** Populations from two RCTs: ONTARGET and TRANSCEND ONTARGET: rampiril 10 mg/d vs. telmisartan 80 mg/d vs. their combination in 25,620 patients. TRANSCEND: telmisartan 80 mg/d vs. placebo in 5,926 ACE-inhibitor intolerant participants This analysis combined the 2 cohorts to assess the association between urinary sodium and potassium and CV events. Morning fasting urine sample obtained prior to run-in period of the RCTs	*(continued from previous table)* **SEX, FEMALE *N* (%):** G1: 438 (53.5) G2 + G3: 3172 (38.0) G4: 3764 (26.6) G5 + G6: 952 (20.2) G7: 178 (21.0) **RACE/ETHNICITY, *N* (%):** White/European G1: 521 (63.7) G2 + G3: 5851 (70.0) G4: 10249 (72.4) G5 + G6: 3387 (72.0) G7: 620 (73.2) **BMI, MEAN KG/M² (SD):** G1: 27.32 (4.63) G2 + G3: 27.48 (4.51) G4: 28.05 (4.38) G5 + G6: 29.13 (4.70) G7: 30.17 (4.70) **WEIGHT, MEAN KG (SD):** NR **HYPERTENSION, *N* (%):** G1: 640 (78.2) G2 + G3: 5761 (69.0) G4: 9616 (67.9) G5 + G6: 3488 (74.1) G7: 695 (82.1) **SBP, MEAN MMHG (SD):** G1: 138.61 (17.63) G2 + G3: 140.81 (17.32)	*(continued from previous table)* **Association between estimated 24-hour urinary Na excretion and CV events and mortality multivariate analysis, HR (95% CI):** CV death: G1: 1.37 (1.09, 1.73) G2: 1.19 (1.02, 1.39) G3: 1.09 (0.96, 1.23) G4: 1 [reference] G5: 1.11 (0.96, 1.29) G6: 1.53 (1.26, 1.86) G7: 1.66 (1.31, 2.10) MI: G1: 1.10 (0.80, 1.53) G2: 1.04 (0.85, 1.27) G3: 1.11 (0.96, 1.28) G4: 1 [reference] G5: 1.21 (1.03, 1.43) G6: 1.11 (0.85, 1.44) G7: 1.48 (1.11, 1.98) Stroke G1: 1.06 (0.76, 1.46) G2: 1.05 (0.89, 1.28) G3: 0.97 (0.83, 1.13) G4: 1 [reference] G5: 0.95 (0.79, 1.15) G6: 1.06 (0.81, 1.40) G7: 1.48 (1.09, 2.01)	

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
		G4: 141.96 (17.39) G5 + G6: 142.95 (16.80) G7: 142.93 (17.01) *(continued in next table)*		

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
O'Donnell et al. 2011(78) *(continued)*		*(continued from previous table)* **DBP, MEAN MMHG (SD):** NR **URINARY SODIUM, MEAN G/DAY (SD):** G1: 1.55 (0.35) G2 + G3: 3.24 (0.53) G4: 4.93 (0.56) G5 + G6: 6.71 (0.53) G7: 9.40 (1.81)		
Stolarz-Skrzpek et al. 2011(84) Prospective cohort study following participants from 2 population-based cohorts FLEMENGHO set in Northern Belgium, EPOGH set in Europe Fair	**STUDY GROUPS** G1: Outcome cohort G2: Hypertension cohort G3: Blood pressure cohort **DURATION:** **Median followup:** G1: 7.93 years G2: 6.48 years G3: 6.14 years **Other study characteristics:** EXPERIENCED OBSERVERS MEASURED BLOOD PRESSURE AT BASELINE AND FOLLOW-UP; SODIUM AND POTASSIUM EXCRETION MEASURED; OUTCOMES ADJUDICATED AGAINST SOURCE DOCUMENTS IN EACH COUNTRY.	Adults without CVD ***N*:** G1: 3681 G2: 2096 G3: 1499 **AGE, MEAN YEARS (SD):** G1: 40.9 (16.3) G2: 38.6 (14.6) G3: 38.3 (14.2) **SEX, FEMALE %:** G1: 52.7 G2: 54.1 G3: 52.4 **RACE/ETHNICITY, %:** NR **OVERWEIGHT, %:** NR **BMI:** G1: 25.2 (4.6) G2: 24.5 (4.0)	**OUTCOMES BY TERTILE OF 24-HOUR URINARY SODIUM EXCRETION (TERTILES: LOW, MEDIUM, HIGH) ADJUSTED HR (95% CI):** Cardiovascular mortality: Low: 1.56 (1.02–2.36) Medium: 1.05 (0.72–1.53) High: 0.95 (0.66–1.38) All CV events (fatal and nonfatal) Low: 1.13 (0.90–1.42) Medium: 1.11 (0.90–1.36) High: 0.90 (0.73–1.11) Coronary events (fatal and nonfatal) Low: 1.42 (0.99–2.04) Medium: 1.17 (0.89–1.54) High: 0.86 (0.55–1.13) Stroke (fatal and nonfatal) Low: 1.07 (0.57–2.00) Medium: 1.29 (0.75–2.20) High: 0.78 (0.45–1.33)	**LOSS TO FOLLOWUP:** During followup, 219 participants died, 16 became seriously ill, and 259 moved out of the study areas, potentially leaving 3,187 participants, 2,856 (89.6%) of whom agreed to take part in examinations. **OTHER METHODOLOGICAL DETAILS:** Used 24-hour urine excretion. Reference group is entire study population rather than group with highest or lowest sodium excretion. Considerable amount of missing data but no sensitivity analyses

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
		G3: 24.6 (4.0) *(continued in next table)*		

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
Stolarz-Skrzpek et al. 2011(84) *(continued)*		*(continued from previous table)* **HYPERTENSION, %:** G1: 25.8 G2: 0 G3: 9.9 **SBP, MEAN MMHG (SD):** G1: 124.7 (17.1) G2: 118.7 (10.4) G3: 120.9 (12.8) **DBP, MEAN MMHG (SD):** G1: 76.3 (10.6) G2: 73.3 (8.0) G3: 74.6 (8.9) **URINARY SODIUM, MEAN MMOL/DAY (SD):** G1: 178.0 (74.8) G2: 174.2 (74.1) G3:172.7 (62.5)		
Takachi et al. 2010(80) Prospective cohort study Japan, 11 public health centers Fair	**STUDY GROUPS** G1: Lowest Quintile of Sodium intake G2: Second Quintile of Sodium intake G3: Third Quintile of Sodium intake G4: Fourth Quintile of Sodium intake G5: Highest Quintile of Sodium intake **DURATION:** Followup: 7 to 9 years **Other study characteristics:** EXAMINATION OF ASSOCIATIONS BETWEEN SODIUM AND SALTED FOOD CONSUMPTION AND CVD RISK USING VALIDATED FOOD FREQUENCY QUESTIONNAIRES.	Japanese adults, age 40 to 59 years (cohort I), age 40 to 69 years (cohort II) **AGE, MEAN YEARS (SD):** G1: 56.1 (8.0) G2: 56.4 (7.8) G3: 56.7 (7.7) G4: 57.1 (7.6) G5: 57.9 (7.6) **SEX, FEMALE *N*:** G1: 5930 G2: 7450 G3: 8371 G4: 9468	**CVD BY SODIUM CONSUMPTION, HR (95% CI):** G1: 1.00 (reference) G2: 1.11 (0.96, 1.29) G3: 1.02 (0.87, 1.19) G4: 1.10 (0.94, 1.29) G5: 1.19 (1.01, 1.40) *p*=0.06 for trend **STROKE BY SODIUM CONSUMPTION, HR (95% CI):** G1: 1.00 (reference) G2: 1.05 (0.90, 1.24) G3: 0.97 (0.82, 1.14) G4: 1.08 (0.92, 1.28) G5: 1.21 (1.01, 1.43)	**Loss to followup:** **OTHER METHODOLOGICAL DETAILS:** Questionnaire not sensitive for sodium intake

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
		G5: 10551 **RACE/ETHNICITY, %:** NR *(continued in next table)*	*p*=0.03 for trend	

CQ2 Summary Table C–6. Sodium and CVD Outcomes: Observational Data (continued)

Study Cited Design Setting Quality Rating	Study Groups and Details Duration	Sample Characteristics	Results	Loss to followup Methodological details
Takachi et al. 2010(80) *(continued)*		*(continued from previous table)* **OVERWEIGHT, %:** NR **BMI, MEAN KG/M^2:** G1: 28.2 G2: 28.0 G3: 28.7 G4: 29.8 G5: 31.1 **SBP, MEAN MMHG (SD):** NR **DBP, MEAN MMHG (SD):** NR **URINARY SODIUM, MEAN MMOL/DAY (SD):** NR **MEAN SODIUM CONSUMPTION, MG:** G1: 3084 G2: 4005 G3: 4709 G4: 5503 G5: 6844		

CQ2 Summary Table C–7. Potassium and Blood Pressure and CVD Outcomes

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Nutrient Intake
Charlton et al. 2008(62) RCT South Africa, Cape Town township Good	**TREATMENT GROUPS:** G1: Food-based intervention G2: Control G1: Intervention comprised 5 commonly consumed food items (brown bread, margarine, stock cubes, soup mixes, and Aromat) modified in Na, K, Mg and Ca content plus a salt replacement and 500 ml of maas (fermented milk). G2: Control diet provided the same foods but of standard commercial composition, as well as artificially sweetened cold drink instead of maas. Based on laboratory-determined chemical food analyses, compared to control foods, the intervention foods were planned to provide 41% less Na (100.3 vs. 170.3 mmol/d), 826% more K (70.9 vs. 8.6 mmol/d), 388% more Ca (857 vs. 221 mg/d) and 368% more Mg (13.8 v. 3.7 mmol/d.) **DURATION:** **Run-in:** 3 weeks Treatment: 8 weeks **INTERVENTION DELIVERY:** Subjects were instructed to consume their usual amounts of food and sufficient food was provided for the whole family. A single dietitian was responsible for food-packing and all food was locked and sealed in large shopping bags, labeled only with participants' names and contact details. A driver delivered the food three times a week.	Black residents of a Cape Town township, 50 to 75 years of age, with drug-treated mild-to-moderate hypertension (SBP≤160 mmHg, DBP≤95 mmHg) ***N*:** G1: 47 G2: 45 **AGE, MEAN YEARS (SD):** G1: 61.8 (6.6) G2: 60.4 (7.4) **SEX, MALE, *N*:** G1: 7 G2: 6 **SEX, FEMALE, *N*:** G1: 33 G2: 34 **RACE, % BLACK:** G1: 100 G2: 100 **WEIGHT, MEAN KG (SD):** G1: 83.3 (13.7) G2: 88.8 (15.5) **BMI, KG/M² (SD):** G1: 32.9 (5.8) G2: 35.3 (6.0) **MEAN SBP, MMHG (SD):** G1: 133.9 (14.6) G2: 135.4 (16.7)	**Mean net difference (G1–G2), mmHg (95% CI)** **SBP, OFFICE:** –6.194 (–11.442, –0.945) *p*=0.021 **DBP, OFFICE:** –0.595 (–3.019, 1.829) **24-HOUR ABPM, AVG SBP:** –4.527 (–9.047, –0.006) *p*=0.050 **24-HOUR ABPM, AVG DBP:** –2.494 (–5.160, 0.173) *p*=0.066	**Mean within group change from baseline** **URINARY NA, MMOL/24H (SD):** G1: –14.6 (54.4) G2: –5.9 (54.3) **URINARY K, MMOL/24H (SD):** G1: 20.0 (22.7) G2: –4.6 (14.8) **URINARY MG, MMOL/24H (SD):** G1: +0.88 (1.20) G2: +0.19 (0.81) **URINARY CA, MMOL/24H (SD):** G1: +0.27 (1.00) G2: +0.32 (1.11) **Mean between group difference (G1–G2)** **URINARY NA, MMOL/24H (SD):** –8.7 (46.9) **URINARY K, MMOL/24H (SD):** +24.6 (16.5) *p*<0.001 **URINARY MG, MMOL/24H (SD):** +0.68 (0.88) *p*<0.05 **URINARY CA, MMOL/24H (SD):** –0.05 (0.91)	**WITHDRAWALS, *N* (%):** G1: 7 (14.9) G2: 5 (11.1) **ADHERENCE:** Dietary compliance was monitored using data from 24-hour recalls and 24-hour urinary electrolyte concentrations; returned salt and Aromat shakers were weighed weekly. **REPORTED DAILY DIETARY INTAKE: MEAN DIFFERENCE (G1–G2)** Na, mg (SD) –1,167 (1532) *p*<0.01 K, mg (SD) 867 (890) *p*<0.0001 Mg, (SD) 71 (89) *p*<0.001 Ca, mg (SD) 310 (392) *p*<0.001

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Nutrient Intake
		MEAN DBP, MMHG (SD): G1: 79.8 (8.6) G2: 82.3 (7.5)			

CQ2 Summary Table C–7. Potassium and Blood Pressure and CVD Outcomes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Nutrient Intake
China Salt Substitute Study China Salt Study Collaborative Group, 2007(61); Hu et al. 2009(60) RCT China, 39 sites distributed between 6 regional coordinating centers Good	**TREATMENT GROUPS:** G1: Salt substitute G2: Normal salt G1: Salt substitute was 65% Na Cl, 25% K Cl, and 10% Mg sulphate G2: normal salt was 100% Na Cl **DURATION:** **Run-in:** 4 week run-in on salt substitute Treatment: 12 months **CHARACTERISTICS OF TREATMENT DELIVERY:** Participants were instructed to use study salt for all food preparation throughout the study duration; existing salt and foods previously pickled in salt were not removed from participants' households. Salt (substitute & normal) was delivered in identical 1 kg bags; up to 3 kg/month available to each randomized participant to cover all household uses.	Adult males and females, living in rural China, at elevated risk of future vascular disease ***N*:** G1: 306 G2: 302 **AGE, MEAN YEARS (SD):** G1: 59 (10.0) G2: 61 (9.7) **SEX, FEMALE, *N* (%):** G1:166 (52) G2:174 (58) **RACE/ETHNICITY:** All were "rural Chinese" **WEIGHT:** NR **BMI, MEAN KG/M² (SD):** G1: 26 (3.6) G2: 25 (3.9) **MEAN SBP, MMHG (SD):** G1: 159 (25) G2: 159 (26) **MEAN DBP, MMHG (SD):** G1: 93 (14) G2: 93 (14) **URINARY SODIUM, MEAN MMOL/DAY (IQR):** G1: 151 (92–201) G2: 154 (94–200)	**SBP** **SBP LOWER IN G1 VS. G2 AT 6, 9 AND 12 MONTH VISITS; (DATA REPORTED IN FIGURE)** *p*<0.002) **MAXIMUM NET REDUCTION ACHIEVED AT 12 MONTHS:** 5.4 (2.3, 8.5) **Over 12 months:** **SBP MEAN DIFFERENCE, MMHG (95% CI):** G1 vs. G2: 3.7 (1.6, 5.9) *p*<0.001 **DBP** No differences between groups at any time (*p*>0.20)	No significant differences between groups in first morning urine sodium concentrations at 6 months or 12 months. G1 had significantly higher first morning urine concentrations of potassium at 6 months and 12 months. **6 MONTHS, MMOL/L (IQR)** 6.8 (1.8, 11.8) **12 MONTHS, MMOL/L (IQR):** 7.2 (2.2, 12.3)	**WITHDRAWALS, *N* (%):** G1: 14 (4.6) G2: 9 (3) **NUTRIENT INTAKE:** Concentrations of sodium and potassium were measured.

CQ2 Summary Table C–7. Potassium and Blood Pressure and CVD Outcomes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27); Obarzanek et al. 2001(28) RCT USA, outpatient medical setting Good	**TREATMENT GROUPS:** G1: DASH diet G2: Fruits and vegetables diet G3: Control diet Run-in: 37% fat, 48% CHO, 15% protein, 16% SF, 9 g fiber, and 300 mg/d of cholesterol G1: Diet rich in fruits, vegetables, and low-fat dairy foods; reduced in saturated fat, total fat, and cholesterol; and modestly increased in protein. Diet was designed to provide 27% kcal from fat, 55% CHO, 18% protein, 6% SF, 13% MUFA, 8% PUFA, 31 g fiber, 150 mg/d of cholesterol, 4,700 mg potassium, 500 mg magnesium, 1,240 mg calcium, 3,000 mg sodium. G2: Diet rich in fruits and vegetables otherwise similar to control. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 31 g fiber, 300 mg/d of cholesterol, 4,770 mg potassium, 500 mg magnesium, 450 mg calcium, 3,000 mg sodium G3: Control diet typical of that consumed by Americans. 37% fat, 48% CHO, 15% protein, 16% SF, 13% MUFA, 8% PUFA, 9 g fiber, 300 mg/d of cholesterol, 1,700 mg potassium, 165 mg magnesium, 450 mg calcium, 3,000 mg sodium There were four calorie levels of 1,600, 2,100, 2,600, or 3,100 kcals for each diet. Weight was and was kept stable by changing calorie level. Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal	Adults ≥22 years; SBP <160 mmHg and a DBP of 80–95 mmHg ***N*:** G1: 151 G2: 154 G3: 154 **AGE, MEAN YEARS (SD):** G1: 44 (10) G2: 45 (11) G3: 44 (11) **SEX, *N* (%):** Male G1: 74 (49.0) G2: 79 (51.3) G3: 81 (52.6) Female G1: 77 (51.0) G2: 75 (48.7) G3: 73 (47.4) **RACE/ETHNICITY, *N** (%):** Black G1: 93 (61.1) G2: 90 (58.4) G3: 92 (59.7) Non-minority G1: 47 (31.1) G2: 55 (35.7) G3: 54 (35.1) Other Minority G1: 11 (7.3) G2: 9 (5.8) G3: 8 (5.2) *(continued in next table)*	**At 8 weeks** **MEAN CHANGE IN SBP, MMHG (97.5% CI)** G1 vs. G2: –2.7 (–4.6, –0.9) *p*=0.001 G1 vs. G3: –5.5 (–7.4, –3.7) *p*<0.001 G2 vs. G3:–2.8 (–4.7, –0.9) *p*<0.001 **MEAN CHANGE IN DBP, MMHG (97.5% CI)** G1 vs.G2: –1.9 (–3.3, –0.6) *p*=0.002 G1 vs. G3: –3.0 (–4.3, –1.6) *p*<0.001 G2 vs. G3: –1.1 (–2.4, 0.3) *p*=0.07	NR	**WITHDRAWALS, *N* (%):*:** G1: 2 (1.3) G2: 4 (2.6) G3: 7 (4.5)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Nutrient Intake
	(continued in next table)				

CQ2 Summary Table C–7. Potassium and Blood Pressure and CVD Outcomes (continued)

Study Cited Design Setting Quality Rating	Intervention Groups and Details Duration	Sample Characteristics	Blood Pressure Outcomes	Urinary Excretion	Attrition Adherence/Compliance Nutrient Intake
DASH Appel et al. 1997(26); Sacks et al. 1999(27); Obarzanek et al. 2001(28) *(continued)*	*(continued from previous table)* **DURATION** Run-in: 3 wks Treatment: 8 wks **INTERVENTION DELIVERY** Participants attended the clinic each weekday to be weighed and to consume one meal onsite (lunch or dinner). All other food was provided, including weekend meals. 0.2 g of sodium was provided daily for discretionary use. Beverages and salt were discretionary items and participants were required to record their consumption. Three servings of designated nonalcoholic beverages and up to 2 servings of specific alcoholic beverages were allowed. *Nutrient values presented for all diets are representative of the diets at the energy level of 2,100 kcal	*(continued from previous table)* **MEAN WEIGHT, KG:** G1: 83.4 G2: 81.8 G3: 81.5 **MEAN BMI, KG/M2*:** G1: 28.5 G2: 28.2 G3: 28.0 **SBP, MMHG (SD):** G1: 131.2 (10.0) G2: 132.3 (10.5) G3: 132 (10.7) **DBP, MMHG (SD):** G1: 85.1 (3.6) G2: 84.8 (3.9) G3: 85.3 (4.0)			

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
CVD-FACTS **(CardioVascular Disease risk FACtor Two-township study)** Weng et al. 2008 (92) Prospective cohort study Fair	**Study groups:** G1: Nonevent Group G2: Ischemic Event Group **DURATION** Followup: 10.6 years Potassium intake obtained from food frequency questionnaire. Nutrient intakes were calorie-adjusted by residual method.	Adults >40 years of age who were stroke and cancer free at baseline from CVD-FACTS ***N*:** G1: 1640 G2: 132 **AGE, MEAN YEARS (SD):** G1: 56.1 (9.8) G2: 62.2 (8.1) **SEX, MALE (%):** G1:43.7 G2:49.2 **RACE/ETHNICITY:** NR **WEIGHT:** NR **BMI, MEAN KG/M² (SD):** G1: 24.4 (3.3) G2: 25.3 (3.4) **SBP:** NR **DBP:** NR	**QUARTILES OF POTASSIUM INTAKE, MG:** Q4 + Q3 High: >3,150 Q2: 2,556–3,150 Q1 Low: <2,555 **HAZARD RATIOS FOR INCIDENT IS BY QUARTILES OF POTASSIUM INTAKE HR* (95% CI):** Q4 + Q3: 1 Q2: 1.20 (0.77, 1.86) Q1: 1.69 (1.12, 2.56) *p* for trend = 0.017 *Adjusted for age, sex, hypertension, use of antihypertensive drugs, DM, area (township), central obesity, alcohol consumption habits, smoking habit, sex-smoking habit interaction, BMI, self-report heart disease hypercholesterolemia, hypertriglyceridemia, physical activity, fibrinogen, apolipoprotein B, and plasminogen
Green et al. 2002(91) Prospective cohort study Fair	**STUDY GROUPS:** By quintile based on serum potassium and by quintile based on dietary potassium **SERUM POTASSIUM, MEQ/L:** G1: 2.6–3.8 G2: 3.81–4.0	Adult men and women >65 years of age who were stroke-free at baseline **AGE, YEARS:** G1: G2: 72.4 G3: G5: 72.9 G6: 72.7 G7: G10: 72.8	**RELATIVE RISK* (95% CI) FOR STROKE FOR SERUM POTASSIUM:** Nondiuretic user: 1.01 (0.88, 1.15); *p*=NS Diuretic user: 1.38 (1.20, 1.59); *p*<0.0001 *p* for interaction <0.005 **RELATIVE RISK* (95% CI) FOR STROKE FOR DIETARY**

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
	G3: 4.01–4.2 G4: 4.21–4.4 G5: 4.41–5.8 *(continued in next table)*	**SEX, FEMALE, *N* (%):** G1: G2: 1340 (68) G3: G5: 1894 (53) G6: 601 (60) G7: G10: 2268 (57) *(continued in next table)*	**POTASSIUM:** Nondiuretic user: 1.18 (1.04, 1.33); *p*<0.01 Diuretic user: 0.89 (0.77, 1.03); *p*=NS *p* for interaction <0.005 *Cox models included age, sex, history of DM, HTN, CAD, CHF, AF, SBP, serum creatinine, potassium supplement use, and serum potassium in the dietary potassium model RR are for one SD decrease *(continued in next table)*

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Green et al. 2002(91) *(continued)*	*(continued from previous table)* **DIETARY POTASSIUM, G/D:** G6: ≤2.34 G7: 2.35–2.92 G8: 2.93–3.47 G9: 3.48–4.16 G10: ≥4.17 **DURATION:** **Followup:** 4 to 8 years Dietary potassium intake determined by food frequency questionnaire administered at single time. Baseline testing included potassium level	*(continued from previous table)* **RACE, AFRICAN AMERICAN, *N* (%):** G1: G2: 398 (20) G3: G5: 419 (12) G6: 52 (5) G7: G10: 177 (4) **WEIGHT:** NR **SBP, MEAN MMHG:** G1; G2: 138 G3: G5: 135 G6: 137 G7: G10: 135 **DBP, MEAN MMHG:** G1: G2: 72 G3: G5: 70 G6: 71 G7: G10: 70	*(continued from previous table)* **RELATIONSHIP OF SERUM POTASSIUM LEVELS IN QUINTILES TO STROKE RISK BY DIURETIC USE, RR[†] (95% CI):** Nonusers of diuretics G1: 1.07 (0.68, 1.69) G2: 0.94 (0.63, 1.4) G3: 1.07 (0.77, 1.49) G4: 1.10 (0.8, 1.53) G5: 1.0 *p*=0.96 Users of diuretics G1: 2.37 (1.33, 4.23) G2: 2.21 (1.21, 4.03) G3: 0.77 (0.37, 1.59) G4: 1.06 (0.53, 2.14) G5: 1.0 *p*<0.001 [†]Cox models included age, sex, history of DM, HTN, CAD, CHF, AF, SBP, serum creatinine, and potassium supplement use. **RELATIONSHIP OF DIETARY POTASSIUM LEVELS IN QUINTILES TO STROKE RISK BY DIURETIC USE, RR[‡] (95% CI):** Nonusers of diuretics G6: 1.76 (1.21, 2.57) G7: 1.22 (0.81, 1.83) G8: 1.11 (0.73, 1.67) G9: 1.37 (0.93, 2.04) G10: 1.0 *p*<0.025 Users of diuretics G6: 0.87 (0.54, 1.40) G7: 0.66 (0.40, 1.11) G8: 0.66 (0.40, 1.10) G9: 1.09 (0.69, 1.73) G10: 1.0 *p*=NS

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
			‡Cox models included age, sex, history of DM, HTN, CAD, CHF, AF, SBP, serum creatinine, serum potassium and potassium supplement use

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Health Professionals Followup Study Al-Delaimy et al. 2004(89) Prospective cohort study Fair	**STUDY GROUPS:** By quintile based on median potassium intake, mg/d G1: 2,632 G2: 3,042 G3: 3,341 G4: 3,672 G5: 4,250 **DURATION:** **Followup:** 12 years Food frequency questionnaire administered in 1986 and updated in 1990 and 1994.	Health professionals 40 to 75 years of age who completed a food frequency questionnaire for the Health Professionals Followup Study, had a daily caloric intake of 800 to 4,200 kcal, and had <70 blanks on the food item questionnaire, did not have MI or CVD at baseline, and had no diagnosis of cancer at baseline Baseline characteristics were reported by magnesium quintile and not by potassium quintile so not reported here. Total sample was predominantly white ***N:*** Total: 39,633 NR by potassium group	**NUMBER OF CHD CASES:** G1: 268 G2: 248 G3: 296 G4: 283 G5: 354 **ADJUSTED RELATIVE RISK OF DEVELOPING CHD BY POTASSIUM QUINTILE:** Age-adjusted RR (95% CI) G1: 1.00 G2: 0.87 (0.74, 1.04) G3: 1.01 (0.86, 1.20) G4: 0.89 (0.75, 1.05) G5: 0.99 (0.84, 1.16) Multivariate* RR (95% CI) G1: 1.00 G2: 0.92 (0.77, 1.10) G3: 1.06 (0.90, 1.26) G4: 0.95 (0.80, 1.12) G5: 1.01 (0.86, 1.20) *p*=0.83 Multi-nutrient† RR (95% CI) G1: 1.00 G2: 0.99 (0.82, 1.19) G3: 1.18 (0.97, 1.43) G4: 1.10 (0.89, 1.32) G5: 1.27 (1.01, 1.58) *p*=0.03 *Covariates: age, time period, energy intake, history of diabetes, history of high cholesterol, family history of MI, smoking history, aspirin intake, BMI, alcohol intake, physical activity, vitamin E intake †The above covariates plus nutrient variables: *trans* fatty acid, total protein intake, cereal fiber, folate, omega–3 fatty acid, magnesium

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Health Professionals Followup Study Ascherio et al. 1998(90) Prospective cohort study Fair	**STUDY GROUPS:** By quintile based on median potassium intake, mg/d G1: 2632 G2: 3042 G3: 3341 G4: 3672 G5: 4250 **DURATION:** **Followup:** 8 years Food frequency questionnaire administered in 1986 and updated in 1990 and 1994.	Health professionals 40 to 75 years of age who completed a food frequency questionnaire for the Health Professionals Followup Study, had a daily caloric intake of 800 to 4,200 kcal, and had <70 blanks on the food item questionnaire. ***N*:** Total: 43,738 **AGE, MEAN YEARS (SD):** NR **SEX, MALE %:** 100 **RACE/ETHNICITY, %:** NR **WEIGHT:** NR **BMI:** NR **SBP, MEAN MMHG:** G1: 131 G5: 129 **DBP, MEAN MMHG:** G1: 82 G5: 81	**STROKE, NUMBER OF CASES:** G1: 76 G2: 65 G3: 62 G4: 64 G5: 61 **ADJUSTED RELATIVE RISK OF STROKE BY POTASSIUM INTAKE:** Age-adjusted RR G1: 1.0 G2: 0.80 G3: 0.71 G4: 0.68 G5: 0.59 *p*=0.004 Multivariate* RR (95% CI) G1: 1.0 G2: 0.85 (0.61, 1.18) G3: 0.78 (0.55, 1.10) G4: 0.76 (0.54, 1.07) G5: 0.62 (0.43, 0.88) *p*=0.007 Further Adjusted† RR (95% CI) G1: 1.0 G2: 0.86 (0.61, 1.23) G3: 0.82 (0.56, 1.20) G4: 0.83 (0.56, 1.24) G5: 0.69 (0.45, 1.07) *p*=0.110 *Model includes age, total energy intake, smoking, alcohol consumption, history of hypertension, history of hypercholesterolemia, parental history of MI before age 65, profession, and quintiles of BMI and physical activity † Above model plus fiber and magnesium intake

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Japan Collaborative Cohort Study for Evaluation of Cancer Risks Umesawa et al. 2008(71) Prospective cohort study Fair	Divided into quintiles (low to high) based on potassium intake **STUDY GROUPS, MEDIAN MMOL/D (SD):** G1: 35 (6) G2: 44 (2) G3: 51 (2) G4: 58 (2) G5:68 (6) **DURATION:** **AVERAGE FOLLOWUP:** 12.7 YEARS Potassium intake obtained from food frequency questionnaire	Adults, 40 to 79 years of age, who provided valid responses to dietary questionnaires, no medical history of stroke, CHD, or cancer ***N*:** G1: 11,746 G2: 11,746 G3: 11,746 G4: 11,746 G5: 11,746 **AGE, YEARS (SD):** G1: 55 (10) G2: 56 (10) G3: 56 (10) G4: 57 (10) G5: 58 (10) **SEX, % MALE:** G1: 67 G2: 44 G3: 35 G4: 29 G5: 23 **RACE/ETHNICITY:** NR **WEIGHT:** NR **BMI*, MEAN KG/M^2:** G1: 22.8 G2: 22.8 G3: 22.8 G4: 22.9 G5: 22.9 *Age- and sex-adjusted **SBP:**	**HAZARD RATIOS OF MORTALITY FROM STROKE:** Age- and sex-adjusted HR (95% CI): G1: 1.00 G2: 0.88 (0.72, 1.08) G3: 0.84 (0.69, 1.03) G4: 0.88 (0.72, 1.07) G5:0.77 (0.63, 0.94) *p* for trend = 0.021 **MULTIVARIABLE HR* (95% CI):** G1: 1.00 G2: 0.93 (0.71, 1.17) G3: 0.91 (0.70, 1.19) G4: 1.01 (0.77, 1.34) G5: 0.96 (0.70, 1.31) *p* for trend = 0.967 **MULTIVARIABLE HR† (95% CI):** G1: 1.00 G2: 0.89 (0.71, 1.13) G3: 0.84 (0.65, 1.10) G4: 0.91 (0.69, 1.22) G5: 0.83 (0.60, 1.14) *p* for trend = 0.355 **HAZARD RATIOS OF MORTALITY FROM CHD:** Age- and sex-adjusted HR (95% CI): G1: 1.00 G2: 0.79 (0.59, 1.05) G3: 0.72 (0.54, 0.97) G4: 0.65 (0.48, 0.88) G5: 0.57 (0.42, 0.77) *p* for trend <0.001 **MULTIVARIABLE HR* (95% CI):** G1: 1.00 G2: 0.81 (0.58, 1.13) G3: 0.74 (0.51, 1.09)

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
		NR **DBP:** NR *(continued in next table)*	G4: 0.69 (0.45, 1.06) G5: 0.69 (0.43, 1.12) *p* for trend = 0.127 *(continued in next table)*

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Japan Collaborative Cohort Study for Evaluation of Cancer Risks Umesawa et al. 2008(71) *(continued)*		*(continued from previous table)* **CALIBRATED* POTASSIUM INTAKE, MEDIAN MMOL/D (SD):** G1: 44 (8) G2: 56 (3) G3: 65 (2) G4: 73 (3) G5: 86 (8) *from a validation study	*(continued from previous table)* **MULTIVARIABLE HR† (95% CI):** G1: 1.00 G2: 0.80 (0.57, 1.11) G3: 0.72 (0.49, 1.07) G4: 0.66 (0.43, 1.03) G5: 0.65 (0.39, 1.06) *p* for trend = 0.083 **HAZARD RATIO OF MORTALITY FROM TOTAL CVD:** Age- and sex-adjusted HR (95% CI): G1: 1.00 G2: 0.84 (0.73, 0.96) G3: 0.82 (0.72, 0.94) G4: 0.84 (0.73, 0.96) G5: 0.71 (0.62, 0.81) *p* for trend <0.001 **MULTIVARIABLE HR* (95% CI):** G1: 1.00 G2: 0.88 (0.75, 1.02) G3: 0.86 (0.72, 1.03) G4: 0.91 (0.75, 1.10) G5: 0.82 (0.66, 1.02) *p* for trend = 0.153 **MULTIVARIABLE HR† (95% CI):** G1: 1.00 G2: 0.84 (0.72, 0.99) G3: 0.81 (0.67, 0.97) G4: 0.84 (0.69, 1.02) G5: 0.73 (0.59, 0.92) *p* for trend = 0.018 *Cox proportional hazard models adjusted further for BMI, smoking status, ethanol intake, history of HTN, history of diabetes, menopause, HRT, time spent on sports activity, walking time, educational status, perceived mental stress, and calcium intake

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
			†Cox proportional hazard models adjusted further for sodium intake

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Marniemi et al. 2005(79) Case-control study Finland, population-based health survey Fair	**STUDY GROUPS:** G1: AMI cases G2: AMI controls G3: Stroke cases G4: Stroke controls **DURATION:** Followup for up to 10 years Food consumption information obtained from dietary history interview	Elderly men and women, 65 to 99 years of age ***N*:** G1: 130 G2: 559 G3: 70 G4: 590 **AGE, MEAN YEARS (SD):** NR **SEX, FEMALE %:** NR **RACE/ETHNICITY, %:** NR **OVERWEIGHT, %:** NR **BMI:** NR **SBP, MEAN MMHG (SD):** NR **DBP, MEAN MMHG (SD):** NR	**DAILY POTASSIUM, MEAN MG (SD):** G1: 3,900 (1250) G2: 4,090 (1350) G3: 4,110 (1430) G4: 4,140 (1330) **SERUM CONCENTRATION OF POTASSIUM, MEAN MMOL/L (SD):** G1: 4.25 (0.34) G2: 4.22 (0.35) G3: 4.25 (0.37) G4: 4.23 (0.37) **ADJUSTED* RR (95% CI) OF AMI AND STROKE BETWEEN TERTILES OF POTASSIUM INTAKE:** Middle tertile vs. lowest tertile AMI: 0.821 (0.53, 1.27) Stroke: 1.21 (0.68, 2.14) Highest tertile vs. lowest tertile AMI: 0.847 (0.50, 1.43) Stroke: 0.751 (0.35, 1.60) *Adjusted in Cox proportional hazards model for age, gender, smoking, functional capacity and weight adjusted energy intake **ADJUSTED* RR (95% CI) OF AMI AND STROKE BETWEEN TERTILES OF SERUM CONCENTRATION OF POTASSIUM:** Middle tertile vs. lowest tertile AMI: 1.27 (0.82, 1.98) Stroke: 1.39 (0.74, 2.60) Highest tertile vs. lowest tertile AMI: 1.12 (0.72, 1.76) Stroke: 1.40 (0.75, 2.60) *Adjusted for age, gender, smoking, and functional capacity

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
NHANES Bazzano et al. 2001(88) Prospective cohort study Fair	Participants were divided into quartile groupings based on their potassium intake, mmol/24h **STUDY GROUPS:** G1: <34.6 G2: 34.6–49.8 G3: 49.8–68.4 G4: >68.4 **DURATION:** **Average followup:** 19 years	NHANES I participants who were aged 25 to 74 years at their baseline examinations between 1971 and 1975 ***N*:** G1: 2,452 G2: 2,451 G3: 2,450 G4: 2,452 **AGE YEARS, MEAN (SD):** G1: 50.1 (15.9) G2: 50.7 (15.8) G3: 49.3 (15.5) G4: 46.6 (14.8) **SEX, MALE, %:** G1: 23.0 G2: 31.0 G3: 39.6 G4: 60.0 **RACE/ETHNICITY, %:** White: G1: 68.5 G2: 84.9 G3: 89.6 G4: 92.0 **WEIGHT:** NR **BMI, KG/M² MEAN (SD):** G1: 26.4 (5.8) G2: 25.8 (5.2) G3: 25.2 (4.8) G4: 25.1 (4.6) **SBP MMHG MEAN (SD):** G1: 137.8 (26.6)	**STROKE INCIDENCE, EVENTS:** G1: 287 G2: 230 G3: 235 G4: 175 **STROKE HR (95% CI), ADJUSTED FOR AGE, RACE, SEX, ENERGY:** G1: 1.0 G2: 0.76 (0.65, 0.88) G3: 0.84 (0.72, 0.99) G4: 0.76 (0.60, 0.97) *p* for trend = 0.07 **STROKE HR (95% CI) MULTIVARIATE:*** G1: 1.0 G2: 0.75 (0.63, 0.88) G3: 0.85 (0.71, 1.01) G4: 0.76 (0.58, 1.01) *p* for trend = 0.14 **CHD INCIDENCE, EVENTS:** G1: 456 G2: 504 G3: 456 G4: 431 **CHD HR (95% CI), ADJUSTED FOR AGE, RACE, SEX, ENERGY:** G1: 1.0 G2: 1.00 (0.86, 1.15) G3: 0.90 (0.77, 1.06) G4: 0.97 (0.79, 1.19) *p* for trend=0.57 **CHD HR (95% CI) MULTIVARIATE:*** G1: 1.0 G2: 10.4 (0.89, 1.20) G3: 0.95 (0.78, 1.17)

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
		G2: 135.4 (24.8) G3: 133.5 (24.3) G4: 130.6 (20.4) *(continued in next table)*	G4: 1.01 (0.78, 1.33) *p* for trend=0.93 *(continued in next table)*

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
NHANES Bazzano et al. 2001(88) *(continued)*		*(continued from previous table)* **DBP MMHG MEAN (SD):** G1: 84.5 (13.8) G2: 83.1 (13.2) G3: 82.8 (13.0) G4: 82.4 (12.0)	*(continued from previous table)* **STROKE INCIDENCE ASSOCIATED WITH LOW DIETARY POTASSIUM INTAKE, HR (95% CI):** Age, energy adjusted: 1.37 (1.20, 1.54); *p*<0.0001 Age, race, sex, energy adjusted: 1.26 (1.11, 1.45); *p*=0.0007 Multivariate*: 1.28 (1.11, 1.47); *p*=0.0001 **CHD INCIDENCE ASSOCIATED WITH LOW DIETARY POTASSIUM INTAKE, HR (95% CI):** Age, energy adjusted: 1.04 (0.92, 1.18); *p*=0.54 Age, race, sex, energy adjusted: 1.04 (0.91, 1.19); *p*=0.53 Multivariate*:1.00 (0.86, 1.15); *p*=0.95 *Additionally adjusted for SBP, serum cholesterol, BMI, history of diabetes, physical activity, education level, regular alcohol consumption, current cigarette smoking, vitamin supplement use, sat fat intake, cholesterol intake, sodium intake, calcium intake, dietary fiber, vitamin C intake and vitamin A intake
NHANES I Epidemiological followup study Fang et al. 2000(87) Prospective cohort study Fair	**Study groups:** G1: Men, White, Tertile I: Potassium <2,003 mg/d G2: Men, White, Tertile II: Potassium 2,003–2,879 mg/d G3: Men, White, Tertile III: Potassium >2,879 mg/d G4: Men, Black, Tertile I: Potassium <1,260 mg/d G5: Men, Black, Tertile II: Potassium 1,260–2206 mg/d G6: Men, Black, Tertile III: Potassium >2,206 mg/d G7: Women, White, Tertile I: Potassium <1,508 mg/d G8: Women, White, Tertile II: Potassium 1,508–2,207 mg/d G9: Women, White, Tertile III: Potassium >2,207 mg/d G10: Women, Black, Tertile I: Potassium <1,017 mg/d G11: Women, Black, Tertile II: Potassium 1,017–1,641 mg/d G12: Women, Black, Tertile III: Potassium >1,641 mg/d **DURATION:** **Mean followup:** 16.7 years Data on nutrient intake were available from a single 24-hour dietary recall	NHANES I survey examined adults, 25 to 74 years of age ***N*:** G1: 1056 G2: 1057 G3: 1056 G4: 198 G5: 199 G6: 198 G7: 1691 G8: 1690 G9: 1692 G10: 343 G11: 343 G12: 343 *(continued in next table)*	**AGE-ADJUSTED STROKE MORTALITY, RATES PER 1,000 PERSON-YEARS (DEATHS):** G1: 1.94 (37) G2: 2.28 (39) G3: 1.17 (17) G3 vs. G1: *p*=0.042 RR (95% CI): 1.66 (1.32, 2.14) G4: 5.08 (14) G5: 3.40 (11) G6: 1.19 (3) G6 vs. G4: *p*=0.0016 RR (95% CI): 4.27 (1.88, 9.19) G7: 1.61 (50) G8: 1.52 (49) G9: 1.43 (37) G9 vs. G7: *p*=0.53 RR (95% CI): 1.13 (0.84, 1.66) *(continued in next table)*

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
NHANES I Epidemiological followup study Fang et al. 2000(87) *(continued)*		*(continued from previous table)* **AGE, MEAN YEARS (SD):** G1: 55.4 G2: 52.5 G3: 47.9 G4: 58.3 G5: 56.0 G6: 48.2 G7: 48.5 G8: 48.9 G9: 45.3 G10: 46.8 G11: 48.9 G12: 45.8 **SEX, FEMALE %:** 61.8 **RACE/ETHNICITY, %:** White: 83.5 **BMI:** G1: 25.5 G2: 25.6 G3: 25.4 G4: 24.5 G5: 26.0 G6: 25.6 G7: 25.9 G8: 25.0 G9: 24.1 G10: 27.5 G11: 27.5 G12: 27.5 **SBP, MEAN MMHG (SD):** G1: 139.2	*(continued from previous table)* **AGE-ADJUSTED STROKE MORTALITY, RATES PER 1,000 PERSON-YEARS (DEATHS):** G10: 2.46 (14) G11: 2.74 (17) G12: 3.04 (16) G12 vs. G10: *p*=0.5425 RR (95% CI): 0.80 (0.21, 2.01) **AGE/RACE-ADJUSTED STROKE MORTALITY BY SEX AND HTN STATUS:** Hypertensive Men Tertile I: 6.02 (19) Tertile II: 4.63 (17) Tertile III: 2.82 (9) III vs. I: *p*=0.0242 RR (95% CI): 2.13 (1.09, 6.78) Hypertensive women Tertile I: 4.43 (36) Tertile II: 3.34 (30) Tertile III: 3.80 (27) III vs. I: *p*=0.746 RR (95% CI): 1.16 (0.86, 3.59) Nonhypertensive men Tertile I: 1.66 (30) Tertile II: 1.42 (24) Tertile III: 1.34 (22) III vs. I: 0.458 RR (95% CI): 1.23 (0.84, 3.89) Nonhypertensive women Tertile I: 1.19 (35) Tertile II: 1.17 (33) Tertile III: 1.07 (22) III vs. I: 0.415 RR (95% CI):1.11 (0.85, 3.54)

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
		G2: 136.2 G3: 132.7 *(continued in next table)*	

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
NHANES I Epidemiological followup study Fang et al. 2000(87) *(continued)*		*(continued from previous table)* **SBP, MEAN MMHG (SD):** G4: 149.4 G5: 144.1 G6: 139.9 G7: 134.4 G8: 132.6 G9: 128.5 G10: 140.5 G11: 141.1 G12: 138.6 **DBP, MEAN MMHG (SD):** G1: 85.5 G2: 85.0 G3: 83.8 G4: 91.3 G5: 88.6 G6: 88.8 G7: 82.1 G8: 81.1 G9: 79.6 G10: 86.1 G11: 86.6 G12: 86.3 **POTASSIUM INTAKE, MG/D:** G1: 1492.6 G2: 2432.6 G3: 3745.8 G4: 866.4 G5: 1672.8 G6: 2993.6 G7: 1094 G8: 1841 G9: 2889 G10: 716	

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
		G11: 1309 G12: 2383	

CQ2 Summary Table C–8. Potassium and CVD Outcomes (continued)

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Nurse's Health Study Iso et al. 1999(94) Prospective cohort study Fair	**STUDY GROUPS:** Participants divided into quintiles (lowest to highest) based on potassium intake, median mg/d: G1: 2,017 (Lowest) G2: 2,412 G3: 2,708 (Intermediate) G4: 3,030 G5: 3,555 (Highest) **DURATION:** **Followup:** 14 years Potassium intake determined by food frequency questionnaire	Women who returned the 1980 dietary questionnaire and left <10 items blank, had no history of cancer, angina, MI, stroke, or other CVD; predominantly White ***N*:** Total: 86,368 NR by quintile **AGE, MEAN YEARS:** G1: 44.9 G2: NR G3: 46.1 G4: NR G5: 47.3 **SEX, % FEMALE:** 100 **RACE/ETHNICITY:** NR **WEIGHT:** NR **BMI ≥29 KG/M^2:** G1: 15.9 G2: NR G3: 12.9 G4: NR G5: 13.4 **SBP:** NR **DBP:** NR	**All Stroke** **CASES, *N*:** G1: 147 G2: 117 G3: 146 G4: 134 G5: 146 **RELATIVE RISK (95% CI):** G1: 1.0 G2: 0.75 (0.59, 0.95) G3: 0.90 (0.72, 1.14) G4: 0.80 (0.63, 1.01) G5: 0.83 (0.66, 1.04) P for trend = 0.34 **MULTIVARIATE RELATIVE RISK OF ISCHEMIC STROKE:** Adjusted RR* (95% CI) G1: 1.0 G2: 0.69 (0.49, 0.97) G3: 0.85 (0.62, 1.16) G4: 0.71 (0.52, 0.99) G5: 0.69 (0.50, 0.95) *p* for trend = 0.04 *Adjusted for age, smoking status, time interval, and history of HTN Adjusted RR† (95% CI) G1: 1.0 G2: 0.72 (0.51, 1.01) G3: 0.90 (0.66, 1.25) G4: 0.75 (0.54, 1.05) G5: 0.72 (0.51, 1.01) *p* for trend = 0.10 †Adjusted for * plus BMI, alcohol intake, menopausal status and postmenopausal hormone use, vigorous exercise, usual aspirin use, multivitamin use, vitamin E use, omega–3 fatty acid intake, and histories of diabetes and high cholesterol levels *(continued in next table)*

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Nurse's Health Study Iso et al. 1999(94) *(continued)*			*(continued from previous table)* **MULTIVARIATE RELATIVE RISK OF ISCHEMIC STROKE:** Adjusted RR‡ (95% CI) G1: 1.0 G2: 0.78 (0.55, 1.10) G3: 1.03 (0.73, 1.44) G4: 0.89 (0.62, 1.27) G5: 0.87 (0.58, 1.30) *p* for trend = 0.67 ‡Adjusted for † plus calcium intake
Rotterdam Study Geleijnse et al. 2007(93) Case-cohort study Good	**STUDY GROUPS:** G1: Random sample G2: Cases of incident MI G3: Cases of incident stroke G4: Cases of CVD mortality G5: Cases of all-cause mortality **DURATION:** Median followup: 5.5 years	Adult men and women, ≥55 years of age ***N*:** G1: 1,448 G2: 206 G3: 181 G4: 217 G5: 795 **AGE MEAN YEARS (SD):** G1: 69.2 (8.7) G2: 71.0 (8.0) G3: 74.0 (8.5) G4: 76.8 (8.4) G5: 76.9 (8.9) **SEX, MALE (%):** G1: 41 G2: 62 G3: 45 G4: 51 G5: 49 **RACE/ETHNICITY:** NR **WEIGHT:**	**INCIDENT MI, ALL SUBJECTS:** RR (95% CI), model 1* Urinary potassium excretion: 1.10 (0.89, 1.35) Dietary potassium intake: 0.98 (0.85, 1.13) RR (95% CI), model 2† Urinary potassium excretion: 1.16 (0.94, 1.43) Dietary potassium intake: 0.94 (0.81, 1.09) RR (95% CI), model 3‡ Urinary potassium excretion: 1.11 (0.87, 1.43) Dietary potassium intake: 0.90 (0.65, 1.24) **INCIDENT STROKE, ALL SUBJECTS:** RR (95% CI), model 1* Urinary potassium excretion: 1.09 (0.87, 1.36) Dietary potassium intake: 0.99 (0.84, 1.17) RR (95% CI), model 2† Urinary potassium excretion: 1.12 (0.89, 1.42) Dietary potassium intake: 0.99 (0.84, 1.16) RR (95% CI), model 3‡ Urinary potassium excretion: 1.17 (0.86, 1.58) Dietary potassium intake: 1.02 (0.71, 1.46) *(continued in next table)*

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
		NR *(continued in next table)*	

CQ2 Summary Table C–8. ***Potassium and CVD Outcomes (continued)***

Study Cited Design Setting	Study Groups and Details Duration	Sample Characteristics	Results
Rotterdam Study Geleijnse et al. 2007(93) *(continued)*		*(continued from previous table)* **BMI, MEAN KG/M² (SD):** G1: 26.4 (3.8) G2: 26.3 (3.4) G3: 26.0 (3.3) G4: 26.2 (3.8) G5: 25.7 (3.8) **SBP, MEAN MMHG (SD):** G1: 140 (22) G2: 145 (23) G3: 149 (24) G4: 146 (25) G5: 145 (25) **DBP, MEAN MMHG (SD):** G1: 74 (11) G2: 74 (12) G3: 75 (13) G4: 73 (13) G5: 73 (14) **URINARY POTASSIUM EXCRETION, MEAN MMOL/24 H:** G1: 45 (22) G2: 47 (22) G3: 45 (23) G4: 44 (24) G5: 44 (22) Based on one timed overnight urine sample **POTASSIUM DIETARY INTAKE, MEAN G/D (SD):** G1: 3.6 (0.8) G2: 3.7 (0.8) G3: 3.6 (0.8) G4: 3.6 (0.9) G5: 3.6 (0.9)	*(continued from previous table)* **CVD MORTALITY, ALL SUBJECTS:** RR (95% CI), model 1* Urinary potassium excretion: 1.13 (0.90, 1.41) Dietary potassium intake: 0.97 (0.82, 1.14) RR (95% CI), model 2† Urinary potassium excretion:1.14 (0.92, 1.42) Dietary potassium intake: 0.95 (0.81, 1.12) RR (95% CI), model 3‡ Urinary potassium excretion: 1.23 (0.94, 1.60) Dietary potassium intake: 0.97 (0.72, 1.31) *Adjusted for age, sex and (for urinary potassium) 24-h urinary creatinine excretion †Adjusted for * plus FMI, smoking status, diabetes, use of diuretics, and highest completed education ‡Adjusted for † plus daily intake of total energy, alcohol, calcium, sat fat, and 24-h urinary sodium excretion

CQ3 Systematic Review and Meta-Analyses Evidence Summary

CQ3 Summary Table D–1: ***Aerobic Exercise and LDL-C***

Cite	Type	LDL Cholesterol	Exercise Program Characteristics				
			Duration (Weeks)	Sessions per Week	Minutes per Session	Intensity	Increase in Steps per Day
Kelley et al. 2005, Int J. Obes. (122)	Meta-analysis	Nonsignificant decrease of –3.0 mg–dL	19.8±10.2 wks	3.9±1.0	41.5±13.5	63.9±10.8% VO2max	
Kelley et al. 2005, Preventive Cardiology(116)	Meta-analysis	----------	22.5±17.8 wks	4.9±2.6	38.4±16.4	64.9±9.3% VO2max	
Kelley et al. 2005, Preventive Cardiology(115) (older adults)	Meta-analysis	Significant decrease of –3.9 mg/dL (–2.5%)	35.3±31.8 wks	3.5±1.0	42.4±12.1	67.8±9.8% VO2max	
Kelley et al. 2004(113)	Meta-analysis	Significant decrease of –5.5 mg/dL	23.19±17.7 wks	4.75±2.5	38.4±15.6	64.2±9.4% VO2max	
Kelley et al. 2004, Journal of Women's Health(114) (Women Only)	Meta-analysis	Significant decrease of –4.4 mg/dL	21.8±19.5 wks	3.7±1.1	36.3±13.2	69.2±10.1% VO2max	
Kelley and Kelley, 2007, Public Health(117) (type 2 diabetes)	Meta-analysis	Significant decrease of –6.4 mg/dL	15.1±5.5 wks	4.2±1.8	47.1±14.4	68.3±3.0% VO2max	
Kelley and Kelley, 2006, Atherosclerosis(185)	Meta-analysis	----------	24.4±22.4 wks	4.0±1.1	40.6±12.7	68.3±11.3% VO2max	
Bravata et al. 2007, JAMA(119)	Systematic Review	Significant decrease of –0.06 mmol/L					+2492 (1098–3885)
Kodama et al. 2007. Arch Int Med(118)	Meta-analysis	----------	27.0 weeks	3.7	40.5	64.8% VO2max (5.3 METS)	
Taylor et al. 2004, Am J. Med.(123) (pts with CVD)	Systematic Review and Meta-analysis	Nonsignificant decrease of 7.7 mg/dL					
Leon and Sanchez 2001, Med Sci Sports Exerc(121)	Systematic Review	Inconsistent improvement					
Durstine et al. 2001, Sports Medicine(120)	Systematic Review	Infrequent improvement					
Physical Activity Guidelines 2008(106)	----------	Inconsistent evidence of improvement					

CQ3 Summary Table D–2: ***Resistance Exercise and LDL-C***

Cite	Type	LDL Cholesterol	Exercise Program Characteristics				
			Duration (Weeks)	Sessions per Week	Minutes per Session	Intensity	Other Details
Kelley and Kelley 2009 (Preventive Medicine)	Meta-analysis	Significant decrease of –6.1 mg/dL	24.0±19.0 wks	2.9±0.4	47.7±11.5	70.3±10.4% 1RM	2.6±1.1 sets 11.5±6.6 reps 9.2±3.1 exercises
Gordon et al. 2009, Diabetes Research and Clinical Practice(125)	Systematic Review	Generally showed improvement	4–6 wks to 12 months	Typically 3 days per week		Varied	Varied

CQ3 Summary Table D–3: ***Aerobic Exercise and HDL-C***

Cite	Type	HDL Cholesterol	Exercise Program Characteristics				
			Duration (Weeks)	Sessions per Week	Minutes per Session	Intensity	Increase in Steps per Day
Kelley et al. 2005, Int J. Obes(122)	Meta-analysis	Nonsignificant increase of 1.6 mg/dL	19.8±10.2 wks	3.9±1.0	41.5±13.5	63.9±10.8% VO2max	
Kelley et al. 2005, Preventive Cardiology(116)	Meta-analysis	Nonsignificant increase of 1.4 mg/dL (3%)	22.5±17.8 wks	4.9±2.6	38.4±16.4	64.9±9.3% VO2max	
Kelley et al. 2005, Preventive Cardiology(115) (older adults)	Meta-analysis	Significant increase of 2.5 mg/dL (5.6%)	35.3±31.8 wks	3.5±1.0	42.4±12.1	67.8±9.8% VO2max	
Kelley et al. 2004(113)	Meta-analysis	Nonsignificant increase of 1.2 mg/dL	23.19±17.7 wks	4.75±2.5	38.4±15.6	64.2±9.4% VO2max	
Kelley et al. 2004. Journal of Women's Health(114) (Women Only)	Meta-analysis	Significant increase of 1.8 mg/dL	21.8±19.5 wks	3.7±1.1	36.3±13.2	69.2±10.1% VO2max	
Kelley and Kelley, 2007, Public Health(117) (type 2 diabetes)	Meta-analysis	Nonsignificant increase of 0.9 mg/dL	15.1±5.5 wks	4.2±1.8	47.1±14.4	68.3±3.0% VO2max	
Kelley and Kelley, 2006, Atherosclerosis(185)	Meta-analysis	Significant increase of 2.6 mg/dL	24.4±22.4 wks	4.0±1.1	40.6±12.7	68.3±11.3% VO2max	
Bravata et al. 2007, JAMA(119)	Systematic Review	Nonsignificant increase of 0.06 mmol/L					+2492 (1098–3885)
Kodama et al. 2007, Arch Int Med(118)	Meta-analysis	Significant increase of 2.63 mg/dL	27.0 weeks	3.7	40.5	64.8% VO2max (5.3 METS)	

Cite	Type	HDL Cholesterol	Exercise Program Characteristics				
			Duration (Weeks)	Sessions per Week	Minutes per Session	Intensity	Increase in Steps per Day
Taylor et al. Am J. Med. 2004(123) (pts with CVD)	Systematic Review and Meta-analysis	Nonsignificant decrease of –1.9 mg/dL					

CQ3 Summary Table D–3: Aerobic Exercise and HDL-C (continued)

Cite	Type	HDL Cholesterol	Exercise Program Characteristics				
			Duration (Weeks)	Sessions per Week	Minutes per Session	Intensity	Increase in Steps per Day
Leon and Sanchez. Med Sci Sports Exerc, 2001(121)	Systematic Review	More consistent improvement					
Durstine et al. Sports Medicine 2001(120)	Systematic Review	More consistent improvement					
Physical Activity Guidelines 2008(106)	----------	Favorable improvement					

CQ3 Summary Table D-4: Resistance Exercise and HDL-C

Cite	Type	HDL Cholesterol	Exercise Program Characteristics				
			Duration (Weeks)	Sessions per Week	Minutes per Session	Intensity	Other Details
Kelley and Kelley 2009 (Preventive Medicine)	Meta-analysis	Nonsignificant increase of 0.7 mg/dL	24.0±19.0 wks	2.9±0.4	47.7±11.5	70.3±10.4% 1RM	2.6±1.1 sets 11.5±6.6 reps 9.2±3.1 exercises
Gordon et al. Diabetes Research and Clinical Practice, 2009(125)	Systematic Review	Generally showed improvement	4–6 wks to 12 months	Typically 3 days per week		Varied	Varied

CQ3 Summary Table D-5: Aerobic Exercise and Blood Pressure

Reference (quality)	Subject Characteristics	SBP	DBP	Exercise Program Characteristics (Median or Mean)			
				Duration (Weeks)	Sessions per Week	Min per Session	Intensity
Aerobic Exercise:							
Cornelissen 2005(140) (poor)	72 trials ≥4 weeks aerobic exercise (*n*=3936; 46.6 y)	Normotensive: Sig decrease 2.4 mmHg Pre-HTN: Sig decrease 1.7 mmHg HTN: Sig decrease 6.9 mmHg	Normotensive: Sig decrease 1.6 mmHg Pre-HTN: Sig decrease 1.7 mmHg HTN: Sig decrease 4.9 mmHg	16	3	40	65% HR_{res}
Whelton 2002(139) (fair)	54 trials ≥2 weeks aerobic exercise (*n*=2419; mean ages 21–79 y)	Normotensive: Sig decrease 4.0 mmHg HTN: Sig decrease 4.9 mmHg	Normotensive: Sig decrease 2.3 mmHg HTN: Sig decrease 3.7 mmHg	N/A	N/A	N/A	N/A
Kelley et al. 2001(131) (fair)	16 trials ≥4 weeks walking (*n*=650; 84% female; mean age 58 y)	Sig decrease 3 mmHg	Sig decrease 1 mmHg	25	4	42	63% VO_2 max

CQ3 Summary Table D-5: Aerobic Exercise and Blood Pressure (continued)

Reference (quality)	Subject Characteristics	SBP	DBP	Exercise Program Characteristics (Median or Mean)			
				Duration (Weeks)	Sessions per Week	Min per Session	Intensity
Aerobic Exercise:							
Murphy 2007(136) (fair)	24 trials ≥4 weeks walking (*n*=1128; 83% female; mean age 52 y) BP data only from 9 trials, *n*=356	Nonsig decrease 1 mmHg	Sig decrease 2 mmHg	35	4	38	56% VO_2 max
Guo 2008(128) (fair)	9 trials of qigong (*n*=908) (age mainly 40s and 50s)	Vs. drug (*n*=278): Nonsig decrease 1 mmHg Vs. aerobic ex (*n*=157): Nonsig increase 2 mmHg Vs. no treatment (*n*=130) Nonsig increase17 mmHg	Vs. drug (*n*=333): Non-sig increase2 mmHg Vs. aerobic ex (*n*=157): Non-sig decrease 2 mmHg Vs. no treatment (*n*=130) Non-sig increase10 mmHg	N/A	N/A	N/A	N/A

Reference (quality)	Subject Characteristics	SBP	DBP	Exercise Program Characteristics (Median or Mean)			
				Duration (Weeks)	Sessions per Week	Min per Session	Intensity
Lee 2007(134) (good)	12 trials of qigong (*n*=1218) (age mainly 40–70 y)	Vs. no treatment (*n*=94) Sig decrease 19 mmHg Vs. aerobic ex (*n*=172): Nonsig increase 1 mmHg	Vs. no treatment N/A Vs. aerobic ex (*n*=172): Nonsig increase 2 mmHg	N/A	N/A	N/A	N/A
Kelley 2001(132) (good)	7 trials of aerobic exercise in ≥50 y (*n*=802; mean age 68.5 y)	Sig decrease 2 mmHg	Nonsig decrease 1 mmHg	35	3	40	63% VO_2 max
Asikainen 2004(127) (fair)	7 trials of postmenopausal women Qualitative review	1 of 5 walking studies in normotensives showed sig decrease in BP 1 aerobic + resistance exercise study in HTN and overweight showed sig decrease in BP	1 aerobic exercise + diet study did not show any effect on BP	N/A	N/A	N/A	N/A
Taylor 2004(123) (good)	Trials ≥6 months of CHD patients; 8 trials (*n*=774) for SBP, 5 trials (482) for DBP (mean age 55 y)	Sig decrease 3.19 mmHg	Nonsig decrease 1.18 mmHg	N/A	4	53	76% VO_2 max
Jolly 2006(130) (fair)	5 trials of CHD patients (*n*=574; age N/A)	Sig decrease 4.2 mmHg	N/A	N/A	N/A	N/A	N/A
Thomas 2006(138) (good)	Trials ≥8 weeks of T2D patients; 4 trials (*n*=127) for SBP, 3 trials (*n*=78) for DBP	Nonsig decrease 4.16 mmHg	Nonsig decrease 0.13 mmHg	N/A	N/A	N/A	N/A

CQ3 Summary Table D–6: ***Resistance Exercise and Blood Pressure***

Reference (Quality)	Subject Characteristics	SBP	DBP	Exercise Program Characteristics (Median or Mean)			
				Duration (Weeks)	Sessions per Week	Min per Session	Intensity
Resistance Training:							
Cornelissen 2005(141) (poor) (PAGAC)	9 trials resistance training; 9 included normotensive, 3 HTN (*n*=341; mean ages 18–72 y)	Nonsig decrease 3.2 mmHg	Sig decrease 3.5 mmHg	16	3	10 exerc, 2 sets, 1–25 reps	61% 1RM
Gordon 2009(125) (fair)	10 trials resistance training (*n* N/A; age N/A) Qualitative review	3 of 10 “beneficial” changes in SBP”	“improvements in DBP were less frequently observed”	N/A	N/A	N/A	N/A

Appendix F. Abbreviations and Acronyms

AAD	average American diet
ABP	ambulatory blood pressure
ABPM	ambulatory blood pressure monitoring
ACC	American College of Cardiology
ADA	American Dietetic Association
AHA	American Heart Association
AHRQ	Agency for Healthcare Research and Quality
AND	Academy of Nutrition and Dietetics
APO	apolipoprotein
ApoA	apolipoprotein A
ApoB	apolipoprotein B
ATP	Adult Treatment Panel
AVD	atrioventricular
BMI	body mass index
BP	blood pressure
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CCD	Canadian Trial of Carbohydrates in Diabetes
CCE	conventional carbohydrate exchange
CHD	coronary heart disease
CI	confidence interval
COI	conflict of interest
COR	Class of Recommendation
CQ	critical question
CV	cardiovascular
CVD	cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
DASH- Na	Dietary Approaches to Stop Hypertension- Sodium
DBP	diastolic blood pressure
EPC	Evidence-based Practice Center
ESRD	end-stage renal disease
FFQ	food frequency questionnaire
GFR	glomerular filtration rate
GI	glycemic index
GLIA	GuideLine Implementability Appraisals
GRT	group-randomized trial
HDL	high-density lipoprotein

HDL-C	HDL cholesterol
HF	heart failure
High-CHO	high-carbohydrate
HR	hazard ratio
HTN	hypertension
IOM	Institute of Medicine
ITT	Intent-to-Treat Analysis
JNC	Joint National Committee
kcal	kilocalorie
LDL-C	LDL cholesterol
LDL-P	LDL particle number
LOE	Level of Evidence
Low-CHO	low-carbohydrate
Lp (a)	lipoprotein (a)
LTF	Lost-to-Followup
MA	meta-analyses
MED	Mediterranean-style diet
MET	metabolic equivalent task
MI	myocardial infarction
MUFA	monounsaturated fatty acids
NA	Not applicable
NCEP	National Cholesterol Education Program
NHANES	National Health and Nutrition Examination Survey
NHLBI	National Heart, Lung, and Blood Institute
NHLBAC	NHLBI Advisory Council
NR	not reported
NSTEMI	non-ST-segment elevation myocardial infarction
OMNI	Optimal Macronutrient Intake Strategies Against Heart Disease
PAGAC	Physical Activity Guidelines Advisory Committee
PICO	Population, Intervention, Comparator, Outcome
PICOS	Population, Intervention, Comparator, Outcomes/Setting
PICOTS	Population, Intervention, Comparator, Outcomes, Timing, and Setting
PUFA	polyunsaturated fatty acids
RCT	randomized controlled trial
RWI	relationships with industry
SBP	systolic blood pressure
SD	standard deviation
SFA	saturated fat
SR	systematic review

STEMI	ST-segment elevation myocardial infarction
SUN	Seguimiento Universidad de Navarra
Task Force	ACC/AHA Task Force on Practice Guidelines
TG	triglycerides
TLC	Therapeutic Lifestyle Changes
TOHP	Trials of Hypertension Prevention
TOHP II	Trials of Hypertension Prevention II
TONE	Trial of Nonpharmacologic Interventions in the Elderly
USPSTF	U.S. Preventive Services Task Force
VCW	Virtual Collaborative Workspace
WHI	Women’s Health Initiative

Appendix G. Author Relationships With Industry and Other Entities (Relevant)

Committee Member	Employment	Consultant	Speaker's Bureau	Ownership/ Partnership/Principal	Personal Research	Expert Witness
Robert H. Eckel, *Co-Chair*	University of Colorado, Anschutz Medical Campus—Professor of Medicine, Professor of Physiology and Biophysics; and Charles A. Boettcher II Chair in Atherosclerosis	**2008-2012:** Foodminds	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None
		2013: Foodminds	**2013:** None	**2013:** None	**2013:** None	**2013:** None
John M. Jakicic, *Co-Chair*	University of Pittsburgh—Chair and Professor of Physical Activity and Weight Management Research Center	**2008-2012:** Alere Wellbeing JennyCraig Nestle Nutrition	**2008-2012:** None	**2008-2012:** None	**2008-2012:** Body Media—PI	**2008-2012:** None
		2013: Calorie Control Council	**2013:** None	**2013:** None	**2013:** Body Media—PI	**2013:** None
Jamy 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:** None	**2008-2012:** None
		2013: Eisai Nestle Healthcare Nutrition OPTIFAST Division Vivus	**2013:** None	**2013:** None	**2013:** None	**2013:** None
Janet M. de Jesus *Ex-Officio*	NHLBI—Nutritionist, 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
Nancy Houston Miller	Stanford University School of Medicine, Department of Cardiology—Associate Director, Stanford Cardiac Rehabilitation Program	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None
		2013: California Walnut Board	**2013:** None	**2013:** None	**2013:** None	**2013:** None
Van S. Hubbard, *Ex-Officio*	National Institute of Diabetes and Digestive and Kidney Diseases—	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None

	Director, NIH Division of Nutrition Research Coordination	**2013:** None	**2013:** None	**2013:** None	**2013:** None	**2013:** None
I-Min Lee	Harvard University—Professor of Medicine, Harvard Medical School	**2008-2012:** Virgin HealthMiles	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None
		2013: None	**2013:** None	**2013:** None	**2013:** None	**2013:** None
Alice H. Lichtenstein	Tufts University, USDA Human Nutrition Research Center on Aging—Senior Scientist and Director, Cardiovascular Nutrition Laboratory Friedman School; Stanley N. Gershoff Professor of Nutrition Science and Policy	**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
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 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	New York City Department 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
Frank M. Sacks	Harvard School of Public Health, Department of Nutrition—Professor of Cardiovascular Disease Prevention; Brigham and Women's Hospital—Senior Physician and Professor of Medicine	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** Federal Trade Commission; Unilever, Keebler
		2013: None	**2013:** None	**2013:** None	**2013:** None	**2013:** None
Sidney C. Smith, Jr	University of North Carolina—Professor of Medicine; Director, Center for	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None	**2008-2012:** None

	Cardiovascular Science and Medicine	**2013:** None	**2013:** None	**2013:** None	**2013:** None	**2013:** None
Laura Svetkey	Duke University, Duke Hypertension Center—Professor; Director, Duke Hypertension Center; Director, Clinical Research, Sarah W. Stedman Nutrition and Metabolism Center	**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	University of Pennsylvania Perelman School of Medicine—Professor of Psychology, 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
Susan Yanovski, *Ex-Officio*	National Institute of Diabetes and Digestive and Kidney Diseases, Division of Digestive Diseases and Nutrition—Co-Director, Office of Obesity Research	**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 (RWI) 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/or 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 RWI. 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 RWI, 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.

ACC indicates American College of Cardiology; AHA, American Heart Association; IOM, Institute of Medicine; NHLBI, National Heart, Lung, and Blood Institute; NIH, National Institutes of Health; PI, primary investigator; and USDA, United States Department of Agriculture.

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