Part D. Chapter 6: Cross-Cutting Topics of Public Health Importance

INTRODUCTION

The *Dietary Guidelines for Americans, 2010* included guidance on sodium, saturated fat, and added sugars, and the 2015 DGAC determined that a reexamination of the evidence on these topics was necessary to evaluate whether revisions to the guidance were warranted. These topics were considered to be of public health importance because each has been associated with negative health outcomes when over-consumed. As the Committee considered it essential to address these topics across two or more Subcommittees, Working Groups were formed with representatives from the relevant Subcommittees to ensure that the topics were thoroughly addressed in a coordinated way. Additionally, the Committee acknowledged that a potential unintended consequence of a recommendation on added sugars might be that consumers and manufacturers replace added sugars with low-calorie sweeteners. As a result, the Committee also examined evidence on low-calorie sweeteners to inform statements on this topic. The updated findings in this chapter will help inform recommendations on these topics for the *2015 Dietary Guidelines for Americans*.

Although sodium, saturated fat, and added sugars are receiving particular focus here, it is important to consider these aspects of the diet in the context of a healthy dietary pattern. A healthy dietary pattern has little room for sodium, saturated fat, and added sugars. That said, these components of the diet are modifiable, and strategies at various levels of the socio-ecologic model, ranging from policy to consumer education, can promote shifts in intake to support healthy dietary patterns.

The sodium, saturated fat, and added sugars sections of this chapter provide introductory text related to the topic including the rationale and approach for the Committee's review. Because the questions within each topic are so complementary, the DGAC choose to develop only one implications section for each topic.

LIST OF QUESTIONS

Sodium

1. What is the relationship between sodium intake and blood pressure in adults?
2. What is the relationship between sodium intake and blood pressure in children?
3. What is the relationship between sodium intake and cardiovascular disease outcomes?

4. What effect does the interrelationship of sodium and potassium have on blood pressure and cardiovascular disease outcomes?

Saturated Fat

5. What is the relationship between intake of saturated fat and risk of cardiovascular disease?

Added Sugars and Low-Calorie Sweeteners

6. What is the relationship between the intake of added sugars and cardiovascular disease, body weight/obesity, type 2 diabetes, and dental caries?
7. What is the relationship between the intake of low-calorie sweeteners and body weight/obesity and type 2 diabetes?

METHODOLOGY

To answer the questions in this chapter, the Committee relied on existing reports, original Nutrition Evidence Library (NEL) systematic reviews, and NEL updates. The Committee followed the methods described in ***Part C. Methodology*** without modification to answer these questions. Because the DGAC knew strong existing reports, systematic reviews (SRs), and meta-analyses (MA) were available related to most of the cross-cutting questions, to prevent duplication of efforts, the DGAC relied on these reviews in lieu of conducting original NEL systematic reviews. In some cases, existing reviews, SRs, or MA were not available or required updating. In these cases, NEL systematic reviews or updates were conducted. Complete information on the NEL reviews and updates is provided at www.NEL.gov. The reader also is directed to the original existing reports, which are referenced throughout the chapter, for additional information.

Four questions addressed dietary sodium intake. For Question 1, the Committee used the 2013 National Heart, Lung, and Blood Institute (NHLBI) *Lifestyle Interventions to Reduce Cardiovascular Risk: Systematic Evidence Review from the Lifestyle Work Group*[1] and the associated American Heart Association (AHA)/ American College of Cardiology (ACC) *Guideline on Lifestyle Management to Reduce Cardiovascular Risk.*[2] Although new studies examining the relationship between sodium and blood pressure have been published since the completion of the NHLBI review, including findings from the Prospective Urban Rural Epidemiology (PURE) study,[3] the Committee determined the evidence presented in the SR conducted by NHLBI, linking sodium and blood pressure, was strong and that consideration of more recent findings would not change the conclusions. Thus, the Committee did not update the review. For Question 2, the Committee updated the NEL systematic review on sodium and blood pressure in children conducted by the 2010 DGAC. The data reviewed for this question by the 2010 DGAC included children, birth to age 18, and the 2015 DGAC updated the sodium review

using the same age range. For Question 3, the Committee relied on the NHLBI systematic review from the Lifestyle Work Group[1] as well as the 2013 Institute of Medicine (IOM) report, *Sodium Intake in Populations*.[4] Additionally, because the quality and quantity of the evidence on sodium and cardiovascular disease (CVD) that was used in the two reports is limited, the Committee updated the sodium and CVD review using a NEL systematic review update from January 2013 to July 2014. The final question in the sodium section, Question 4, also was answered using the recent NHLBI systematic review from the Lifestyle Work Group.[1] The Committee also used the 2010 IOM Report on *Strategies to Reduce Sodium Intake in the United States* to inform the implications statements for these questions.[5]

Regarding saturated fat, Question 5 was answered using the NHLBI systematic review[1] and related AHA/ACC *Guideline on Lifestyle Management to Reduce Cardiovascular Risk*,[2] which focused on randomized controlled trials (RCTs), as well as existing SRs and MA addressing this question published in peer-reviewed literature between January 2009 and August 2014. Particular emphasis was placed on reviews that examined the macronutrient replacement for saturated fat.

The remaining questions in this chapter examined added sugars and low-calorie sweeteners. For Question 6, the DGAC relied on systematic reviews commissioned by the World Health Organization (WHO) to address body weight[6] and dental caries.[7] Additionally, to capture new research, the Committee searched for SRs and MA published since January 2012, the completion of the WHO reviews. Type 2 diabetes was not addressed by the WHO, and therefore, the Committee relied on existing SRs/MA published since January 2010 to address this health outcome. No existing SRs/MA examine added sugars and CVD, so the Committee conducted an original NEL systematic review to address this question (see http://NEL.gov/topic.cfm?cat=3376 for complete information on this review). Question 7 on low-calorie sweeteners was answered using existing SRs/MA published from January 2010 to August 2014. For low-calorie sweeteners, the Committee was initially interested in the health outcomes of body weight, type 2 diabetes, CVD, and dental caries. However, existing reviews were available only for body weight and type 2 diabetes. The Committee did not conduct an original NEL systematic review on CVD or dental caries because of limited time and resources, and because the Committee did not think sufficient evidence was available to address these health outcomes.

SODIUM

Introduction

From its first edition in 1980, the *Dietary Guidelines for Americans* consistently recommended the public reduce dietary sodium intakes in order to prevent and treat hypertension, CVD, and

stroke. This recommendation is based on evidence supporting a dose-dependent relationship between sodium intake and blood pressure and observational data identifying associations between sodium intake and blood pressure and cardiovascular outcomes. However, despite many years of accumulating evidence and public health guidelines focused on changing individual behavior to achieve a reduced sodium intake among Americans, consumption continues to far exceed recommendations. The DGAC has identified dietary sodium as a nutrient of public health concern because of overconsumption, with usual intakes for those ages 2 years and older at 3,463 mg/day.[8] Sodium is ubiquitous in the current U.S. food supply and multiple food categories contribute to excessive sodium intake (see ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends,*** Figure D1.35).

Currently, 30 percent of U.S. adults have high blood pressure (see ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends***). Furthermore, the estimated lifetime risk of developing hypertension in the U.S. is 90%. The rate of borderline high blood pressure (defined as a systolic or diastolic blood pressure ≥90th percentile but <95th percentile or blood pressure levels ≥120/80 mm Hg) in youth ages 8 to 17 years is highest in those who are obese (16.2 percent), slightly lower in those who are overweight (11 percent); and this condition is present even in those who are normal weight (5 percent). Dietary sodium reduction can effectively prevent and reduce high blood pressure.[9-11] Given the long-standing awareness of this health concern and scientific foundation for dietary treatment, the DGAC conducted a focused review of dietary sodium and its relationship with blood pressure as well as its relationship with CVD.

Question 1: What is the relationship between sodium intake and blood pressure in adults?

Source of evidence: Existing reports

Conclusions

The DGAC concurs with the three conclusions from the 2013 AHA/ACC Lifestyle Guideline that apply to adults who would benefit from blood pressure lowering.

The DGAC concurs that adults who would benefit from blood pressure lowering should "lower sodium intake." AHA/ACC Grade: Strong; **DGAC Grade: Strong**

The DGAC concurs that adults who would benefit from blood pressure lowering should "Consume no more than 2,400 mg of sodium/day." The report also indicates that "Further reduction of sodium intake to 1,500 mg/d can result in even greater reduction in blood pressure";

and concludes that "Even without achieving these goals, reducing sodium intake by at least 1,000 mg/d lowers blood pressure." AHA/ACC Grade: Moderate; **DGAC Grade: Moderate**

The DGAC concurs that adults who would benefit from blood pressure lowering should "Combine the DASH dietary pattern with lower sodium intake." AHA/ACC Grade: Strong; **DGAC Grade: Strong**

Review of the Evidence

The 2013 AHA/ACC Lifestyle Guideline and associated NHLBI Lifestyle Report summarized strong and consistent evidence that supports dietary sodium reduction as a means to prevent and treat high blood pressure. The studies used to inform the conclusion to lower sodium intake were conducted in older and younger adults, individuals with prehypertension and hypertension, men and women, and African American and non-African American adults. The trials also documented positive effects of sodium reduction that were independent of weight change; and include behavioral interventions where individuals were counseled to reduce sodium, as well as feeding studies.

The recommendation to combine the DASH dietary pattern with lower sodium is based heavily on the results of the DASH sodium trial, which showed clinically significant lowering of blood pressure with sodium intake of 2,400 mg/day and even lower blood pressure with sodium intake of 1,500 mg/day. The goal of 2,400 or less mg/day was selected because it is the estimated average urinary sodium excretion in the DASH sodium trial.

The recommendation to reduce sodium intake by 1,000 mg/day even if goals for 2,400 mg/day or 1,500 mg/day cannot be reached comes from studies where this level of sodium reduction was beneficial for blood pressure lowering.

The differences in the evidence grade for the three conclusions related to sodium and blood pressure in adults results from the differences in the number and power of clinical trials supporting each recommendation. For example, a grade of "moderate" was assigned to the second conclusion because fewer clinical trials informed the goals of 2,400 and 1,500 mg/day than for the overall goal of sodium reduction.

For additional details on this body of evidence, visit: References 1, 2, 4 and 9 and ***Appendix E-2.42***

Question 2: What is the relationship between sodium intake and blood pressure in children?

Source of evidence: Existing systematic review with a NEL systematic review update

Conclusions

The 2015 DGAC concurs with the 2010 DGAC that "a moderate body of evidence has documented that as sodium intake decreases, so does blood pressure in children, birth to age 18 years." **DGAC Grade: Moderate**

Review of the Evidence

The 2010 DGAC conducted a systematic review to examine the relationship between sodium intake and blood pressure in children from birth to age 18 years, examining studies published from January 1970 to May 2009. That systematic review included 19 articles from 15 intervention studies and four prospective cohort studies.

The 2015 DGAC updated this systematic review and identified two additional articles published since May 2009, including one RCT and one prospective cohort study.[12, 13]

The 2015 DGAC considered the evidence reviewed by the 2010 DGAC related to dietary sodium intake and blood pressure in children, and determined that, based on the two new studies identified in the updated search, changes were not warranted to the conclusion statement or grade. In aggregate, the data reviewed by the 2010 DGAC indicated that sodium reduction modestly lowers BP in infants and children. Neither of the two studies identified in the update found a relationship between dietary sodium intake and blood pressure in healthy, normotensive children.

For additional details on this body of evidence, visit:
http://NEL.gov/conclusion.cfm?conclusion_statement_id=250452

Question 3: What is the relationship between sodium intake and cardiovascular disease outcomes?

Source of evidence: Existing report with a NEL systematic review update

Conclusions

The DGAC concurs with the IOM Report: *Sodium Intake in Populations*, which concluded that "although the reviewed evidence on associations between sodium intake and direct health outcomes has methodological flaws and limitations, when considered collectively, it indicates a positive relationship between higher levels of sodium intake and risk of CVD. This evidence is consistent with existing evidence on blood pressure as a surrogate indicator of CVD risk." IOM Grade: Grade not determined, outside the statement of task; **DGAC Grade: Moderate**

The DGAC concurs with the IOM Report: *Sodium Intake in Populations* that "evidence from studies on direct health outcomes is inconsistent and insufficient to conclude that lowering sodium intakes below 2,300 mg/day either increases or decreases risk of CVD outcomes (including stroke and CVD mortality) or all-cause mortality in the general U.S. population." IOM Grade: Grade not determined, outside the statement of task; **DGAC Grade: Grade not assignable**

The DGAC concurs with the NHLBI Lifestyle Report, which concluded that "a reduction in sodium intake by approximately 1,000 mg/day reduces CVD events by about 30 percent" and that "higher dietary sodium intake is associated with a greater risk for fatal and nonfatal stroke and CVD." NHLBI Strength of Evidence: Low; **DGAC Grade: Limited**

The DGAC concurs with the NHLBI Lifestyle Report that "evidence is not sufficient to determine the association between sodium intake and the development of heart failure." NHLBI Strength of Evidence: Not assigned due to insufficient evidence; **DGAC Grade: Grade not Assignable**

Review of the Evidence

The DGAC updated systematic reviews done in 2013 by the IOM[4] and NHLBI,[1] and identified four additional articles published since 2013, all of which were prospective cohort studies.[14-17]

Of note, the evidence reviewed for the 2013 IOM report was published between 2003 and December 2012. The DGAC concluded that the reviewed evidence on associations between sodium intake and direct health outcomes has methodological flaws and limitations. Specifically, the Committee documented the small number of well-conducted studies evaluating sodium intake and direct health outcomes; the inconsistency in findings across the published literature, possibly due to methodological factors; the lack of comparability in sodium intake levels across studies particularity in international studies; and the absence of strong data related to sodium goals and direct health outcomes, not including hypertension.

The DGAC considered the conclusions reached by the IOM and NHLBI related to dietary sodium intake and risk of CVD, and determined that the findings from the four new studies identified in the updated search did not warrant changes to the conclusion statements. In aggregate, the data indicate a relationship between higher sodium intake and higher risk of CVD.

For additional details on this body of evidence, visit:
http://NEL.gov/conclusion.cfm?conclusion_statement_id=250457

Question 4: What effect does the interrelationship of sodium and potassium have on blood pressure and cardiovascular disease outcomes?

Source of evidence: Existing report

Conclusions

The DGAC concurs with the NHLBI Lifestyle Report that: "Evidence is not sufficient to determine whether increasing dietary potassium intake lowers blood pressure." NHLBI Strength of Evidence: Not assigned due to insufficient evidence; **DGAC Grade: Not Assignable**

The DGAC concurs with the NHLBI Lifestyle Report that: "In observational studies with appropriate adjustments (e.g., blood pressure, sodium intake), higher dietary potassium intake is associated with lower risk for stroke." NHLBI Strength of Evidence: Low; **DGAC Grade: Limited**

The DGAC concurs with the NHLBI Lifestyle Report that: "Evidence is not sufficient to determine an association between dietary potassium intake and coronary heart disease (CHD), heart failure, and cardiovascular mortality." NHLBI Strength of Evidence: Not assigned due to insufficient evidence; **DGAC Grade: Grade not Assignable**

Review of the Evidence

The NHLBI Lifestyle Report summarized limited evidence on the relationship between potassium intake and blood pressure, CHD, heart failure, cardiovascular mortality, or stroke. Although it is postulated that a high ratio of sodium intake to potassium intake is a stronger risk factor for hypertension than either factor alone, the evidence base to support this hypothesis is insufficient for drawing definitive conclusions. Although results of epidemiologic studies suggest that potassium consumption influences the risk of CVD, the strength of the evidence is insufficient to draw conclusions about CHD, heart failure, or cardiovascular mortality. The evidence is limited with regard to stroke, coming from studies with weaker designs in which investigators were able to make appropriate statistical adjustments for potential confounders of the relationship.

For additional details on this body of evidence, visit: References 1 and 2

Implications

The current average sodium intake in the United States is 3,478 mg/d, far exceeding recommendations. Given the well-documented relationship between sodium intake and high blood pressure, sodium intake should be reduced and combined with a healthful dietary pattern

(as described in ***Part D. Chapter 2: Dietary Patterns, Foods and Nutrients, and Health Outcomes***).

The general population, ages 2 years and older, should rely on the recommendations of the IOM Panel on Dietary Reference Intakes for Electrolytes and Water.[9] A tolerable upper limit was set by the Panel at 2,300 mg/day based on evidence showing associations between high sodium intake, high blood pressure, and subsequent risk of heart disease, stroke, and mortality. Of note, the AHA/ACC recommendation of less than 2,400 mg/day (see conclusions for sodium question 1) is slightly different than the less than 2,300 mg/day recommended by the IOM Panel on Dietary Reference Intakes or the 2010 Dietary Guidelines for Americans; less than 2,400 mg/day was selected because it was the estimated average urinary sodium excretion in the DASH-sodium trial.

Individuals who would benefit from blood pressure lowering (i.e., those with prehypertension or hypertension), should rely on the recommendations in the 2013 AHA/ACC Lifestyle Guideline. These include: lowering sodium intake in general; or consuming no more than 2,400 mg of sodium/day; or lowering sodium intake to 1,500 mg per day for even greater reduction in blood pressure; or lowering sodium intake by at least 1,000 mg per day even if the goals of 2,400 or 1,500 mg per day cannot be met.

For decades, sodium intake in the United States has exceeded recommendations in spite of numerous national campaigns, through programs such as the NHLBI's National High Blood Pressure Education Program and the CDC's State Heart Disease and Stroke Prevention Program, focused on individual behavior change for sodium reduction. As described in ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends***, sodium is ubiquitous in the U.S. food supply and almost all food categories contribute to intake levels. This unique feature of sodium makes it difficult for individuals to achieve recommended intake. As such, we recommend that a primary emphasis be placed on policies and population-based strategies for sodium reduction while at the same time paying attention to consumer education. Local, state, and Federal agencies should consider a comprehensive and coordinated strategy, that includes partnerships with the food industry, to reduce the sodium content of foods in the United States based on the socio-ecological model highlighted in the 2015 DGAC's conceptual model (see ***Part B. Chapter 1: Introduction***).

These strategies should be consistent with the recommendation described in the 2010 IOM report on *Strategies to Reduce Sodium Intake in the United States*.[5] The primary strategy that was recommended is that "The FDA should expeditiously initiate a process to set mandatory national standards for the sodium content of foods". This would include: 1) "a modification of the generally recognized as safe (GRAS) status of salt added to processed foods in order to reduce the salt content of the food supply in a stepwise manner"; 2) "FDA should likewise extend its

stepwise application of the GRAS modification, adjusted as necessary, to encompass salt added to menu items offered by restaurant/foodservice operations that are sufficiently standardized so as to allow practical implementation"; and 3) "FDA should revisit the GRAS status of other sodium-containing compounds as well as any food additive provisions for such compounds and make adjustments as appropriate, consistent with changes for salt in processed foods and restaurant/foodservice menu items."

Population sodium reductions efforts should consider: 1) the varied technical and functional roles that sodium plays in foods and the complexity of reducing sodium in foods; 2) the recent accomplishments and voluntary reduction efforts by the food industry; and 3) consumer demand for lower-sodium products. More information about strategies for reducing sodium intake in the United States can be found in the IOM report, at http://www.iom.edu/Reports/2010/Strategies-to-Reduce-Sodium-Intake-in-the-United-States.aspx.

Informative food labels should be used to effectively promote awareness of sodium content in foods. Consumers would benefit from a standardized, easily understood front-of-package (FOP) label on all food and beverage products to give clear guidance about a food's healthfulness. An example is the FOP label recommended by the IOM,[18] which included calories, and 0 to 3 "nutritional" points for added sugars, saturated fat, and sodium. This would be integrated with the Nutrition Facts Panel, allowing consumers to quickly and easily identify nutrients of concern for over-consumption, in order to make healthier choices.

Public-private-community partnerships should be created to reduce sodium levels in commercially processed and restaurant foods.

Strategies that complement policies and support consumers to make dietary behavior changes also are needed. These include (but are not limited to): 1) nutrition services and comprehensive lifestyle interventions by multidisciplinary teams;[2] 2) widely available diet planning tools that include sodium as an area of focus; and 3) educational programs that teach adults simple recipes that emphasize flavoring unsalted foods with spices and herbs.

Although the evidence on potassium and blood pressure is limited, the DGAC recognizes potassium as a nutrient of concern (see ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends***) and encourages increased potassium intake through potassium-rich foods such as vegetables and fruits (see Table D1.7).

Interventions, preferably nonpharmacologic, are needed for children because borderline high blood pressure occurs concomitantly with overweight, obesity, and other cardio-metabolic risk factors (see ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends***). Evidence-based strategies in clinical and public health settings need to be implemented

and complemented by environmental approaches to reverse these high priority health problems in children.

For blood pressure lowering and hypertension prevention, action is needed at both the individual and population levels.

Sodium reduction in youth will require changes in their food environments and school and community-based education on healthful eating.

School systems should adopt mandatory age-appropriate nutrition and physical activity curricula (K-12) that incorporate the core principles of the future *2015 Dietary Guidelines*.

SATURATED FAT

Introduction

The relationship between different types of dietary fats and risk of CVD has been extensively studied in RCTs and epidemiologic studies. It is now well-established that higher intake of *trans* fat from partially hydrogenated vegetable oils is associated with increased risk of CVD and thus, should be minimized in the diet. Numerous RCTs have demonstrated that saturated fat (SFA) as compared to mono- (MUFA) or polyunsaturated fats (PUFA) or carbohydrates increases total and LDL cholesterol. Thus, limiting saturated fat consumption has been a longstanding dietary recommendation to reduce risk of CVD. In particular, previous DGACs have recommended consuming no more than 10 percent of daily calories from saturated fat.

However, recent meta-analyses of prospective observational studies did not find a significant association between higher saturated fat intake and risk of CVD in large populations. These data have re-ignited the debate regarding the current recommendation to limit saturated fat intake. Therefore, the DGAC chose to conduct a focused review of published systematic reviews and meta-analyses on saturated fat intake and CVD. A central issue in the relationship between saturated fat and CVD is the specific macronutrients that are used to replace it because consuming unsaturated fats versus carbohydrates in place of saturated fat can have different effects on blood lipids and risk of CVD. Thus, the Committee's assessment of the available evidence puts greater emphasis on the replacement macronutrient for saturated fat.

In the United States, the top sources of foods contributing to saturated fat intake are mixed dishes, particularly burgers and sandwiches, and snacks and sweets (see ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends***). Although saturated fat intake has declined in the past decades, current intake is still high at a median of 11.1 percent of

daily calories (see ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends***). Therefore, saturated fat continues to be an area of public health concern and the DGAC deemed it important to re-evaluate and update the knowledge base on saturated fat intake and CVD risk.

Question 5: What is the relationship between intake of saturated fat and risk of cardiovascular disease?

Source of evidence: Existing reports

Conclusions

Strong and consistent evidence from RCTs shows that replacing SFA with unsaturated fats, especially PUFA, significantly reduces total and LDL cholesterol. Replacing SFA with carbohydrates (sources not defined) also reduces total and LDL cholesterol, but significantly increases triglycerides and reduces HDL cholesterol.

Strong and consistent evidence from RCTs and statistical modeling in prospective cohort studies shows that replacing SFA with PUFA reduces the risk of CVD events and coronary mortality. For every 1 percent of energy intake from SFA replaced with PUFA, incidence of CHD is reduced by 2 to 3 percent. However, reducing total fat (replacing total fat with overall carbohydrates) does not lower CVD risk. Consistent evidence from prospective cohort studies shows that higher SFA intake as compared to total carbohydrates is not associated with CVD risk. **DGAC Grade: Strong**

Evidence is limited regarding whether replacing SFA with MUFA confers overall CVD (or CVD endpoint) benefits. One reason is that the main sources of MUFA in a typical American diet are animal fat, and because of the co-occurrence of SFA and MUFA in foods makes it difficult to tease out the independent association of MUFA with CVD. However, evidence from RCTs and prospective studies has demonstrated benefits of plant sources of monounsaturated fats, such as olive oil and nuts on CVD risk. **DGAC Grade: Limited**

Implications

Recommendations on saturated fat intake should specify replacement macronutrients and emphasize replacing saturated fat with unsaturated fats, especially polyunsaturated fats. The Committee recommends retaining the 10 percent upper limit for saturated fat intake. In practice, non-hydrogenated vegetable oils that are high in unsaturated fats and relatively low in SFA (e.g., soybean, corn, olive, and canola oils) instead of animal fats (e.g., butter, cream, beef tallow, and lard) or tropical oils (e.g., palm, palm kernel, and coconut oils) should be recommended as the primary source of dietary fat. Partially hydrogenated oils containing *trans* fat should be avoided.

In low-fat diets, fats are often replaced with refined carbohydrates and this is of particular concern because such diets are generally associated with dyslipidemia (hypertriglyceridemia and low HDL-C concentrations). Therefore, dietary advice should put the emphasis on optimizing types of dietary fat and not reducing total fat.

When individuals reduce consumption of refined carbohydrates and added sugars, they should not replace them with foods high in saturated fat. Instead, refined carbohydrates and added sugars should be replaced by healthy sources of carbohydrates (e.g., whole grains, legumes, vegetables, and fruits), and healthy sources of fats (e.g., non-hydrogenated vegetable oils that are high unsaturated fats, and nuts/seeds). The consumption of "low-fat" or "nonfat" products with high amounts of refined grains and added sugars should be discouraged.

Dietary recommendations on macronutrient composition for reducing CVD risk should be dietary pattern-based emphasizing foods that characterize healthy dietary patterns (see ***Part D. Chapter 2: Dietary Patterns, Foods and Nutrients, and Health Outcomes***). Individuals are encouraged to consume dietary patterns that emphasize vegetables, fruits, whole grains, legumes, and nuts; include low- and non-fat dairy products, poultry, seafood, non-tropical vegetable oils; limit sodium, saturated fat, refined grains, sugar-sweetened foods and beverages, and are lower in red and processed meats. Multiple dietary patterns can achieve these food and nutrient patterns and are beneficial for cardiovascular health, and they should be tailored to individuals' biological needs and food preferences.

Review of the Evidence

The DGAC drew evidence from SRs or MA published between January 2009 and August 2014 in English in a peer-reviewed journal, which included RCTs and/or prospective cohort studies. Participants included healthy volunteers as well as individuals at elevated chronic disease risk. The main exposure was SFA, and the main outcomes included LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), triglycerides (TG), blood pressure (BP), and incidence of CVD and CHD, CVD- and CHD-related death, myocardial infarction, or stroke. All reviews were high-quality, with ratings ranging from 8 to 11 on AMSTAR. The Committee drew evidence on blood lipids and blood pressure outcomes from the AHA/ACC Lifestyle Guideline and the associated NHLBI Lifestyle Report, which included primarily RCTs on intermediate CVD risk factors. The Committee drew evidence on CVD endpoints and effect size estimates from seven published MA that included one or more studies not covered in these reports.[19-25] Little evidence on the contribution of SFA to cardiovascular risk factors in the pediatric populations was available, and that which was published has not been systematically reviewed.

Effects of Replacing SFA on LDL-C, HDL-C, and TG

Macronutrients may affect plasma lipids and lipoproteins, which are strong predictors of CVD risk. The NHLBI Lifestyle Report summarized evidence from three feeding trials examining effects on LDL-C of dietary patterns with varying SFA levels: DASH (Dietary Approaches to Stop Hypertension), DASH-Sodium, and DELTA (Dietary Effects on Lipoproteins and Thrombogenic Activity). The results from these trials indicate that reducing total and saturated fat led to a significant reduction in LDL cholesterol in the context of the DASH dietary pattern and the National Cholesterol Education Program (NCEP) Step 1 diet. To estimate the effects of replacing SFA by specific macronutrients such as carbohydrates, MUFA, or PUFA, the NHLBI Lifestyle Report also included two MA from Mensink and Katan (n=1,672), covering the period from 1970 to 1998 (27 controlled trials in the first MA and 60 controlled trials in the second MA) and using the same inclusion/exclusion criteria to estimate changes in plasma lipids when substituting dietary SFA with carbohydrates or other fat types and holding dietary cholesterol constant.[26, 27] Mensink and Katan found that replacing 1 percent of SFA with an equal amount of carbohydrates, 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 carbohydrates, MUFA, or PUFA also lowered HDL-C by 0.4, 1.2, and 0.2 mg/dL, respectively. Replacing 1 percent of carbohydrates 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. The 2003 MA by Mensink and Katan[27] indicated that the ratio of total to HDL-C, a stronger predictor of CVD risk than total or LDL cholesterol alone, did not change when SFA was replaced by carbohydrates, but the ratio significantly decreased when SFA was replaced by unsaturated fats, especially PUFA.

In summary, strong and consistent evidence from RCTs shows that replacing SFA with unsaturated fats, especially PUFA, significantly reduces total and LDL cholesterol. Replacing SFA with carbohydrates also reduces total and LDL cholesterol, but significantly increases TG and reduces HDL cholesterol. However, the evidence of beneficial effects on one risk factor does not rule out neutral or opposite effects on unstudied risk factors. To better assess the overall effects of intervention to reduce or modify SFA intake, studies of clinical endpoints are summarized below.

The Relationship between Consumption of Total Fat and SFA and Risk of CVD

A MA by Skeaff et al. in 2009 included 28 U.S. and European cohorts (6,600 CHD deaths among 280,000 participants) and found no clear relationship between total or SFA intake and CHD events or deaths.[25] Similarly, Siri-Tarino et al., 2010 found that SFA intake was not associated with risk of CHD, stroke or cardiovascular disease.[24] The Siri-Tarino et al., 2010 meta-analysis included data from 347,747 participants (11,006 developed CVD) in 21 unique studies, with 16 studies providing risk estimates for CHD and 8 studies providing data for stroke as an endpoint. In the 2012 MA of trials to reduce or modify intake of SFA, Hooper et al. also found no significant associations of total fat reduction with cardiovascular events or mortality.

Consistent with these prior studies, Chowdhury et al.'s 2014 MA of total SFA also did not specify what macronutrient substituted SFA and again found no association of dietary SFA intake, nor of circulating SFA, with coronary disease.[19] Chowdhury et al. included data from 32 observational studies (530,525 participants) of fatty acids from dietary intake, 17 observational studies (25,721 participants) of fatty acid biomarkers, and 27 RCTs (103,052 participants) of fatty acid supplementation.

The results described above do not explicitly specify the comparison or replacement nutrient, but typically it consists largely of carbohydrates (sources not defined). These results suggest that replacing SFA with carbohydrates is not associated with CVD risk. Taken together, these results suggest that simply reducing SFA or total fat in the diet by replacing it with any type of carbohydrates is not effective in reducing risk of CVD.

Effects of Replacing SFA with Polyunsaturated Fat or Carbohydrates on CVD Events

Hooper et al.'s 2012 Cochrane MA of trials of SFA reduction/modification found that reducing SFA by reducing and/or modifying dietary fat reduced the risk of cardiovascular events by 14 percent (pooled RR = 0.86; 95% CI = 0.77 to 0.96, with 24 comparisons and 65,508 participants of whom 7 percent had a cardiovascular event, I= 50%).[21] Subgroup analyses revealed this protective effect was driven by dietary fat *modification* rather than reduction and was only apparent in longer trials (2 years or more). Despite the reduction in total cardiovascular events, there was no clear evidence of reductions in any individual outcome (total or non-fatal myocardial infarction, stroke, cancer deaths or diagnoses, diabetes diagnoses), nor was there any evidence that trials of reduced or modified SFA reduced cardiovascular mortality. These results suggest that modifying dietary fat by replacing some saturated (animal) fats with plant oils and unsaturated spreads may reduce risk of heart and vascular disease.

Emphasizing the benefits of replacement of saturated with polyunsaturated fats, Mozaffarian et al., 2010 found in a MA of 8 trials (13,614 participants with 1,042 CHD events) that modifying fat reduced the risk of myocardial infarction or coronary heart disease death (combined) by 19 percent (RR = 0.81; 95% CI = 0.70 to 0.95; p = 0.008), corresponding to 10 percent reduced CHD risk (RR = 0.90; 95% CI = 0.83 to 0.97) for each 5 percent energy of increased PUFA.[23] This magnitude of effect is similar to that observed in the Cochrane MA. In secondary analyses restricted to CHD mortality events, the pooled RR was 0.80 (95% CI = 0.65 to 0.98). In subgroup analyses, the RR was greater in magnitude in the four trials in primary prevention populations but non-significant (24 percent reduction in CHD events) compared to a significant reduction of 16 percent in the four trials of secondary prevention populations. Mozaffarian et al. argue that the slightly greater risk reduction in studies of CHD events, compared with predicted effects based on lipid changes alone, is consistent with potential additional benefits of PUFA on other non-lipid pathways of risk, such as insulin resistance. Many of the included trials used

vegetable oils containing small amounts of plant-derived n-3 PUFA in addition to omega-6 PUFA.

Consistent with the benefits of replacing SFA with PUFA for prevention of CHD shown in other studies, Farvid et al., 2014 conducted an SR and MA of prospective cohort studies of dietary linoleic acid (LA), which included 13 studies with 310,602 individuals and 12,479 total CHD events (5,882 CHD deaths).[20] Farvid et al. found dietary LA intake is inversely associated with CHD risk in a dose-response manner: when comparing the highest to the lowest category of intake, LA was associated with a 15 percent lower risk of CHD events (pooled RR = 0.85; 95% CI = 0.78 to 0.92; I^2=35.5%) and a 21% lower risk of CHD deaths (pooled RR = 0.79; 95% CI = 0.71 to 0.89; I^2=0.0%). A 5 percent of energy increment in LA intake replacing energy from SFA intake was associated with a 9 percent lower risk of CHD events (RR = 0.91; 95% CI = 0.86 to 0.96) and a 13 percent lower risk of CHD deaths (RR = 0.87; 95% CI = 0.82 to 0.94). In the meta-analysis conducted by Chowdhury et al., there was no significant association between LA intake and CHD risk, but the analysis was based on a limited number of prospective cohort studies.

In Jakobsen et al.'s 2009 pooled analysis of 11 cohorts (344,696 persons with 5,249 coronary events and 2,155 coronary deaths), a 5 percent lower energy intake from SFAs and a concomitant higher energy intake from PUFAs reduced risk of coronary events by 13 percent (hazard ratio [HR] = 0.87; 95% CI = 0.77 to 0.97) and coronary deaths by 16 percent (hazard ratio = 0.74; 95% CI = 0.61 to 0.89).[22] By contrast, a 5 percent lower energy intake from SFAs and a concomitant higher energy intake from carbohydrates, there was a modest significant direct association between carbohydrates and coronary events (hazard ratio = 1.07; 95% CI = 1.01 to 1.14) and no association with coronary deaths (hazard ratio = 0.96; 95% CI = 0.82 to 1.13). Notably, the estimated HRs for carbohydrate intake in this study could reflect high glycemic carbohydrate intake rather than total carbohydrate, as fiber was controlled for in the analyses. MUFA intake was not associated with CHD incidence or death.

Taken together, strong and consistent evidence from RCTs and statistical modeling in prospective cohort studies shows that replacing SFA with PUFA reduces the risk of CVD events and coronary mortality. For every 1 percent of energy intake from SFA replaced with PUFA, incidence of CHD is reduced by 2 to 3 percent. The evidence is not as clear for replacement by MUFA or replacement with carbohydrate, and likely depends on the type and source.

Methodological Issues

When individuals in natural settings reduce calories from SFA, they typically replaced them with other macronutrients, and the type and source of the macronutrients substituting SFA determine effects on CVD. For this reason, studies specifying the macronutrient type replacing SFA are more informative than those examining only total SFA intake, and the strongest and most

consistent evidence for CVD reduction is with replacement of SFA with PUFA in both RCTs and observational studies.

The differing effects of the type and source of macronutrient substituted may be one reason for the limited evidence regarding whether replacing SFA with MUFA confers CVD benefits and the lack of benefit from carbohydrate substitution. The main sources of MUFA in a typical American diet are animal fats, which could confound potential benefits of SFA-replacement with plant-source MUFA, such as nuts and olive oil, which have demonstrated benefits on CVD risk. To date, evidence testing replacement of SFA by MUFA from different sources is insufficient to reach a firm conclusion. Similarly, most analyses did not distinguish between substitution of saturated fat by different types of carbohydrates (e.g., refined carbohydrate vs. whole grains).

Of the RCTs included in this evidence summary, the intervention methods used varied from long-term dietary counseling with good generalizability but variable compliance, to providing a whole diet for weeks (e.g., controlled feeding studies) with maximal compliance but limited generalizability. Though the content of the recommended or provided diet is known with greater precision in the RCTs than in observational studies, adherence to the diet is likely variable and could result in lack of compliance and high rates of dropout in long-term trials. Additionally, bias may arise from the lack of blinding in non-supplement dietary intervention trials.

In prospective observational studies, misclassification of dietary fatty acid intake could bias associations towards the null. In addition, residual confounding by other dietary and lifestyle factors cannot be ruled out through statistical adjustment. Despite these methodological issues, there is high consistency of the evidence from prospective cohort studies and RCTs in supporting the benefits of replacing saturated fat with unsaturated fats especially PUFA in reducing CVD risk.

For additional details on this body of evidence, visit: References 1, 2, 19-25 and ***Appendix E-2.43***

ADDED SUGARS AND LOW-CALORIE SWEETENERS

INTRODUCTION

Added sugars are sugars that are either added during the processing of foods, or are packaged as such, and include sugars (free, mono- and disaccharides), syrups, naturally occurring sugars that are isolated from a whole food and concentrated so that sugar is the primary component (e.g., fruit juice concentrates), and other caloric sweeteners.[28] Added sugars have been discussed in

previous iterations of the *Dietary Guidelines*, including a key recommendation in the *2010 Dietary Guidelines* to "Reduce the intake of calories from solid fats and added sugars." The *2010 Dietary Guidelines* also included guidance stating that, for most people, no more than about 5 to 15 percent of calories from solid fats and added sugars (combined) can be reasonably accommodated in a healthy eating pattern. However, as discussed in ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends***, the current intake of added sugars still remains high at 268 calories, or 13.4 percent of total calories per day among the total population ages 1 year and older.

Similar to the healthy eating patterns modeled for the 2010 DGAC, in the three healthy eating patterns modeled for the 2015 DGAC (Healthy U.S.-style Pattern, Healthy Mediterranean-style Pattern, and Healthy Vegetarian Pattern), a limited number of calories are available to be consumed as added sugars (see ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends***). As shown in Table D.6.1, the full range of these three patterns at all calorie levels allow for 3 to 9 percent of calories from added sugars, after meeting food group and nutrient recommendations. For the patterns appropriate for most people (1600 to 2400 calories), the range is 4 to 6 percent of calories from added sugars (or 4.5 to 9.4 teaspoons). The total empty calorie allowance in these patterns is 8 to 19 percent of calories, and based on current consumption patterns, 45 percent of empty calories are allocated to limits for added sugars, with the remainder (55 percent) allocated to solid fats.

Table D6.1. Added sugars available in the USDA Food Patterns (Healthy U.S.-Style, Healthy Mediterranean-Style, and Healthy Vegetarian Patterns) in calories, teaspoons, and percent of total calories per day*

CALORIE LEVEL	1000	1200	1400	1600	1800	2000	2200	2400	2600	2800	3000	3200
	Empty calorie limits available for **added sugars** (assuming 45% empty calories from added sugars and 55% from solid fat)											
Healthy U.S.-style	68	50	50	54	77	122	126	158	171	180	212	275
Healthy Med-style	63	50	50	81	72	117	126	135	149	158	194	257
Healthy Vegetarian	77	77	81	81	81	131	131	158	158	158	185	234
Average	69	59	60	72	77	123	128	150	159	165	197	255
Average (tsp)	4.3	3.7	3.8	4.5	4.8	7.7	8.0	9.4	9.9	10.3	12.3	15.9
Healthy U.S.-style	7%	4%	4%	3%	4%	6%	6%	7%	7%	6%	7%	9%
Healthy Med-style	6%	4%	4%	5%	4%	6%	6%	6%	6%	6%	6%	8%
Healthy Vegetarian	8%	6%	6%	5%	5%	7%	6%	7%	6%	6%	6%	7%
Average	7%	5%	4%	5%	4%	6%	6%	6%	6%	6%	7%	8%

* See ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends*** and Appendix E-3.7 for a full discussion of the food pattern modeling.

Although food pattern modeling evaluates the amount of added sugars that can be consumed while meeting food group and nutrient needs, the DGAC also reviewed scientific literature examining the relationship between the intake of added sugars and health to inform recommendations. The Committee focused on the health outcomes most commonly researched related to added sugars, specifically, body weight and risk of type 2 diabetes, CVD, and dental caries.

As noted above, the Committee acknowledged that a potential unintended consequence of a recommendation on added sugars might be that consumers and manufacturers replace added sugars with low-calorie sweeteners. As a result, the Committee also examined evidence on low-calorie sweeteners to inform statements on this topic. The Committee approached this topic broadly, including sweeteners labeled as low-calorie sweeteners, non-caloric sweeteners, non-nutritive sweeteners, artificial sweeteners, and diet beverages. This work is complemented by a food safety evidence review on aspartame (see ***Part D. Chapter 5: Food Sustainability and Safety***). As the evidence on added sugars was considered collectively, the added sugars conclusions are presented together below, and a similar approach was taken for low-calorie sweeteners.

Question 6: What is the relationship between the intake of added sugars and cardiovascular disease, body weight/obesity, type 2 diabetes, and dental caries?

Source of evidence: CVD: NEL systematic review; Body weight/obesity, type 2 diabetes, and dental caries: Existing reports

Conclusions

Strong and consistent evidence shows that intake of added sugars from food and/or sugar-sweetened beverages are associated with excess body weight in children and adults. The reduction of added sugars and sugar-sweetened beverages in the diet reduces body mass index (BMI) in both children and adults. Comparison groups with the highest versus the lowest intakes of added sugars in cohort studies were compatible with a recommendation to keep added sugars intake below 10 percent of total energy intake. **DGAC Grade: Strong**

Strong evidence shows that higher consumption of added sugars, especially sugar-sweetened beverages, increases the risk of type 2 diabetes among adults and this relationship is not fully explained by body weight. **DGAC Grade: Strong**

Moderate evidence from prospective cohort studies indicates that higher intake of added sugars, especially in the form of sugar-sweetened beverages, is consistently associated with increased risk of hypertension, stroke, and CHD in adults. Observational and intervention studies indicate a consistent relationship between higher added sugars intake and higher blood pressure and serum triglycerides. **DGAC Grade: Moderate**

The DGAC concurs with the World Health Organization's commissioned systematic review that moderate consistent evidence supports a relationship between the amount of free sugars intake and the development of dental caries among children and adults. Moderate evidence also indicates that caries are lower when free sugars intake is less than 10 percent of energy intake. **DGAC Grade: Moderate**

Review of the Evidence

Added Sugars and Body Weight/Obesity

These findings come from three recent reports, all using SRs and MA that examined the relationship between the intake of added sugars and measures of body weight.[6, 29, 30] Te Morenga et al.[6] considered "free sugars," * while Malik[29] and Kaiser et al.[30] focused on sugar-sweetened

* Free sugar is defined by WHO as "all monosaccharides and disaccharides added to foods by the manufacturer, cook, or consumer, plus sugars naturally present in honey, syrups, and fruit juices." It is used to distinguish between the sugars that are naturally present in fully unrefined carbohydrates such as brown rice, whole wheat pasta, and fruit and those sugars (or carbohydrates) that have been, to some extent, refined

beverages. All reviews reported on body weight. The Te Morenga report also reported on body fatness. In the Te Morenga et al. study, 30 trials and 38 cohort studies were included in the analyses. In the Malik et al. study, 10 trials and 22 cohort studies were included in the analyses. Kaiser et al. provided an updated meta-analysis to a previous publication (Mattes[31]) and included a total of 18 trials. In total, 92 articles were considered in these reviews, of which 21 were included in two or more reviews. Children and adults were included in the analyses as were females and males. Diverse demographics (race/ethnicity and geographic location) also were represented by the participants in the respective research studies. All three reviews were high-quality, with ratings of 11 out of 11 using the AMSTAR tool, and they specifically addressed the Committee's question of interest.

The reviews by Malik et al. and Te Morenga et al. were very consistent. The findings from both reports provide strong evidence that among free-living people consuming ad libitum diets, the intake of added sugars or sugar-sweetened beverages is associated with unfavorable weight status in children and adults. Increased added sugars intake is associated with weight gain; decreased added sugars intake is associated with decreased body weight. Although a dose response cannot be determined at this time, the data analyzed by Te Morenga et al. support limiting added sugars to no more than 10 percent of daily total energy intake based on lowest versus highest intakes from prospective cohort studies. Te Morenga et al. state that, "despite significant heterogeneity in one meta-analysis and potential bias in some trials, sensitivity analyses showed that the trends were consistent and associations remained after these studies were excluded." Despite these limitations the DGAC gave this evidence a grade of **Strong**, as the limitations are those inherent to the primary research on which they are based, notably inadequacy of dietary intake data and variations in the nature and quality of the dietary interventions.

The Kaiser et al. review concluded that the currently available randomized evidence for the effects of reducing sugar-sweetened beverage intake on obesity is equivocal. However, the DGAC noted methodological issues with this review, particularly the inclusion of both efficacy studies (in more controlled settings) and effectiveness studies (in real world). The outcomes from the effectiveness trials vary substantially, depending how effective the interventions are. As a result, the Committee viewed the reviews by Te Morenga et al. and Malik et al. to be stronger than the Kaiser et al. review.

Added Sugars and Type 2 Diabetes

Evidence for this question and conclusion came from five SRs and MA published between January 2010 and August 2014.[33-37] Four of the reviews focused on sugar-sweetened

(normally by humans but sometimes by animals, such as the free sugars present in honey). They are referred to as "sugars" since they cover multiple chemical forms, including sucrose, glucose, fructose, dextrose, and others.[32]

beverages[33-35, 37] and one review examined sugar intake.[36] Combined, a total of 17 articles were considered in these reviews, of which nine were included in two or more reviews. Increased consumption of sugar-sweetened beverages was consistently associated with increased risk of type 2 diabetes. Pooled estimated relative risks ranged from 1.20 to 1.28, and included 1.20 (95% CI = 1.12 to 1.29)/330 ml/day of sugar-sweetened soft drinks;[33]1.26 (95% CI = 1.12 to 1.41) for sugar-sweetened beverages,[35] and 1.28 (95% CI = 1.04 to 1.59) for sugar-sweetened fruit juices.[37] Comparably, a hazard ratio of 1.29 (1.02, 1.63) was identified for sugar-sweetened beverages.[34] These consistently positive associations between sugar-sweetened beverages and type 2 diabetes were attenuated, but still existed, after adjustment for BMI, suggesting that body weight only partly explains the deleterious effects of sugar-sweetened beverages on type 2 diabetes. Although the studies were highly heterogeneous, findings from the MA by Malik et al. tentatively showed that consumption of more than one 12-ounce serving per day of sugar-sweetened beverage increased the risk of developing type 2 diabetes by 26 percent, compared to consuming less than one serving per month. Insufficient high-quality data are available to determine a dose-response line or curve between sugar-sweetened beverage consumption and type 2 diabetes risk.

The issue of generalizability, whether the participants included in this body of evidence are representative of the general U.S. population, was not specifically addressed in the literature reviewed, but the large sample sizes of the pooled data (several hundred thousand subjects from different populations) are noteworthy.

Added Sugars and Cardiovascular Disease

This NEL systematic review included 23 articles published since 2000 that examined the relationship between added sugars and risk of CVD or CVD risk factors such as blood lipids and blood pressure.[38-60] This literature included 11 intervention studies and 12 prospective cohort studies.

The majority of intervention and observational studies included in this SR provide some evidence among adults in support of an association between higher intake of added sugars, especially in the form of sugar-sweetened beverages, and higher risk of CVD or increased CVD risk factors. More consistent associations were seen between added sugars and elevated serum triglycerides, blood pressure, and increased risk of hypertension, stroke, or CHD. Evidence for associations between added sugars and dyslipidemia (i.e., low HDL, high LDL, and high total cholesterol) was not as consistent, especially among intervention studies.

The body of evidence examined in this SR had a number of limitations. For example, the intervention studies had extensive heterogeneity in terms of the types and forms of sugars used (i.e., fructose, glucose, sucrose, sugar-sweetened beverages, sweetened milk) and the type of control and/or isocaloric condition used. In addition, most intervention studies had a short

duration of the intervention and a small sample size. Most of the observational studies assessed dietary intake only at baseline, and did not take assessments during follow-up. Residual confounding by other dietary and lifestyle factors in observational analyses could not be completely ruled out.

Added Sugars and Dental Caries

These findings were extracted from a World Health Organization (WHO)-commissioned SR by Moynihan et al. published in 2014 examining the association between the amount of sugars intake and dental caries.[7] The search for SRs/MA published since completion of the WHO review did not yield any additional reviews that met the DGAC's inclusion criteria.

Moynihan et al. examined total sugars, free sugars, added sugars, sucrose, and non-milk extrinsic (NME) sugars. In the review, eligible studies reported the absolute amount of sugars. Dental caries outcomes included caries prevalence, incidence and/or severity.

Several databases were searched from 1950 through 2011. From 5,990 papers identified, 55 studies (from 65 papers) were eligible, including 3 interventions, 8 cohort studies, 20 population studies, and 24 cross-sectional studies. No RCTs were included. Data variability limited the ability to conduct meta-analysis. Of the 55 studies included in the review, the majority were in children and only four studies were conducted in adults. The terminology used for reporting sugars varied, but most were described as pertaining to free sugars or added sugars.

The findings indicated consistent evidence of moderate quality supporting a relationship between the amount of sugars consumed and dental caries development across age groups. Of the studies, 42 out of 50 studies in children and five out of five in adults reported at least one result for an association between sugars intake with increased caries. Moderate evidence also showed that caries incidence is lower when free sugars intake is less than 10 percent of energy intake. When a less than 5 percent energy intake cutoff was used, a significant relationship between sugars and caries was observed, but the evidence was judged to be of very low quality. Although meta-analysis was limited, analysis of existing data indicated a large effect size (e.g., Standardized Mean Difference for Decayed/Missing/Filled Teeth [DMFT] = 0.82 [CI = 0.67-0.97]) for the relationship of sugars intake and risk of dental caries. A strength of the in-depth SR was the consistency of data, despite methodological weaknesses in many studies, which included unclear definitions of endpoints, questions about outcomes ascertainment, and lack of clarity about the generalizability of individual study results given the study populations used.

For additional details on this body of evidence, visit: References 6, 7, 29, 30, 33-37, and 38-60 and ***Appendices E-2.44*** *(body weight),* ***E-2.45*** *(type 2 diabetes),* ***E-2.46*** *(dental caries),* and http://NEL.gov/topic.cfm?cat=3376 *(CVD)*

Question 7: What is the relationship between the intake of low-calorie sweeteners and body weight/obesity and type 2 diabetes?

Source of evidence: Existing reports

Conclusions

Moderate and generally consistent evidence from short-term RCTs conducted in adults and children supports that replacing sugar-containing sweeteners with low-calorie sweeteners reduces calorie intake, body weight, and adiposity. **DGAC Grade: Moderate**

Long-term observational studies conducted in children and adults provide inconsistent evidence of an association between low-calorie sweeteners and body weight as compared to sugar-containing sweeteners. **DGAC Grade: Limited**

Long-term observational studies conducted in adults provide inconsistent evidence of an association between low-calorie sweeteners and risk of type 2 diabetes. **DGAC Grade: Limited**

Review of the Evidence

Low-Calorie Sweeteners and Body Weight/Obesity

The evidence to support these conclusions comes from three SRs/MA published between January 2010 and August 2014.[61-63] In total, 39 articles were considered in these reviews, of which six were included in two or more reviews. Experimentally, the protocols described in the 39 articles included RCTs and prospective cohort studies. Although results from both experimental designs were carefully assessed, the DCAC deemed evidence from RCTs to be scientifically stronger and used it as the foundation for conclusions pertaining to body weight.

Among prospective cohort studies, low-calorie sweetener intake was not associated with body weight or fat mass, but was significantly associated with slightly higher BMI (0.03; 95% CI = 0.01 to 0.06).[62] These findings should be viewed with caution, however, because of the high risk of reverse causality and the possibility that people with higher body weights would consume more low-calorie sweetener-containing foods and beverages as a weight-control strategy.

Evidence from short-term RCTs consistently indicated that low-calorie sweeteners (vs. sugar-containing foods and beverages) modestly reduce body weight in adults. When evidence from adults and children were combined, low-calorie sweeteners modestly reduced BMI, fat mass, and waist circumference. The primary research articles used by Miller and Perez for the MA contained findings from both adults (n=5 cohorts) and children (n=4 cohorts).[62] The results of interventions lasting 3 to 78 weeks indicated that low-calorie sweeteners reduced body weight in adults (-0.72 kg; 95% CI = -1.15 to -0.30) and children (-1.06 kg; 95% CI = -1.17 to -0.56). Age-

887 specific results were not provided for BMI, fat mass, or waist circumference, but data from both
888 age groups were pooled to show the impact of low-calorie sweeteners vs. sugar-containing
889 foods/beverages on these outcomes.
890
891 In contrast, Brown et al. summarized that very limited evidence from three short-term (12 to 25
892 week) RCTs, which suggested that consumption of low-calorie sweeteners does not influence
893 body weight or BMI in predominantly pre-teenage and teenage youth (ages 10 to 21 years),
894 compared to sugar-sweetened beverage or placebo.[61] The authors cautioned that insufficient data
895 exist to assess causality of low-calorie sweeteners on body weight. The evidence reported in this
896 2010 publication was obtained from very heterogeneous experimental designs and interventions.
897 One study tested the effects of encapsulated aspartame vs. placebo during weight loss; another
898 allowed subjects to exchange sugar-sweetened beverages with either low-calorie sweetener
899 beverages or water (precluding assessment of low-calorie sweetener beverages specifically); and
900 a third was described as a "pilot study."
901
902 Collectively, evidence is mixed on the impact of low-calorie sweeteners vs. sugar-containing
903 foods/beverages on body weight in children. However, the DGAC deemed evidence presented by
904 Miller and Perez[62] to be stronger than from Brown et al.[61] because it culminated from a larger,
905 more recent research base and include both systematic review and meta-analysis assessment and
906 evaluation techniques.
907
908 ***Low-Calorie Sweeteners and Type 2 Diabetes***
909 Evidence to address the impact of low-calorie sweeteners (specifically artificially sweetened soft
910 drinks, ASSD) on risk of type 2 diabetes comes from two SRs/MA published between January
911 2010 and August 2014.[33, 34] The data from one of the reviews also is represented in the second
912 review.
913
914 Greenwood et al. reported that higher consumption of ASSD predicts increased risk of type 2
915 diabetes.[33] The summary RR for ASSD on type 2 diabetes risk was 1.13 (95% CI = 1.02 to 1.25,
916 $p<0.02$) per 330 ml/day, based on four analyses from three prospective observational studies.
917 Although the finding indicates a positive association between ASSD and type 2 diabetes risk, the
918 trend was not consistent and may indicate an alternative explanation, such as confounding by
919 lifestyle factors or reverse causality (e.g., individuals with higher BMI at baseline may use
920 ASSD as a means to control weight).
921
922 Romaguera et al. also reported that higher consumption of ASSD was associated with increased
923 risk of type 2 diabetes.[34] In adjusted models, one 336 g (12 oz) daily increment in ASSD
924 consumption was associated with a hazard ratio for type 2 diabetes of 1.52 (95% CI = 1.26 to
925 1.83). High consumers of ASSD showed almost twice the hazard ratio of developing type 2
926 diabetes compared with low consumers (adjusted HR = 1.93; 95% CI = 1.47 to 2.54; p for trend

<0.0001). However, the association was attenuated and became statistically not significant when BMI was included in the model (HR = 1.13, 95% CI = 0.85 to 1.52; p for trend = 0.24). The authors offered these interpretations of the findings: "In light of these findings, we have two possible explanations of the association between artificially sweetened soft drinks and diabetes: (1) the observed association is driven by reverse causality and residual confounding, given that the underlying health of people consuming artificially sweetened soft drinks may be compromised and their risk of type 2 diabetes increased; or (2) the association between artificially sweetened soft drinks and type 2 diabetes is mediated through increased BMI." The authors argued that explanation 1 is more likely correct based on reverse causality, but new research would be needed to clarify the issue.

Collectively, both studies report a positive association between ASSD and type 2 diabetes risk that was confounded by baseline BMI. The experimental designs of the studies included in these reviews analyzed associations, but precluded the assessment of cause and effect relationships, and future experimental studies should examine the relationship between ASSD and biomarkers of insulin resistance and other diabetes biomarkers.

For additional details on this body of evidence, visit: References 33, 34, and 61-63 and ***Appendices E-2.47*** (body weight) and ***E-2.48*** (type 2 diabetes)

Implications

Obesity, type 2 diabetes, CVD, and dental caries are major public health concerns. Added sugars intake negatively impacts all of these conditions, and strong evidence supports reducing added sugars intake to reduce health risks. Added sugars are frequently used in food/beverage processing and provide calories but no other nutrients. Since 39 percent of added sugars are from sugar-sweetened beverages, efforts are needed to reduce these beverages (see Figure D1.36. Food Sources of Added Sugars). Currently, the mean intake of added sugars in the U.S. population is 13%, and from 15% to 17% in children 9 and older, adolescents, and young adults.

The DGAC recommends limiting added sugars to a maximum of 10% of total daily caloric intake. This recommendation is supported by: 1) the food pattern modeling analysis conducted by the 2015 DGAC and 2) the scientific evidence review on added sugars and chronic disease risk conducted by the Committee. The food pattern analysis, based on the Healthy U.S.-Style Pattern, the Healthy Vegetarian Pattern, and the Healthy Mediterranean-Style Pattern (see ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends*** and ***Appendix E-3.7***), demonstrates that when added sugars in foods and beverages exceeds 3% to 9% of total calories, depending on calorie level, a healthful food pattern may be difficult to achieve and nutrient density may be adversely affected (Table D6.1). The scientific evidence on added sugars and chronic disease risk also supports this limit.

The recommendation to limit added sugars, especially sugar-sweetened beverages, is consistent with recommendations from national and international organizations including the American Academy of Pediatrics, World Health Organization, American Heart Association, Centers for Disease Control and Prevention, and the American Diabetes Association (Table D6.2).

When low-calorie sweeteners are used to replace sugar, the resulting reduction in calories can help to achieve short-term weight loss. However, there is insufficient evidence (due to a paucity of data) to recommend the use of low-calorie sweeteners as a strategy for long-term weight loss and weight maintenance. Since the long-term effects of low-calorie sweeteners are still uncertain, those sweeteners should not be recommended for use as a primary replacement/substitute for added sugars in foods and beverages.

Policies and programs at local, state, and national levels in both the private sector and public sector are necessary to support efforts to lower added sugars in beverages and foods and to limit availability of sugar-sweetened beverages and snacks. Suggested specific approaches for reducing added sugars intake include:

- Water is the preferred beverage choice. Strategies are needed to encourage the US population, especially children and adolescents, to drink water when they are thirsty. Water provides a healthy, low-cost, zero-calorie beverage option. Free, readily accessible, safe water should be available in public settings, as well as child care facilities, schools, worksites and other community places and promoted in all settings where beverages are offered.
- The Nutrition Facts Panel (NFP) should include added sugars (in grams and teaspoons) and include a percent daily value, to assist consumers in making informed dietary decisions by identifying the amount of added sugars in foods and beverages.
- Consumers would benefit from a standardized, easily understood front-of-package (FOP) label on all food and beverage products to give clear guidance about a food's healthfulness. An example is the FOP label recommended by the IOM,[18] which included calories, and 0 to 3 "nutritional" points for added sugars, saturated fat, and sodium. This would be integrated with the NFP, allowing consumers to quickly and easily identify nutrients of concern for over-consumption, in order to make healthier choices.
- Economic and pricing approaches, using incentives and disincentives should be explored to promote the purchase of healthier foods and beverages. For example, higher sugar-sweetened beverage taxes may encourage consumers to reduce sugar-sweetened beverage consumption. Using the revenues from the higher sugar-sweetened beverage taxes for nutrition health promotion efforts or to subsidize fruits and vegetables could have public health benefits.

- Efforts to reduce added sugars in foods and sugar-sweetened beverages in school meals and through the new smart snacks in schools should continue and also be expanded to other settings, including early child care (through the Child and Adult Care Food Program-CACFP), parks, recreation centers, sports leagues, after school programs, work sites and other community settings.
- Policies that limit exposure and marketing of foods and beverages high in added sugars to young children, youth and adolescents are needed as dietary preferences are established early in life.
- Young adults (ages 20-29 years) are among the greatest consumers of sugar-sweetened beverages and are directly targeted in sugar-sweetened beverage marketing campaigns. Health promotion efforts and policies are needed to reduce sugar-sweetened beverages in settings, such as postsecondary institutions and worksites.
- Policy changes within the federal Supplemental Nutrition Assistance Program (SNAP), similar to policies in place for the WIC program, should be considered to encourage purchase of healthier options, including foods and beverages low in added sugars. Pilot studies using incentives and restrictions should be tested and evaluated.
- Public education campaigns are needed to increase the public's awareness of the health effects of added sugars and help consumers reduce added sugars intake and reduce intake of sugar-sweetened beverages through policy, food environment and education initiatives.

Table D6.2. Recommendations or statements related to added sugars or sugar-sweetened beverages from international and national organizations

Organization	Recommendation/Statement Related to Added Sugars and/or Sugar-Sweetened Beverages
World Health Organization (WHO)[64]	• WHO recommends reduced intake of free sugars throughout the life-course (*strong recommendation*). • In both adults and children, WHO recommends that intake of free sugars not to exceed 10% of total energy (*strong recommendation*). • WHO suggests further reduction to below 5% of total energy (*conditional recommendation*).
American Heart Association (AHA)[65]	The AHA recommends reductions in added sugars with an upper limit of half of the discretionary calorie allowance that can be accommodated within the appropriate energy intake level needed for a person to achieve or maintain a healthy weight based on the USDA food intake patterns. Most American women should eat or drink no more than 100 calories per day from added sugars (about 6 teaspoons), and most American men should eat or drink no more than 150 calories per day from added sugars (about 9 teaspoons).
HealthyPeople 2020[66]	Objective NWS-17.2: Reduce consumption of calories from added sugars (Target: 10.8%)
American Academy of Pediatrics (AAP)[67-69]	Limit consumption of sugar-sweetened beverages (consistent evidence) Pediatricians should work to eliminate sweetened drinks in schools *Note: Due to limited studies in children, the American Academy of Pediatrics (AAP) has no official recommendations regarding the use of non-caloric sweeteners.*
American Diabetes Association (ADA)[70, 71]	<u>Prevention</u> Research has shown that drinking sugary drinks is linked to type 2 diabetes, and the American Diabetes Association recommends that people limit their intake of sugar-sweetened beverages to help prevent diabetes. <u>Diabetes Management</u> People with diabetes should limit or avoid intake of sugar-sweetened beverages (from any caloric sweetener including high fructose corn syrup and sucrose) to reduce risk for weight gain and worsening of cardiometabolic risk profile. (Evidence rating B)
NHLBI Expert Panel Guidelines for Cardiovascular Health and Risk Reduction in Childhood[72]	Reduced intake of sugar-sweetened beverages is associated with decreased obesity measures (Grade B).

CHAPTER SUMMARY

The DGAC encourages the consumption of healthy dietary patterns that are low in saturated fat, added sugars, and sodium. The conclusions in this chapter complement the findings from ***Part D. Chapter 1: Food and Nutrient Intakes, and Health: Current Status and Trends*** and ***Part D. Chapter 2: Dietary Patterns, Foods and Nutrients, and Health Outcomes***. The goals for the general population are: less than 2,300 mg dietary sodium per day (or age-appropriate Dietary Reference Intake amount), less than 10 percent of total calories from saturated fat per day, and a maximum of 10 percent of total calories from added sugars per day.

Sodium, saturated fat, and added sugars are not intended to be reduced in isolation, but as a part of a healthy dietary pattern. Rather than focusing purely on reduction, emphasis should be placed on replacement and shifts in food intake and eating patterns. Sources of saturated fat should be replaced with unsaturated fat, particularly polyunsaturated fatty acids. Similarly, added sugars should be reduced in the diet and not replaced with low-calorie sweeteners, but rather with healthy options, such as water in place of sugar-sweetened beverages. For sodium, emphasis should be placed on expanding industry efforts to reduce the sodium content of foods and helping consumers understand how to flavor unsalted foods with spices and herbs.

Achieving reductions in sodium, saturated fat, and added sugars, can all be accomplished and are more attainable by eating a healthy dietary pattern. For all three of these components of the diet, policies and programs at local, state, and national levels in both the private and public sector are necessary to support reduction efforts. Similarly, the Committee supports efforts in labeling and other campaigns to increase consumer awareness and understanding of sodium, saturated fats, and added sugars in foods and beverages. The Committee encourages the food industry to continue reformulating and making changes to certain foods to improve their nutrition profile. Examples of such actions include lowering sodium and added sugars content, achieving better saturated fat to polyunsaturated fat ratio, and reducing portion sizes in retail settings (restaurants, food outlets, and public venues, such as professional sports stadiums and arenas). The Committee also encourages the food industry to market these improved products to consumers.

NEEDS FOR FUTURE RESEARCH

1. Design and conduct studies with sufficient power to define the impact of improving dietary quality, including the lowering of dietary sodium intake, on hypertension and relevant disease outcomes, including cardiovascular disease, stroke, peripheral vascular disease, kidney disease, and others. The interactions with patterns of therapeutic medication use (e.g., diuretics, antihypertensives, and lipid-lowering) should be considered.

Rationale: The current literature is incomplete, limited in power and durations, and often compromised by methodological challenges that must be addressed in well-designed studies with relevant clinical outcomes.

2. Assess the accuracy of 24-hour urine collections for sodium assessment in populations with different health conditions (e.g., diabetes, chronic kidney disease, heart failure, cardiovascular disease) and interactions with different patterns of medication use (e.g., diuretics, antihypertensives).

   Rationale: If there is systematic error in sodium assessment because individuals with various co-morbidities who are taking medications systematically do not provide accurate urine collections, paradoxical findings between sodium and health outcomes may be observed.

3. Examine the effect of behavioral interventions, with novel approaches (e.g., flavorful recipes, cooking techniques) on adherence to dietary sodium recommendations.

   Rationale: For decades, the population has exceeded dietary sodium intake recommendations. A public health approach that results in reformulation of commercially processed foods to lower sodium content should be the primary strategy for decreasing sodium intake in the U.S. population. However, individual support for public health policies will be needed to further document demand for changes in the sodium food environment. To this end, interventions that modify individual knowledge, attitudes, and behaviors around sodium intake should be evaluated.

4. Examine the effect of low sodium intake on taste preferences for sodium and healthy dietary patterns.

   Rationale: It has been argued that populations desire higher levels of sodium intake and will inevitably revert to higher levels of sodium intakes after acute reductions in sodium intake. It has also been argued that after six weeks of reduced sodium intake, taste preferences are modified such that higher sodium is no longer desirable. Studies are needed to elucidate the effects of lowering sodium intake on diet preferences.

5. Document the relationship between portion size and sodium intake.

   Rationale: These data are needed to inform whether dietary recommendations for sodium should be adjusted for caloric intake. It is known that the absolute amount of sodium intake is highly correlated with caloric intake. As a result, the absolute recommended amount of sodium is harder to achieve for a larger, high energy consuming person than for a smaller,

low energy consuming person. The science to inform whether sodium density confers different risk than absolute intake of sodium is limited because of methodologic limitations in surveys where both calories and sodium intake can be calculated. Furthermore, the existing correlation between sodium and calories may be an artifact of the current food supply.

6. Determine the effects of replacement of saturated fat with different types of carbohydrates (e.g., refined vs. whole grains) on cardiovascular disease risk.

   Rationale: Most randomized controlled trials and prospective cohort studies compared saturated fat with total carbohydrates. It is important to distinguish different types of carbohydrates (e.g. refined vs. whole grains) in future studies.

7. Examine the effects that replacement of saturated fat with polyunsaturated fat vs. monounsaturated fat has on cardiovascular disease risk.

   Rationale: Most existing studies have examined the effects of substituting PUFA for saturated fat on cardiovascular disease risk. Future studies should also examine the potential benefits of substituting monounsaturated fat from plant sources such as olive oil and nuts/seeds for saturated fat on cardiovascular disease risk.

8. Examine lipid and metabolic effects of specific oils modified to have different fatty acid profiles (e.g. commodity soy oil [high linoleic acid] vs. high oleic soy oil).

   Rationale: As more modified vegetables oils become commercially available, it is important to assess their long-term health effects. In addition, future studies should examine lipid and metabolic effects of plant oils that contain a mix of *n*-9, *n*-6, and *n*-3 fatty acids, as a replacement for animal fat, on cardiovascular disease risk factors.

9. Examine the effects of saturated fat from different sources, including animal products (e.g. butter, lard), plant (e.g., palm vs. coconut oils), and production systems (e.g. refined deodorized bleached vs. virgin coconut oil) on blood lipids and cardiovascular disease risk.

   Rationale: Different sources of saturated fat contain different fatty acid profiles and thus, may result in different lipid and metabolic effects. In addition, virgin and refined coconut oils have different effects in animal models, but human data are lacking.

10. Conduct gene-nutrient interaction studies by measuring genetic variations in relevant genes that will enable evaluation of effects of specific diets for individualized nutrition recommendations.

Rationale: Individuals with different genetic background may respond to the same dietary intervention differently in terms of blood lipids and other cardiovascular disease risk factors. Future studies should explore the potential role of genetic factors in modulating the effects of fat type modification on health outcomes.

11. Identify sources and names of added sugars and low-calorie sweeteners used in the food supply and quantify their consumption levels and trends in the U.S. diet.

Rationale: It is unclear whether all food and nutrient databases capture all added sugars because: 1) added sugars have varied and inconsistent nomenclature and may not be recognized as added sugars in nutrient analyses; and 2) many foods with added sugars have formulations considered proprietary by the manufacturers and for this reason actual added sugars content is difficult to obtain. Accurate assessment of added sugars in the U.S. diet is needed to quantify the population level exposure and subsequent health risks from added sugars. The lack of information on the various added sugars in the food supply hinders efforts to make policy about consumption.

12. Conduct prospective research with strong experimental designs and multiple measurements of the consumption of added sugars and low-calorie sweeteners on health outcomes, such as body weight, adiposity, and clinical markers of type 2 diabetes and cardiovascular disease.

Rationale: High heterogeneity exists among published research with regard to the types and forms of added sugars and low-calorie sweeteners-containing foods/beverages used for interventions, which precludes assessing the effects of specific added sugars and low-calorie sweeteners on body weight, adiposity, and cardio-metabolic health in adults and children. Many studies use single baseline measurements of diet to reflect usual patterns and quantities of intake over time. New research should emphasize assessments within the context of usual dietary intakes and patterns of food and beverage consumption in free-living populations, along with specific added sugars and low-calorie sweeteners, especially those that are currently understudied. Large prospective studies with repeated measurements of low-calorie sweeteners are needed to monitor their long-term effects on cancer and other health outcomes.

13. Design studies that emphasize assessments of relationships between the intakes of added sugars and low-calorie sweeteners and body weight, adiposity, and cardio-metabolic health in diverse sub-populations who are at high risk of obesity and related morbidities.

Rationale: Insufficient evidence exists to assess the impact of added sugars and low-calorie sweeteners contained in foods and beverages on individuals from diverse populations who

have high risk for adverse health outcomes. These include (but not limited to) different race/ethnicity groups; low income groups, especially those with food insecurity; groups who live in specific geographic locations with high prevalence of obesity (e.g. inner city, rural, and Southern regions of the United States); and age and sex groups (women, children, and elderly adults).

14. Assess and improve approaches and policies to reduce the amount of added sugars in the food and beverage supply as well as in school and community settings.

    Rationale: Results from this research would assist policy makers and the private sector in establishing sustainable approaches and policies to limit the availability and consumption of added sugars. These approaches and policies would also be important for multi-component strategies to improve weight control and health among people living in the United States.

15. Conduct consumer research to identify and test elements of a standardized, easily understood front-of-package label.

    Rationale: Research is needed to provide an evidence base to support the need and identify critical elements of a front of package label. This is particularly important to support the Food and Drug Administration in implementing a front-of-package labeling system.

REFERENCES

1. National Heart Lung and Blood Institute. Lifestyle Interventions to Reduce Cardiovascular Risk: Systematic Evidence Review from the Lifestyle Work Group. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health; 2013. Available from: http://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/lifestyle/index.htm.
2. Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston Miller N, Hubbard VS, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63(25 Pt B):2960-84. PMID: 24239922. http://www.ncbi.nlm.nih.gov/pubmed/24239922.
3. Mente A, O'Donnell MJ, Rangarajan S, McQueen MJ, Poirier P, Wielgosz A, et al. Association of urinary sodium and potassium excretion with blood pressure. N Engl J Med. 2014;371(7):601-11. PMID: 25119606. http://www.ncbi.nlm.nih.gov/pubmed/25119606.
4. Institute of Medicine. Sodium Intake in Populations: Assessment of Evidence. Washington, D.C.: The National Academies Press; 2013. Available from: http://www.nap.edu/catalog.php?record_id=18311.

5. Institute of Medicine. Strategies to Reduce Sodium Intake in the United States. Washington D.C.: The National Academies Press; 2010.
6. Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. BMJ. 2013;346:e7492. PMID: 23321486. http://www.ncbi.nlm.nih.gov/pubmed/23321486.
7. Moynihan PJ, Kelly SA. Effect on caries of restricting sugars intake: systematic review to inform WHO guidelines. J Dent Res. 2014;93(1):8-18. PMID: 24323509. http://www.ncbi.nlm.nih.gov/pubmed/24323509.
8. U.S. Department of Agriculture. Agricultural Research Services. Nutrient Intakes from Food: Mean Amounts Consumed per Individual, by Gender and Age, *What We Eat in America,* NHANES 2009-2010. 2012. Available from: www.ars.usda.gov/ba/bhnrc/fsrg.
9. Institute of Medicine. Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate. Washington, D.C.: The National Academies Press; 2005. Available from: http://books.nap.edu/openbook.php?record_id=10925.
10. Graudal NA, Hubeck-Graudal T, Jürgens G. Effects of low-sodium diet vs. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane Review). Am J Hypertens. 2012;25(1):1-15. PMID: 22068710. http://www.ncbi.nlm.nih.gov/pubmed/22068710.
11. Dietary Guidelines Advisory Committee. Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, 2010, to the Secretary of Agriculture and the Secretary of Health and Human Services: U.S. Department of Agriculture, Agricultural Research Service, Washington D.C.; 2010. Available from: http://www.cnpp.usda.gov/DGAs2010-DGACReport.htm.
12. Cotter J, Cotter MJ, Oliveira P, Cunha P, Polonia J. Salt intake in children 10-12 years old and its modification by active working practices in a school garden. J Hypertens. 2013;31(10):1966-71. PMID: 24107730. http://www.ncbi.nlm.nih.gov/pubmed/24107730.
13. Shi L, Krupp D, Remer T. Salt, fruit and vegetable consumption and blood pressure development: a longitudinal investigation in healthy children. Br J Nutr. 2014;111(4):662-71. PMID: 24326147. http://www.ncbi.nlm.nih.gov/pubmed/24326147.
14. Cook NR, Appel LJ, Whelton PK. Lower levels of sodium intake and reduced cardiovascular risk. Circulation. 2014;129(9):981-9. PMID: 24415713. http://www.ncbi.nlm.nih.gov/pubmed/24415713.
15. Joosten MM, Gansevoort RT, Mukamal KJ, Lambers Heerspink HJ, Geleijnse JM, Feskens EJ, et al. Sodium excretion and risk of developing coronary heart disease. Circulation. 2014;129(10):1121-8. PMID: 24425751. http://www.ncbi.nlm.nih.gov/pubmed/24425751.
16. O'Donnell M, Mente A, Rangarajan S, McQueen MJ, Wang X, Liu L, et al. Urinary sodium and potassium excretion, mortality, and cardiovascular events. N Engl J Med. 2014;371(7):612-23. PMID: 25119607. http://www.ncbi.nlm.nih.gov/pubmed/25119607.
17. Pfister R, Michels G, Sharp SJ, Luben R, Wareham NJ, Khaw KT. Estimated urinary sodium excretion and risk of heart failure in men and women in the EPIC-Norfolk study. Eur J Heart Fail. 2014. PMID: 24464931. http://www.ncbi.nlm.nih.gov/pubmed/24464931.
18. Institute of Medicine. Front-of-Package Nutrition Rating Systems and Symbols: Promoting Healthier Choices. Washingon D.C.: The National Academies Press; 2012.

19. Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L, et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. Ann Intern Med. 2014;160(6):398-406. PMID: 24723079. http://www.ncbi.nlm.nih.gov/pubmed/24723079.
20. Farvid MS, Ding M, Pan A, Sun Q, Chiuve SE, Steffen LM, et al. Dietary Linoleic Acid and Risk of Coronary Heart Disease: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. Circulation. 2014. PMID: 25161045. http://www.ncbi.nlm.nih.gov/pubmed/25161045.
21. Hooper L, Summerbell CD, Thompson R, Sills D, Roberts FG, Moore HJ, et al. Reduced or modified dietary fat for preventing cardiovascular disease. Cochrane Database Syst Rev. 2012;5:CD002137. PMID: 22592684. http://www.ncbi.nlm.nih.gov/pubmed/22592684.
22. Jakobsen MU, O'Reilly EJ, Heitmann BL, Pereira MA, Bälter K, Fraser GE, et al. Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. Am J Clin Nutr. 2009;89(5):1425-32. PMID: 19211817. http://www.ncbi.nlm.nih.gov/pubmed/19211817.
23. Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. PLoS Med. 2010;7(3):e1000252. PMID: 20351774. http://www.ncbi.nlm.nih.gov/pubmed/20351774.
24. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. Am J Clin Nutr. 2010;91(3):535-46. PMID: 20071648. http://www.ncbi.nlm.nih.gov/pubmed/20071648.
25. Skeaff CM, Miller J. Dietary fat and coronary heart disease: summary of evidence from prospective cohort and randomised controlled trials. Ann Nutr Metab. 2009;55(1-3):173-201. PMID: 19752542. http://www.ncbi.nlm.nih.gov/pubmed/19752542.
26. Mensink RP, Katan MB. Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. Arterioscler Thromb. 1992;12(8):911-9. PMID: 1386252. http://www.ncbi.nlm.nih.gov/pubmed/1386252.
27. Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. Am J Clin Nutr. 2003;77(5):1146-55. PMID: 12716665. http://www.ncbi.nlm.nih.gov/pubmed/12716665.
28. Department of Health and Human Services. Food and Drug Administration. Proposed definition from FDA in the Proposed Rule to the revision of the Nutrition and Supplement Facts Labels (Docket No. FDA-2012-N-1210). March 2014. Available from: https://www.federalregister.gov/articles/2014/03/03/2014-04387/food-labeling-revision-of-the-nutrition-and-supplement-facts-labels#p-325.
29. Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. Am J Clin Nutr. 2013;98(4):1084-102. PMID: 23966427. http://www.ncbi.nlm.nih.gov/pubmed/23966427.
30. Kaiser KA, Shikany JM, Keating KD, Allison DB. Will reducing sugar-sweetened beverage consumption reduce obesity? Evidence supporting conjecture is strong, but evidence when testing effect is weak. Obes Rev. 2013;14(8):620-33. PMID: 23742715. http://www.ncbi.nlm.nih.gov/pubmed/23742715.

31. Mattes RD, Shikany JM, Kaiser KA, Allison DB. Nutritively sweetened beverage consumption and body weight: a systematic review and meta-analysis of randomized experiments. Obes Rev. 2011;12(5):346-65. PMID: 20524996. http://www.ncbi.nlm.nih.gov/pubmed/20524996.
32. The science behind the sweetness in our diets. Bull World Health Organ. 2014;92(11):780-1. PMID: 25378738. http://www.ncbi.nlm.nih.gov/pubmed/25378738.
33. Greenwood DC, Threapleton DE, Evans CE, Cleghorn CL, Nykjaer C, Woodhead C, et al. Association between sugar-sweetened and artificially sweetened soft drinks and type 2 diabetes: systematic review and dose-response meta-analysis of prospective studies. Br J Nutr. 2014;112(5):725-34. PMID: 24932880. http://www.ncbi.nlm.nih.gov/pubmed/24932880.
34. Romaguera D, Norat T, Wark PA, Vergnaud AC, Schulze MB, van Woudenbergh GJ, et al. Consumption of sweet beverages and type 2 diabetes incidence in European adults: results from EPIC-InterAct. Diabetologia. 2013;56(7):1520-30. PMID: 23620057. http://www.ncbi.nlm.nih.gov/pubmed/23620057.
35. Malik VS, Popkin BM, Bray GA, Després JP, Willett WC, Hu FB. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. Diabetes Care. 2010;33(11):2477-83. PMID: 20693348. http://www.ncbi.nlm.nih.gov/pubmed/20693348.
36. Sonestedt E, Overby NC, Laaksonen DE, Birgisdottir BE. Does high sugar consumption exacerbate cardiometabolic risk factors and increase the risk of type 2 diabetes and cardiovascular disease? Food Nutr Res. 2012;56. PMID: 22855643. http://www.ncbi.nlm.nih.gov/pubmed/22855643.
37. Xi B, Li S, Liu Z, Tian H, Yin X, Huai P, et al. Intake of fruit juice and incidence of type 2 diabetes: a systematic review and meta-analysis. PLoS One. 2014;9(3):e93471. PMID: 24682091. http://www.ncbi.nlm.nih.gov/pubmed/24682091.
38. Aeberli I, Gerber PA, Hochuli M, Kohler S, Haile SR, Gouni-Berthold I, et al. Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: a randomized controlled trial. Am J Clin Nutr. 2011;94(2):479-85. PMID: 21677052. http://www.ncbi.nlm.nih.gov/pubmed/21677052.
39. Aeberli I, Hochuli M, Gerber PA, Sze L, Murer SB, Tappy L, et al. Moderate amounts of fructose consumption impair insulin sensitivity in healthy young men: a randomized controlled trial. Diabetes Care. 2013;36(1):150-6. PMID: 22933433. http://www.ncbi.nlm.nih.gov/pubmed/22933433.
40. Barrio-Lopez MT, Martinez-Gonzalez MA, Fernandez-Montero A, Beunza JJ, Zazpe I, Bes-Rastrollo M. Prospective study of changes in sugar-sweetened beverage consumption and the incidence of the metabolic syndrome and its components: the SUN cohort. Br J Nutr. 2013;110(9):1722-31. PMID: 23534417. http://www.ncbi.nlm.nih.gov/pubmed/23534417.
41. Bernstein AM, de Koning L, Flint AJ, Rexrode KM, Willett WC. Soda consumption and the risk of stroke in men and women. Am J Clin Nutr. 2012;95(5):1190-9. PMID: 22492378. http://www.ncbi.nlm.nih.gov/pubmed/22492378.
42. Black RN, Spence M, McMahon RO, Cuskelly GJ, Ennis CN, McCance DR, et al. Effect of eucaloric high- and low-sucrose diets with identical macronutrient profile on insulin

resistance and vascular risk: a randomized controlled trial. Diabetes. 2006;55(12):3566-72. PMID: 17130505. http://www.ncbi.nlm.nih.gov/pubmed/17130505.

43. Chen L, Caballero B, Mitchell DC, Loria C, Lin PH, Champagne CM, et al. Reducing consumption of sugar-sweetened beverages is associated with reduced blood pressure: a prospective study among United States adults. Circulation. 2010;121(22):2398-406. PMID: 20497980. http://www.ncbi.nlm.nih.gov/pubmed/20497980.

44. Cohen L, Curhan G, Forman J. Association of sweetened beverage intake with incident hypertension. J Gen Intern Med. 2012;27(9):1127-34. PMID: 22539069. http://www.ncbi.nlm.nih.gov/pubmed/22539069.

45. de Koning L, Malik VS, Kellogg MD, Rimm EB, Willett WC, Hu FB. Sweetened beverage consumption, incident coronary heart disease, and biomarkers of risk in men. Circulation. 2012;125(14):1735-41, S1. PMID: 22412070. http://www.ncbi.nlm.nih.gov/pubmed/22412070.

46. Dhingra R, Sullivan L, Jacques PF, Wang TJ, Fox CS, Meigs JB, et al. Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. Circulation. 2007;116(5):480-8. PMID: 17646581. http://www.ncbi.nlm.nih.gov/pubmed/17646581.

47. Duffey KJ, Gordon-Larsen P, Steffen LM, Jacobs DR, Popkin BM. Drinking caloric beverages increases the risk of adverse cardiometabolic outcomes in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Am J Clin Nutr. 2010;92(4):954-9. PMID: 20702604. http://www.ncbi.nlm.nih.gov/pubmed/20702604.

48. Eshak ES, Iso H, Kokubo Y, Saito I, Yamagishi K, Inoue M, et al. Soft drink intake in relation to incident ischemic heart disease, stroke, and stroke subtypes in Japanese men and women: the Japan Public Health Centre-based study cohort I. Am J Clin Nutr. 2012;96(6):1390-7. PMID: 23076619. http://www.ncbi.nlm.nih.gov/pubmed/23076619.

49. Faeh D, Minehira K, Schwarz JM, Periasamy R, Periasami R, Park S, et al. Effect of fructose overfeeding and fish oil administration on hepatic de novo lipogenesis and insulin sensitivity in healthy men. Diabetes. 2005;54(7):1907-13. PMID: 15983189. http://www.ncbi.nlm.nih.gov/pubmed/15983189.

50. Fung TT, Malik V, Rexrode KM, Manson JE, Willett WC, Hu FB. Sweetened beverage consumption and risk of coronary heart disease in women. Am J Clin Nutr. 2009;89(4):1037-42. PMID: 19211821. http://www.ncbi.nlm.nih.gov/pubmed/19211821.

51. Larsson SC, Akesson A, Wolk A. Sweetened beverage consumption is associated with increased risk of stroke in women and men. J Nutr. 2014;144(6):856-60. PMID: 24717367. http://www.ncbi.nlm.nih.gov/pubmed/24717367.

52. Lê KA, Ith M, Kreis R, Faeh D, Bortolotti M, Tran C, et al. Fructose overconsumption causes dyslipidemia and ectopic lipid deposition in healthy subjects with and without a family history of type 2 diabetes. Am J Clin Nutr. 2009;89(6):1760-5. PMID: 19403641. http://www.ncbi.nlm.nih.gov/pubmed/19403641.

53. Lewis AS, McCourt HJ, Ennis CN, Bell PM, Courtney CH, McKinley MC, et al. Comparison of 5% versus 15% sucrose intakes as part of a eucaloric diet in overweight and obese subjects: effects on insulin sensitivity, glucose metabolism, vascular compliance, body composition and lipid profile. A randomised controlled trial. Metabolism. 2013;62(5):694-702. PMID: 23363580. http://www.ncbi.nlm.nih.gov/pubmed/23363580.

54. Lowndes J, Sinnett S, Pardo S, Nguyen VT, Melanson KJ, Yu Z, et al. The effect of normally consumed amounts of sucrose or high fructose corn syrup on lipid profiles, body composition and related parameters in overweight/obese subjects. Nutrients. 2014;6(3):1128-44. PMID: 24642950. http://www.ncbi.nlm.nih.gov/pubmed/24642950.
55. Lowndes J, Sinnett S, Yu Z, Rippe J. The effects of fructose-containing sugars on weight, body composition and cardiometabolic risk factors when consumed at up to the 90th percentile population consumption level for fructose. Nutrients. 2014;6(8):3153-68. PMID: 25111121. http://www.ncbi.nlm.nih.gov/pubmed/25111121.
56. Maersk M, Belza A, Stødkilde-Jørgensen H, Ringgaard S, Chabanova E, Thomsen H, et al. Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study. Am J Clin Nutr. 2012;95(2):283-9. PMID: 22205311. http://www.ncbi.nlm.nih.gov/pubmed/22205311.
57. Raben A, Vasilaras TH, Møller AC, Astrup A. Sucrose compared with artificial sweeteners: different effects on ad libitum food intake and body weight after 10 wk of supplementation in overweight subjects. Am J Clin Nutr. 2002;76(4):721-9. PMID: 12324283. http://www.ncbi.nlm.nih.gov/pubmed/12324283.
58. Tasevska N, Park Y, Jiao L, Hollenbeck A, Subar AF, Potischman N. Sugars and risk of mortality in the NIH-AARP Diet and Health Study. Am J Clin Nutr. 2014;99(5):1077-88. PMID: 24552754. http://www.ncbi.nlm.nih.gov/pubmed/24552754.
59. Yang Q, Zhang Z, Gregg EW, Flanders WD, Merritt R, Hu FB. Added sugar intake and cardiovascular diseases mortality among US adults. JAMA Intern Med. 2014;174(4):516-24. PMID: 24493081. http://www.ncbi.nlm.nih.gov/pubmed/24493081.
60. Yu Z, Lowndes J, Rippe J. High-fructose corn syrup and sucrose have equivalent effects on energy-regulating hormones at normal human consumption levels. Nutr Res. 2013;33(12):1043-52. PMID: 24267044. http://www.ncbi.nlm.nih.gov/pubmed/24267044.
61. Brown RJ, de Banate MA, Rother KI. Artificial sweeteners: a systematic review of metabolic effects in youth. Int J Pediatr Obes. 2010;5(4):305-12. PMID: 20078374. http://www.ncbi.nlm.nih.gov/pubmed/20078374.
62. Miller PE, Perez V. Low-calorie sweeteners and body weight and composition: a meta-analysis of randomized controlled trials and prospective cohort studies. Am J Clin Nutr. 2014;100(3):765-77. PMID: 24944060. http://www.ncbi.nlm.nih.gov/pubmed/24944060.
63. Wiebe N, Padwal R, Field C, Marks S, Jacobs R, Tonelli M. A systematic review on the effect of sweeteners on glycemic response and clinically relevant outcomes. BMC Med. 2011;9:123. PMID: 22093544. http://www.ncbi.nlm.nih.gov/pubmed/22093544.
64. World Health Organization. Draft guidelines on free sugars released for public consultation, 5 March 2014. http://www.who.int/nutrition/sugars_public_consultation/en/.
65. Van Horn L, Johnson RK, Flickinger BD, Vafiadis DK, Yin-Piazza S, Group ASCP. Translation and implementation of added sugars consumption recommendations: a conference report from the American Heart Association Added Sugars Conference 2010. Circulation. 2010;122(23):2470-90. PMID: 21060079. http://www.ncbi.nlm.nih.gov/pubmed/21060079.
66. U.S. Department of Health and Human Services. Office of Disease Prevention and Health Promotion. Healthy People 2020. Objective NWS-17.2. Available from:

https://www.healthypeople.gov/2020/topics-objectives/topic/nutrition-and-weight-status/objectives.

67. Barlow SE, Committee E. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics. 2007;120 Suppl 4:S164-92. PMID: 18055651. http://www.ncbi.nlm.nih.gov/pubmed/18055651.

68. American Academy of Pediatrics Committee on School Health. Soft drinks in schools. Pediatrics. 2004;113(1 Pt 1):152-4. PMID: 14702469. http://www.ncbi.nlm.nih.gov/pubmed/14702469.

69. American Academy of Pediatrics. Sweeteners and Sugar Substitutes. Available from: http://www.healthychildren.org/English/healthy-living/nutrition/Pages/Sweeteners-and-Sugar-Substitutes.aspx.

70. American Diabetes Association. Sugar and Desserts [November 2014]. Available from: http://www.diabetes.org/food-and-fitness/food/what-can-i-eat/understanding-carbohydrates/sugar-and-desserts.html.

71. Evert AB, Boucher JL, Cypress M, Dunbar SA, Franz MJ, Mayer-Davis EJ, et al. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care. 2013;36(11):3821-42. PMID: 24107659. http://www.ncbi.nlm.nih.gov/pubmed/24107659.

72. National Heart Lung and Blood Institute. Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health; 2013.