

The Scientific Basis of Guideline Recommendations on Sugar Intake A Systematic Review

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Background: The relationship between sugar and health is affected by energy balance, macronutrient substitutions, and diet and lifestyle patterns. Several authoritative organizations have issued public health guidelines addressing dietary sugars.

Purpose: To systematically review guidelines on sugar intake and assess consistency of recommendations, methodological quality of guidelines, and the quality of evidence supporting each recommendation.

Data Sources: MEDLINE, EMBASE, and Web of Science (1995 to September 2016); guideline registries; and gray literature (bibliographies, Google, and experts).

Study Selection: Guidelines addressing sugar intake that reported their methods of development and were published in English between 1995 and 2016.

Data Extraction: Three reviewers independently assessed guideline quality using the Appraisal of Guidelines for Research and Evaluation, 2nd edition (AGREE II), instrument. To assess evidence quality, articles supporting recommendations were independently reviewed and their quality was determined by using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methods.

Data Synthesis: The search identified 9 guidelines that offered 12 recommendations. Each of the reviewed guidelines indicated

a suggested decrease in the consumption of foods containing nonintrinsic sugars. The guidelines scored poorly on AGREE II criteria, specifically in rigor of development, applicability, and editorial independence. Seven recommendations provided non-quantitative guidance; 5 recommended less than 25% to less than 5% of total calories from nonintrinsic sugars. The recommendations were based on various health concerns, including nutrient displacement, dental caries, and weight gain. Quality of evidence supporting recommendations was low to very low.

Limitation: The authors conducted the study independent of the funding source, which is primarily supported by the food and agriculture industry.

Conclusion: Guidelines on dietary sugar do not meet criteria for trustworthy recommendations and are based on low-quality evidence. Public health officials (when promulgating these recommendations) and their public audience (when considering dietary behavior) should be aware of these limitations.

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he relationship between sugar and health is complex due to multiple interrelated variables, including state of energy balance, macronutrient substitutions, and underlying diet and lifestyle patterns (1). Existing evidence of a link between sugar intake and adverse health outcomes has been translated into dietary guidance and recommendations for the general public by authoritative health organizations (2). Dietary guidance addresses the types of sugars, especially sources of nonintrinsic sugars, such as added sugars and free sugars (2). Added sugars consist of monosaccharides and disaccharides added during the production and preparation of foods and beverages and do not include sugars naturally found in milk, fruit, and fruit juice. Free sugars comprise sugars added to products as well as sugars naturally found in fruit, honey, and

As research continues to add knowledge, authoritative organizations have issued public health guidance based on the available evidence (2). Recent guidelines have included both qualitative and quantitative recommendations that consistently focus on limiting and reducing sugar consumption, especially sources of non-intrinsic sugars (2). For example, in 2015, the World Health Organization (WHO), the Scientific Advisory Committee on Nutrition (SACN), and the U.S. Depart-

ment of Agriculture and U.S. Department of Health and Human Services issued public health guidelines (PHGs) with specific recommendations for dietary sugar intake (4-6). Each organization conducted its own review of the available evidence and published its recommendations, including the scientific basis for its conclusions. These organizations have crafted different recommendations with regard to sugar consumption, with various rationales for limiting intake.

When respected organizations issue conflicting recommendations, it can result in confusion and raises concern about the quality of the guidelines and the underlying evidence. We conducted a systematic survey and critical appraisal of authoritative PHGs, including an assessment of the quality of evidence supporting recommendations for dietary sugar intake.

| See also: | |
|----------------------|--|
| Editorial comment | |
| Web-Only CME quiz | |

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This article has been corrected. The specific correction appears on the last page of this document. The original version (PDF) is available at www.annals.org.

Methods

We registered the protocol for this systematic review in the PROSPERO database in November 2015 (registration number CRD42015029182) (7).

Data Sources and Searches

Using a search strategy developed with the help of an experienced librarian, we searched MEDLINE, EMBASE, and Web of Science (1995 to September 2016) using subject terms and keywords. We searched 5 gray literature sources, including Google (Appendix Table 1, available at www.annals.org), as well as bibliographies of included studies. We consulted with 3 experts in the field of carbohydrates (Appendix Table 1) to identify additional guidelines we may have missed. Our search was restricted to English-language guidelines.

Study Selection

Our criteria for inclusion were 1) PHGs, defined as documents developed by a nationally recognized committee, a publicly funded institution, or a medical society that provided recommendations for sugar intake in the general population; 2) inclusion of an explicit methodology section, either within the guideline or in supporting documents (for example, definition of the search strategy, evidence quality assessment, and methods used to create recommendations); 3) the most recent version of publications from an organization; and 4) publication between 1995 and 2016.

Our target outcomes of interest were the overall quality of development of the PHGs; the consistency of sugar recommendations, both quantitative and qualitative; the strength of the recommendations; an assessment of the supporting evidence for each recommendation; the use of systematic review methods; explicit links between recommendations and supporting evidence; and the strengths and limitations of the body of evidence.

Data Extraction and Quality Assessment

Two reviewers (B.S. and J.E.) independently screened titles and abstracts, full-text articles, and data extracted from included PHGs by using standardized, pilot-tested forms. We abstracted the following guideline characteristics: title, year, authors, language, organization, whether it was a novel publication or an update, location of development, the recommendations for sugar intake along with the strength of each recommendation, and the authors' assessment of the quality of the supporting evidence. Pairs of reviewers (B.S., J.E., L.L., and B.C.J.) independently identified, extracted, and appraised references to the evidence used to justify each recommendation, including the types of sugars (for example, added, free, or total) referenced in the supporting body of literature. Reviewers resolved disagreements by consensus and, if consensus could not be reached, consulted with senior scientists (B.C.J. and J.S.).

Three reviewers (B.S., J.E., and L.L.) independently appraised guidelines by using the Appraisal of Guidelines for Research and Evaluation, 2nd edition (AGREE

II), instrument, comprising 23 items within 6 domains: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence (Appendix Table 2, available at www.annals.org) (8). In addition, 2 overall assessments were completed for each PHG: a score of 1 to 7, and whether the reviewer would recommend using the guideline (recommended, recommended with modifications, or not recommended). We conducted a calibration exercise using 2 guidelines to ensure consistency and validity and resolved disagreements by consensus. Item rating differences of 3 points or fewer between reviewers were permitted. Senior scientists (B.C.J. and J.S.) were available for discrepancies but were not needed.

Quality Appraisal of Evidence Used in Guidelines

We used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach (9) to independently assess the quality of the evidence underlying each recommendation. For each target outcome linked to a recommendation, GRADE assigns the quality of evidence as high, moderate, low, or very low. Systematic reviews of randomized, controlled trials (RCTs) started with high quality of evidence, whereas systematic reviews of observational studies started with low quality. In instances where only single studies for recommendations were cited, RCTs started with moderate-quality evidence and observational studies started with very-low-quality evidence. For each body of evidence (systematic reviews) and for each citation (single studies), where possible, we considered downgrading the quality of evidence on the basis of 5 domains: risk of bias, indirectness, imprecision, inconsistency, and publication bias. Subsequently, we considered rating up on the basis of 3 domains: large effect size, dose-response, and an absence of residual or unmeasured confounding.

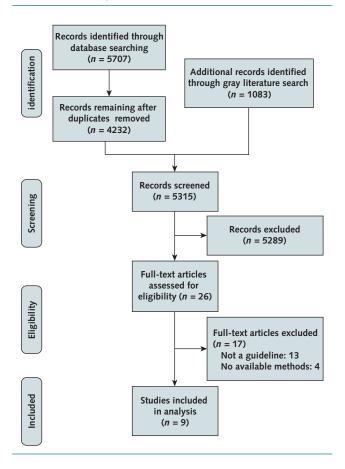
Data Synthesis and Analysis

Agreement for the full-text screening was calculated using the κ statistic and its 95% CI (10). For each guideline, we calculated the AGREE II score for each domain as a percentage of the maximum possible score and standardized range. We considered 60% as a threshold of acceptable quality. Interrater agreement was calculated using the intraclass correlation coefficient with corresponding 95% CIs (11). Agreement of 0.01 to 0.20 was considered poor, 0.21 to 0.40 was considered fair, 0.41 to 0.60 was considered moderate, 0.61 to 0.80 was considered substantial, and 0.81 to 1.00 was considered very good (12). For all AGREE II domains across all PHGs, we calculated the median domain score and the interquartile range (IQR). All analyses were conducted using Excel 2013 (Microsoft).

Role of the Funding Source

This study was supported by the Technical Committee on Dietary Carbohydrates of the North American branch of the International Life Sciences Institute (ILSI North America). ILSI North America is a public, non-profit foundation that provides a forum to advance un-

Figure. Summary of evidence search and selection.



derstanding of scientific issues related to the nutritional quality and safety of the food supply by sponsoring research programs, educational seminars and workshops, and publications. ILSI North America receives 60% of its financial support from its more than 400 industry members. The authors wrote the protocol, which was reviewed for scope clarifications and approved by ILSI. The funding source had no role in the conduct of the review or the interpretation of data, manuscript review, or publication decisions.

RESULTS

A total of 5315 records were screened, 26 records were considered potentially eligible for full-text screening, and 9 PHGs proved eligible (Figure). Eligible guidelines included 1 global guideline (4), 2 international guidelines (13, 14), and 6 national guidelines (5, 6, 15-18). Guidelines were published from 2002 to 2015 by the following agencies: the U.S. Department of Agriculture and the U.S. Department of Health and Human Services (6), WHO (4), SACN and Public Health England (5), the Ministry of Health of Brazil (15), the Australian National Health and Medical Research Council (18), the Nordic Council of Ministers (14), the German Nutrition Society (16), the Food Safety Authority of Ireland (17), and the Institute of Medicine (13) (Table 1).

Recommendation Characteristics

The 9 PHGs provided a total of 12 recommendations on dietary sugar intake. All recommendations advocated for reduced intake of nonintrinsic free or added sugars and/or decreased consumption of foods and beverages high in refined sugars, and 5 recommendations provided specific sugar intake limits (Table 1). Guidelines used variable terminology in sugar recommendations. For example, 2 guidelines used the term "free sugars" (4, 5), 3 used the term "added sugars" (6, 13, 14), 2 made recommendations on sugarsweetened beverages (SSBs) (5, 16), and 3 referred to food and beverage sources of refined sugars (15, 17, 18). Quantitative recommendations ranged from less than 5% of total energy from free sugars (4, 5) to less than 25% of total energy from added sugars (13). The rationale for decreased sugar intake included nutrient displacement, excess energy intake, dental caries, bone health, weight gain, and obesity. Four guidelines assessed the quality of the evidence and used the assessment to develop their recommendations (4, 5, 16, 18), and 5 did not (6, 13, 15, 17, 19).

Quality Assessment of Guidelines: AGREE II Results Scope and Purpose

Items in this domain evaluate the overall objectives, related health questions, and the target population of the guideline (20). Across guidelines, the median score for this domain was 81.5% (IQR, 72.2% to 88.0%), indicating that most items were highly rated (Table 2). Eight of the 9 guidelines reached the 60% threshold for reporting. The main limitation across all guidelines was the description of expected benefit, or outcomes, of the guidelines.

Stakeholder Involvement

Stakeholder involvement criteria focus on the extent of involvement of appropriate participants in the guideline development process and whether it reflects the views of its intended users (20). The median score for this domain was 63.0% (IQR, 38.9% to 77.8%) (Table 2). Four guidelines scored below 60% in this domain (5, 13, 16, 17). Many guidelines did not describe how they sought the views and preferences of their target population (patients or the public), and those that did were vague about the process.

Rigor of Development

Rigor of development relates to the methods used for gathering and synthesizing the evidence for guideline development, formulation of the recommendations, and the process for updating the guideline (20). The median score for this domain was low, at 47.2% (IQR, 24.0% to 69.4%) (Table 2). Three of the guidelines met the 60% threshold (4, 6, 18). Four guidelines did not use systematic methods to search for evidence (6, 13, 15, 17). Four guidelines assigned strength to their recommendations (4, 6, 16, 18), but only the WHO guideline used the GRADE approach (4). Three of the

REVIEW

| Table 1. Identified | d Guidelines and Co | rresponding Sugar Recommendations | | |
|--|---|---|--|---|
| Guideline, Year (Reference) | Guideline Title | Funding | Qualitative Recommendation | Quantitative Recommendation* |
| U.S. Department of Agriculture, U.S. Department of Health and Human Services, 2015 (6) | 2015-2020 Dietary Guidelines for Americans | Unclear | - | "Consume less than 10% of calories per day from added sugars" |
| WHO, 2015 (4) | Sugars Intake for Adults and Children | Ministry of Health, Labour and Welfare of the Government of Japan; Korean Food and Drug Administration; Zhejiang University; and the WHO Regional Office for Europe | "Reduced intake of free sugars throughout the life course" | "In both adults and children, WHO recommends reducing the intake free sugars to less than 10% of total energy intake"; "WHO suggests further reduction of the intake of free sugars to below 5% of total energy intake" |
| Public Health England/SACN, 2015 (5) | Carbohydrates and Health | Unclear | "The consumption of sugars- sweetened beverages should be minimised in both children and adults" | "The population average intake of fre sugars should not exceed 5% of total dietary energy for age groups from 2 years upwards" |
| Ministry of Health of Brazil, Secretariat of Health Care, Primary Health Care Department, 2014 (15) | Dietary Guidelines for the Brazilian Population | Unclear | "Use oils, fats, salt, and sugar in small amounts for seasoning and cooking foods and to create culinary preparations" | - - |
| National Health and Medical Research Council, 2013 (18) | Australian Dietary Guidelines | Unclear | "Limit intake of foods and drinks containing added sugars such as confectionary, sugar-sweetened soft drinks and cordials, fruit drinks, vitamin waters, energy and sports drinks" | - |
| Nordic Council of Ministers, 2012 (14) | Nordic Nutrition Recommendations | Nordic Council of Ministers | · - | "Intake of added sugar should be kept belo 10% of the energy intake" |
| German Nutrition Society, 2012 (16) | Evidence-based Guideline of the German Nutrition Society | Unclear | "The consumption of sugar- sweetened beverages should be limited" | - |
| Food Safety Authority of Ireland, 2011 (17) | Scientific Recommendations for Healthy Eating Guidelines in Ireland | Department of Health and Children | "Healthy eating can be enjoyed with limited amounts of 'other foods' like biscuits, cakes, savoury snacks and confectionery. These foods are rich in calories, fat, sugar and salt so remember–NOT too MUCH and NOT too OFTEN" | - |
| Institute of Medicine, Food and Nutrition Board, 2002 (13) | Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids | U.S. Department of Health and Human Services Office of Disease Prevention and Health Promotion, Health Canada, U.S. Food and Drug Administration, National Institutes of Health, Centers for Disease Control and Prevention, U.S. Department of Agriculture, U.S. Department of Defense, Institute of Medicine, and Dietary Reference Intakes Private Foundation Fund and Corporate Donors Fund, including the Dannon Institute, International Life Sciences Institute, Roche Vitamins Inc., Mead Johnson Nutrition Group, and M&M Mars | - | "A maximal intake leve of 25% or less of energy is suggested to prevent the displacement of foods that are major sources of essential micronutrients" |

| Basis for Recommendation | Methods Used to Determine Recommendations | Sugar Definition in Public Health Guidelines | Types of Sugar in Relevant Evidence |
|---|--|--|---|
| Nutrient displacement | Systematic review, diet modeling, and national intake data | Added sugars include syrups, brown sugar, corn sweetener, corn syrup, dextrose, fructose, glucose, high-fructose corn syrup, honey, invert sugar, lactose, malt syrup, maltose, molasses, raw sugar, sucrose, trehalose, and turbinado sugar | Not applicable; diet modeling used for evidence |
| Dental caries and weight gain | Systematic review | Free sugars include monosaccharides and disaccharides added to foods and beverages by the manufacturer, cook, or consumer and sugars naturally present in honey, syrups, fruit juices, and fruit juice concentrates | Sucrose, added sugar, total sugars, free sugars, SSBs, fructose, and sweet foods |
| Excess energy intake | Systematic review | All monosaccharides and disaccharides added to foods by the manufacturer, cook, or consumer plus sugars naturally present in honey, syrups, and unsweetened fruit juices | Total sugars, individual sugars, SSBs, sweet food, fruit juice, and nonmilk extrinsic sugars |
| Excess energy intake | Consensus | No definition | Not applicable; did not assess the literature |
| Weight gain, dental caries, and bone health | Systematic review and diet modeling | Not applicable | SSBs, energy-dense snack foods, fruit juice, sucrose, and total sugar |
| Dental caries, obesity, and nutrient displacement | Systematic review | Added sugars include sucrose, fructose, glucose, starch hydrolysates (glucose syrup and high-fructose syrup), and other isolated sugar preparations used as such or added during food preparation and manufacturing | SSBs, dietary sugars, fructose, sucrose, sweet foods, added sugar, and fruit juice |
| Excess energy intake | Systematic review | Not applicable | Sweets, SSBs, fructose, and glucose |
| Dental caries | Diet modeling | Not applicable | Total sugar |
| Nutrient displacement | Literature review | Not applicable | Total sugar, added sugar, and nonmilk extrinsic sugars |

SACN = Scientific Advisory Committee on Nutrition; SSB = sugar-sweetened beverage; UK = United Kingdom; WHO = World Health Organization.

* Although scientific reports were commissioned, including systematic reviews, quantitative recommendations were based on modeling and intake Annals of Internal Medicine 5

Table 2. Public Health Guideline Domain Scores on the AGREE II Instrument

| Guideline (Reference) | · · · · · · · · · · · · · · · · · · · | | | | Combined Overall | Systematic Method† | | | |
|--|---------------------------------------|-------------------------|----------------------------|-------------------------|----------------------------|-----------------------|---------------------------|--------|--------|
| (Reference) | Coefficient* | Scope and Purpose | Stakeholder Involvement | Rigor of Development | Clarity of Presentation | Applicability | Editorial Independence | Rating | Wethod |
| Carbohydrates and Health (5) | 0.966 | 81.5 | 37.0 | 47.2 | 48.1 | 0 | 0 | 3.7 | Yes |
| Sugars Intake for Adults and Children (4) | 0.887 | 88.9 | 77.8 | 81.3‡ | 59.3 | 36.1 | 83.3‡ | 4.3 | Yes |
| Nordic Nutrition Recommendations (14) | 0.913 | 83.3 | 63.0 | 50.0 | 53.7 | 15.3 | 33.3 | 4.7 | Yes |
| Dietary Guidelines for the Brazilian Population (15) | 0.873 | 53.7 | 74.1 | 16.7 | 50.0 | 34.7 | 33.3 | 3.7 | No |
| Evidence-based Guideline of the German Nutrition Society (16) | 0.941 | 74.1 | 18.5 | 41.0 | 38.9 | 6.9 | 13.9 | 3.3 | Yes |
| Scientific Recommendations for Healthy Eating Guidelines in Ireland (17) | 0.964 | 70.4 | 40.7 | 10.4 | 72.2 | 58.3 | 0 | 4.0 | No |
| Australian Dietary Guidelines (18) | 0.870 | 92.6‡ | 77.8 | 69.4 | 66.7 | 61.1‡ | 77.8 | 5.3‡ | Yes |
| Dietary Reference Intakes (13) | 0.935 | 75.9 | 46.3 | 31.3 | 70.4 | 18.1 | 52.8 | 3.7 | No |
| 2015-2020 Dietary Guidelines for Americans (6) | 0.873 | 87.0 | 87.0‡ | 69.4 | 79.6‡ | 41.7 | 30.6 | 5.0 | No |

AGREE II = Appraisal of Guidelines for Research and Evaluation, 2nd edition.

guidelines discussed external review by experts before publication (4, 6, 18). Two guidelines appropriately described the process for updating recommendations (4, 6).

Clarity of Presentation

Clarity of presentation relates to whether key recommendations are unambiguous and easily identifiable in the guideline (20). The median score for this domain was 59.3% (IQR, 49.1% to 71.3%), with 4 guidelines meeting the 60% threshold (6, 13, 17, 18) (Table 2). The main limitation in this domain was that the different options for management of the health issue (for example, ways to limit sugar intake) were not clearly presented.

Applicability

Items in the applicability domain focus on the likely barriers to and facilitators of implementation, strategies to improve uptake, and resource implications of applying the guideline (20). The median score for this domain was low, at 34.7% (IQR, 11.1% to 50.0%) (Table 2). Only 1 guideline met the 60% threshold (18). The most common issue was failing to discuss the facilitators and barriers to the guideline's application and failing to address the resource implications of applying the recom-

mendations. Only 1 guideline (4) presented monitoring and auditing criteria.

Editorial Independence

Editorial independence relates to unbiased formulation of recommendations and competing interests (20). This domain had the lowest median score (33.3% [IQR, 6.9% to 65.3%]), with only 2 guidelines meeting the 60% threshold (Table 2). Most of the guidelines either did not provide a statement about funding and its influence in the process of guideline development or failed to state conflicts of interest of authors or the guideline panel (Appendix Table 3, available at www .annals.org).

Overall Assessment

Overall guideline quality was moderate (median score, 4.0 [IQR, 3.7 to 4.8]), with only the Australian guideline meeting the 60% threshold for all 6 domains. Scores ranged from 3.3 (German guideline [16]) to 5.3 (Australian guideline [18]) (Table 2). All of the guidelines were categorized as "recommended with modifications."

^{*} Agreement among reviewers for inclusion of guideline.

[†] Denotes whether systematic review methods (for example, systematic search and selection of criteria and quality assessment of studies) were used in the development of the guideline.

[‡] Highest-rated guideline in this domain.

Quality Assessment of Supporting Evidence for Recommendations: GRADE Results

There were a total of 66 unique publications across 9 eligible guidelines supporting the 12 dietary sugar recommendations. Evidence included systematic reviews; RCTs; nonrandomized, controlled trials; prospective cohort studies; case-control studies; national surveys; and cross-sectional studies (Appendix Table 4, available at www.annals.org). The Dietary Guidelines for the Brazilian Population and the 2015-2020 Dietary Guidelines for Americans did not cite any previously published studies as evidence for their recommendations (6, 15), and Public Health England conducted its own systematic reviews for its Carbohydrates and Health report that have not been published in a peer-reviewed journal but were publicly available (5).

Sixteen systematic reviews were used to inform 7 recommendations across 5 guidelines (4, 5, 14, 16, 18) (Appendix Table 5, available at www.annals.org). Evidence was low to very low for each systematic review. Fourteen reviews (87.5%) were downgraded for inconsistency, 11 (68.8%) were downgraded for imprecision, 2 (14%) were downgraded for publication bias, and 2 (12.5%) were downgraded for indirectness.

Two large RCTs (21, 22), both on SSBs and body weight, informed 2 recommendations from the German and Australian guidelines (16, 18) (Appendix Table 5). Our independent review indicated that the evidence was of very low quality for both and was downgraded for imprecision (wide CIs and trivial treatment effects based on the lower bound of the 95% CI) and indirectness. Eight small RCTs (<300 events for dichotomous outcomes or <400 participants for continuous outcomes) started at moderate quality and were all downgraded to very low quality due to imprecision and indirectness.

Eight large cohort studies (Appendix Table 5), all on SSBs and health outcomes (such as type 2 diabetes and body weight), informed 3 recommendations across the Nordic, German, and Australian guidelines (14, 16, 18). Evidence was considered very low quality for 6 studies (75%) (23-28) and low quality for 2 studies (25%) (29, 30). Three studies were downgraded for indirectness (37.5%), and 2 were downgraded for imprecision (25%). Two studies were rated up for a doseresponse (25%) (29, 30). Twenty-eight small cohort studies started at very low quality, and we did not rate up given their imprecision and indirectness.

Although a Dietary Guidelines Advisory Committee drafted an extensive scientific report (31) to inform the 2015-2020 Dietary Guidelines for Americans (6), the guidelines cited food pattern modeling and U.S. national caloric intake data from added sugars to inform recommendations. We planned to use GRADE to evaluate the quality of the evidence used in the model components as well as the accuracy of the modeling procedure; however, these details were not publicly available, and we were unable to assess the quality of the evidence for the recommendations.

The WHO guideline was the only one to use the GRADE approach (9). The WHO conducted 2 system-

atic reviews, one of which included observational studies evaluating effects of free sugars on dental caries (assessed as moderate-quality by the WHO and graded up for large effect size) and the other including RCTs and observational studies evaluating effects of free sugars on body weight (assessed as moderate-quality by the WHO and downgraded for publication bias). Although the WHO guideline recommendations are for free sugars, included studies among both systematic reviews used various forms of sugar, including sucrose, added sugars, and total sugars for the dental caries review (32) and free sugars, SSBs, fructose, sucrose, sweet foods, and added sugars for the body weight review (33). Similar discrepancies were found in 5 additional guidelines (Table 1).

We independently reviewed the WHO evidence profiles and deemed the quality of evidence on sugars and body weight to be low (with additional downgrading for inconsistency). We also reasoned that the evidence on sugar and dental caries was low (unlike WHO's rationale, we did not rate up for a large effect size). The WHO issued a strong recommendation to reduce free sugars to less than 10% of daily caloric intake based on 5 cohort studies (1200 children) assessing the risk for dental caries and a weak recommendation to reduce free sugars to less than 5% of daily caloric intake based on 3 ecological studies on the risk for dental caries.

DISCUSSION

We identified 9 PHGs containing 12 dietary sugar recommendations. The quality of development of the guidelines (assessed using the AGREE II instrument) was moderate, with 3 of 6 AGREE II domains (rigor of development, applicability, and editorial independence) having major limitations. Seven recommendations were qualitative, whereas 5 were quantitative, ranging from less than 5% to less than 25% of total calories from nonintrinsic sugars per day. The rationale for the varied sugar intake recommendations was based primarily on nutrient displacement, dental caries, and weight gain.

Using the GRADE approach, we found that the overall quality of evidence to support recommendations was low to very low. Optimal guidelines should be developed with increased rigor, and recommendations should be specific (population, exposure, comparator group, and outcomes critically important to the general public) and transparent (including explicit conflicts of interest and how the body of evidence was considered for developing each recommendation) and should follow GRADE guidance as intended (weak recommendations if the quality of evidence is low, with few exceptions [34]).

A PubMed search for reviews of dietary sugar guidelines done within the past 5 years identified only 1 other review. Although Hess and colleagues (2) reviewed dietary sugar recommendations around the world, the search was not systematic and the review did not assess the quality of the guidelines or the support-

ing evidence. The authors concluded that no clear link exists between added sugar intake and health outcomes.

The included guidelines examined the potential health effects of sugars and risk for dental caries, obesity, type 2 diabetes, and cardiovascular disease. The WHO and SACN suggested that a strong correlation exists between overall free sugars and health outcomes (4, 5). In both guidelines, most of the cited evidence examined SSB consumption and health outcomes rather than the consumption of free sugars from various foods.

Our review had limitations. This project was funded by ILSI, an organization that is funded primarily by the food and agriculture industry. The authors, having expertise in study methodology (particularly in the development of practice guidelines), wrote the protocol and conducted the study independent of the funding body. However, given our funding source, our study team has a financial conflict of interest and readers should consider our results carefully.

We initially sought to assess the quality of the evidence underlying the recommendations by using the Oxford Levels of Evidence, as indicated in our publicly available protocol. Post hoc, we chose to use the GRADE approach, wherein a body of evidence is categorized using intuitive language (high, moderate, low, or very low quality) and each category is accompanied by an explicit definition. In contrast, the Oxford Levels of Evidence uses numbers associated with specific study designs based on the traditional hierarchy of evidence. We believe that the Oxford Levels of Evidence gives a false impression of the evidence (for example, a systematic review of RCTs rated as level 1 evidence despite potentially serious limitations when comprehensively assessed using the GRADE approach). With GRADE methods, the evidence can be rated up or down on the basis of a set of criteria (such as precision, risk of bias, and publication bias). The criteria are applied using a systematic and explicit approach that includes extensive instructions and transparency with respect to the quality assessment. We believe that the use of GRADE reduces the likelihood of mislabeling the overall certainty of evidence.

Only 9 guidelines that explicitly reported their methods were included in this review. Given our focused eligibility criteria, this was not a review of all available dietary sugar recommendations that may influence the beliefs and actions of the public, regulators, and health care practitioners. For example, we identified 4 publications (35-38) containing dietary sugar recommendations written by influential organizations (American Academy of Pediatrics, European Food Safety Authority, American Heart Association, and India National Institute of Nutrition) that were excluded because they lacked a written methodology section. We did not include these reports because a comprehensive understanding of the methods used to develop a PHG is essential to assessing the quality of the development of a guideline and the quality of evidence for recommendations. We also excluded PHGs that were

not published in English. Although our review included guidelines from around the world, it was not a comprehensive review of all potentially available guidelines.

Our review also had several strengths. A priori, we documented our eligibility criteria, objectives, and planned methods of analysis as publicly registered on PROSPERO (7). We independently assessed the quality of development of dietary guidelines by using AGREE II and the certainty of evidence for sugar recommendations by using the GRADE framework, which has been endorsed by more than 90 health organizations worldwide (39). On the basis of our methodological analysis of PHGs, we believe the range of various recommendations and the evidence that supports these recommendations can be better interpreted by health care professionals and consumers trying to design effective programs and provide guidance to the public about sugar intake.

All of the reviewed guidelines suggested a decrease in consumption of nonintrinsic sugars. Although the overall direction was consistent, the rationale and evidence used to make each recommendation were inconsistent. This lack of evidentiary consistency, with various health concerns cited, creates confusion for practitioners and the public about the role that sugar plays in health.

Quantitative limits on sugar intake were recommended in 5 of the 9 PHGs (4-6, 13, 14). Each of the quantitative sugar recommendations (except the WHO recommendation) was based on an estimate of how much sugar could be consumed while maintaining a "healthy diet." For example, the Dietary Reference Intakes and the 2015-2020 Dietary Guidelines for Americans set limits of less than 25% and less than 10% of energy from added sugars, respectively (6, 13), based on diet modeling and intake data. Similarly, the SACN recommendation was based on the desired energy reduction of 100 calories per day for effective populationwide weight loss. An approximated 100 calories of free sugars was subtracted from the previous sugar recommendation to obtain this 100-calorie deficit, resulting in the specified maximal intake of 5% of total energy from free sugars (5). The method by which the Nordic Council of Ministers determined a limit of 10% of energy from added sugars was not explained in its PHG (14). In contrast, the WHO used 5 cohort studies (moderate quality) and 3 ecological studies (very low quality) on the risk for dental caries to set the limit of intake of free sugars to below 10% and 5% of total energy intake (4).

The quality of available evidence to link sugar with health outcomes was generally rated as low to very low. The prevailing concerns with high sugar intake are directed toward excessive calorie consumption and nutrient displacement. Sugar added to products adds considerable calories without any nutritional benefits and may take the place of other nutrient-dense foods in the diet. From a practical standpoint, added sugars are a source of calories that many public health authorities believe can be easily reduced. Doing so at a population level may result in a reduction in caloric intake and a subsequent decrease in the rate of overweight and

obesity. At present, there seems to be no reliable evidence indicating that any of the recommended daily caloric thresholds for sugar intake are strongly associated with negative health effects. The results from this review should be used to promote improvement in the development of trustworthy guidelines on sugar intake (40).

From University of Minnesota, St. Paul, Minnesota; McMaster University, Hamilton, Ontario, Canada; Kerman University of Medical Sciences, Kerman, Iran; and The Hospital for Sick Children Research Institute and University of Toronto, Toronto, Ontario, Canada.

Note: As the guarantors of the study, Drs. Johnston and Slavin take full responsibility for the work as a whole, including the study design, access to data, and the decision to submit and publish the manuscript.

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Disclosures: Dr. Slavin served on the 2010 Dietary Guidelines for Americans Advisory Committee (DGAC) where she chaired the carbohydrate committee that reviewed the relationships between added sugar intake and health outcomes. The results of that review were published in the 2010 DGACs, in Nutrition Reviews (Slavin J. Beverages and body weight: challenges in the evidence-based review process of the Carbohydrate Subcommittee from the 2010 Dietary Guidelines Advisory Committee. Nutr Rev. 2012;70 Suppl 2:S111-20.). She has presented widely on her work as chair of the carbohydrate and protein committees for the 2010 DGAC. Most of her research is in the areas of dietary fiber and gut health. As a dietitian, she is interested in dietary patterns and whole foods. Her research funding in the area of dietary sugars is summarized below. She received a grant from ILSI-NA Carbohydrate Committee in 2010 to examine sugar recommendations. That work was published in 2012 (Hess J, Latulippe ME, Ayoob K, Slavin J. The confusing world of dietary sugars: definitions, intakes, food sources and international dietary recommendations. Food Funct. 2012;3:477-86.). One of the coauthors of that paper was an employee of ILSI-NA at the time. That information is disclosed in the paper. Dr. Slavin and the University of Minnesota received the grant from ILSI-NA to support the current project. Besides ILSI-NA, Dr. Slavin thanks the following organizations for providing research funds for her laboratory the past 3 years: Minnesota Beef Council (satiety), Minnesota Cultivated Wild Rice Council (literature review), Barilla (snacking), Novartis Consumer Health (GSK) (fiber), American Pulse Association (satiety), MNDrive Global Food Ventures (nutrients in spinach), United States Department of Agriculture (fiber), The Mushroom Council (gut health), Pepsico (oatmeal), Welch's (FODMAPs), Nestle Health

Sciences (FODMAPs), and DSM (fiber). Her laboratory also has received contracts for analytical services in the areas of dietary fiber, whole grains, legumes, FODMAPs, digestive health, protein needs, carbohydrate needs, and snacking. Besides the companies listed, the laboratory has received funds in the past 3 years from Danone (snacking) and Coca-Cola (fiber). When the work is published, the funding source for all work in the laboratory will be disclosed as outlined by the journal. Dr. Slavin speaks widely on a range of human nutrition topics. Some talks on the topic of interest in this paper: "Fluid Consumption: Caloric Contribution to Weight Gain/Loss and Health: Factors That Influence Satiety" (Second International Conference on hydration and Health, sponsored by the ILSI North America Committee on Hydration, November 2011); "The Confusing World of Dietary Sugars: Views From the 2010 Dietary Guidelines Scientific Advisory Committee" (2012 Nutrition News Forecast, Academy of Nutrition and Dietetics, April 2012); "Food Is Not a Talisman: Reflections on the Science and Practice of Nutrition" (WO Atwater Lecture at Experimental Biology, April 2015). For full financial disclosure: ILSI meetings do not pay speakers; other scientific meetings also typically do not pay speakers if you are a member of that society. Dr. Slavin serves on the scientific advisory board for Tate and Lyle, Kerry Ingredients, Atkins Nutritionals, and Midwest Dairy Association. She also owns one-third share of the Slavin Sisters Farm LLC, a 119-acre farm in Walworth, Wisconsin, that is currently rented. Crops in 2016 included corn, soybeans, and pumpkins. Dr. Johnston is a member of GRADE, a working group that has developed a common, sensible, and transparent approach to grading quality of evidence and strength of recommendations. In addition to being a methods consultant to ILSI for this project, over the last 5 years, he has held investigator-initiated grants unrelated to the topic of sugar from BioK+ (a probiotic manufacturer), Genzyme (a manufacturer of enzyme replacement therapy for patients with rare lysosomal storage diseases), and a joint grant funded by Nestle and MITACS Accelerate (a provincially and federally supported not-for-profit organization that works with Canadian universities and companies to build partnerships that support industrial and social innovation in Canada) to assess probiotics for preventing necrotizing enterocolitis. Authors not named here have disclosed no conflicts of interest. Disclosures can also be viewed at www.acponline .org/authors/icmje/ConflictOfInterestForms.do?msNum=M16

Reproducible Research Statement: *Study protocol:* Available at www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015029182. *Statistical code:* Not applicable. *Data set:* See tables and appendices for all relevant data.

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Appendix Table 1. Additional Data Sources

Gray literature sources

- 1. National Guidelines Clearinghouse
- 2. National Institute for Health and Care Excellence
- 3. Scottish Intercollegiate Guidelines Network (SIGN)
- 4. Guidelines International Network
- Google Internet search engine (terms searched: "sugar guidelines" or "recommend* daily sugar"; limited to sites ending in ".gov" or ".org"; limited to the first 20 pages)

Experts in carbohydrates contacted in search for public health guidelines

- Dr. John L. Sievenpiper, MD, PhD, FRCPC, Associate Professor, Department of Nutritional Sciences, University of Toronto; Scientist, Li Ka Shing Knowledge Institute, St. Michael's Hospital; Consultant Physician, Division of Endocrinology & Metabolism, St. Michael's Hospital
- Dr. Julie Miller Jones, PhD, CNS, LN, Fellow of AACCI and ICC, Distinguished Scholar and Professor Emerita, Foods and Nutrition, St. Catherine University
- Dr. Keith-Thomas Ayoob, EdD, RD, FAND, Associate Clinical Professor, Department of Pediatrics, Albert Einstein College of Medicine

Appendix Table 2. AGREE II Instrument

Item, by Domain

Scope and purpose

- The overall objective(s) of the guideline is (are) specifically described.
- The health question(s) covered by the guideline is (are) specifically described.
- The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

Stakeholder involvement

- 4. The guideline development group includes individuals from all the relevant professional groups.
- 5. The views and preferences of the target population (patients, public, etc.) have been sought.
- 6. The target users of the guideline are clearly defined.

Rigor of development

- 7. Systematic methods were used to search for evidence.
- 8. The criteria for selecting the evidence are clearly described.
- The strengths and limitations of the body of evidence are clearly described.
- The methods for formulating the recommendations are clearly described.
- 11. The health benefits, side effects and risks have been considered in formulating the recommendations.
- 12. There is an explicit link between the recommendations and the supporting evidence.
- 13. The guideline has been externally reviewed by experts prior to its publication.
- 14. A procedure for updating the guideline is provided.

Clarity of presentation

- 15. The recommendations are specific and unambiguous.
- 16. The different options for management of the condition or health issue are clearly presented.
- 17. Key recommendations are easily identifiable.

Applicability

- 18. The guideline describes facilitators and barriers to its application.
- 19. The guideline provides advice and/or tools on how the recommendations can be put into practice.
- 20. The potential resource implications of applying the recommendations have been considered.
- 21. The guideline presents monitoring and/ or auditing criteria.

Editorial independence

- 22. The views of the funding body have not influenced the content of the guideline.
- 23. Competing interests of guideline development group members have been recorded and addressed.

Overall guideline assessment

- 1. Rate the overall quality of this guideline.
- 2. I would recommend this guideline for use.

AGREE II = Appraisal of Guidelines for Research and Evaluation, 2nd edition.

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| Appendix Table 3. COI Reporting Across Guidelines | porting Across (| Guidelines | | | |
|--|------------------|--|--|--|--|
| Guideline | COI | Groups Requiring COIs (Number of Members) | | COI Reporting | |
| | Reporting | | Affiliation | Financial | Intellectual |
| Australian Dietary Guidelines | Unclear | Dietary guidelines working committee (11) | Yes | N _O | Marginally-lists their research focuses |
| | | National Health and Medical Research Council project team (4), Department of Health and Ageing Project Team (5), contractors (8), expert reviewers (5) | Yes | ° N | No |
| | | Public consultation contributors; 2 rounds | OZ | No | No |
| Dietary Guidelines for the Brazilian Population | o Z | Listening workshop (59), evaluation workshop (29), working group for consideration of public consultation (10) | Yes | O Z | 0 Z |
| 2 | 2 | Fublic consultation contributors | | 02 2 | 0 2 |
| Nordic Nutrition Recommendations | 0 2 | Working group (11), topic experts ("over 100"; for carbohydrates = 4), topic peer reviewers (unspecified; for carbohydrates = 2), reference group of senior experts (9), steering group with representatives from each national authority (5), librarians (5). | No (country only) | o c Z z | o s 2 Z |
| | | | | | |
| Scientific Recommendations for Healthy Eating | 0 Z | Steering committee (11) | Yes (except for contract researcher) | 0 Z | No |
| Guidelines in Ireland | | Research team (11), Irish Nutrition and Dietetic Institute (unspecified), consultation day contributors (e.g., dietitians, nutritionists, Irish Nutrition and Dietetic Institute members, Irish Heart Foundation; unspecified) | o Z | o Z | 0 Z |
| | | Nutrition and novel foods subcommittee | Yes | No | No |
| Evidence-based Guideline of the German Nutrition Society | o Z | Authors of publication | Yes | °Z | °Z |
| DRI/Institute of Medicine | °Z | Panel on DRI for macronutrients (21), panel on the definition of dietary fiber (7), subcommittee on upper reference levels of nutrients (10), subcommittee on interpretation and uses of DRI (8) | Yes | Marginally–lists some industry work | Marginally—lists their research focuses |
| | | Staff macronutrient panel (8), staff fiber panel (7), staff upper reference levels panel (2), staff interpretation/use panel (3), staff standing committee (8), staff food and nutrition board (5), individuals who provided input (31 and some "unnamed"), federal DRI working committee (23) | ON. | 0 Z | o Z |
| | | Consultants (2), standing committee on the scientific evaluations of DRI (9), technical advisor to the DRI projects (1), U.S. government liaison (1), Canadian government liaison (1), food and nutrition board (15), independent reviewers (18) | Yes | 0 Z | o Z |
| | | Organizations, including industry (15) | NA (these are organizations, not people) | No | No |

| Appendix Table 3-Continued | pen | | | | |
|--|-----------|--|---|----------------|---|
| Guideline | COI | Groups Requiring COIs (Number of Members) | | COI Reporting | |
| | Reporting | | Affiliation | Financial | Intellectual |
| 2015-2020 Dietary Guidelines for Americans | Unclear | Federal advisory committee, divided into subcommittees for each chapter (14) | Yes | No | Marginally—lists their research focuses |
| | | Consultant subcommittee members (3) | Yes | * o Z | Marginally—lists their research focuses |
| | | Co-executive secretaries (4), policy officials (5), dietary guidelines management team (17), nutrition evidence library team (13), data analysis team (18), science writer/editor (1), public consultation contributors throughout commentary period up to December 2014 (918 [number of comments accounted for; comments may be by person or group or organization]), public consultation contributors 2014 | Yes | °Z | ° Z |
| | | Invited expert speakers (32), staff, contract, and/or technical support (20), national service volunteer evidence abstractors (28) | ON. | ° Z | o Z |
| Carbohydrates and Health (SACN) | ON. | Membership of Scientific Advisory Committee on Nutrition: Carbohydrates Working Group (12), observers carbohydrates working group (1), external consultants carb working group (5) | Yes | O Z | No |
| | | Membership of Scientific Advisory Committee on Nutrition (16) | Yes (but unclear affiliation for 2 members) | o _Z | No |
| | | Secretariat nutrition committee (15), secretariat carb working group (12), public consultation contributors (unspecified) | No | OZ | No |
| Sugars Intake for Adults and Children (WHO) | Unclear | WHO secretariat headquarters (11), WHO secretariat regional offices (11), members of the WHO Steering Committee for Nutrition Guideline Development 2012-2014 (17), public consultation contributors planning stage (18), public consultation contributors draft stage (173) | Yes | °Z | °Z |
| | | Members of the guideline development group Nutrition Guidance Expert Advisory Group Subgroup on Diet and Health (15), external resource persons 2012-2014 (10), external peer review group (6) | Yes | Yes | Yes |
| | | | | | |

COI = conflict of interest; DRI = Dietary Reference Intakes; NA = not applicable; SACN = Scientific Advisory Committee on Nutrition; WHO = World Health Organization.
* Dietary Guidelines for Americans do, however, state, "Per Federal Advisory Committee Act rules, Advisory Committee members were thoroughly vetted for conflicts of interest before they were appointed to their positions and were required to submit a financial disclosure form annually."

| Guideline Title | Overall Recommendation | Specific Recommendations, Including Strength (if Reported) | Citations Supporting Recommendation, n | Study Design | GRADE Evidence Quality (Certainty in Estimates of |
|--|---|---|---|--|---|
| Sugars Intake for Adults and Children (WHO)* | | "Reduced intake of free sugars throughout the life course–Strong Recommendation" "In both adults and children, WHO recommends reducing the intake of free sugars to less than 10% of total energy intake–Strong | 0 - | Systematic review | NA Low† |
| | | Recommendation "WHO suggests further reduction of the intake of free sugars to below 5% of total energy intake-Conditional Recommendation" | - | Systematic review | Very low |
| Carbohydrates and Health (Public Health England)‡ | "The population average intake of free sugars should not exceed 5% of total dietary energy for age groups from 2 years upwards" and "The consumption of sugars-sweetened beverages should be minimised, in both children and adults." | "Greater sugar intake is associated with increased energy intake—Adequate Evidence" and "Sugar sweetened beverage intake is associated with risk of type-2 diabetes—Moderate Evidence" | - | Systematic review | Very low |
| | | "Sugar consumption is associated with increased risk of dental caries—Moderate Evidence" and "Amount and frequency of SSB consumption is associated with dental caries—Adequate Evidence" and "Greater SSB consumption is associated with increased BMI-Limited Evidence" | - | Systematic review | Very low |
| Australian Dietary Guidelines | "Limit intake of foods and drinks containing added sugars such as confectionary, sugar-sweetened soft drinks and cordials, fruit drinks, vitamin waters, energy and sports drinks" | "Consumption of sugar-sweetened beverages is associated with increased risk of weight gain in adults and children-Grade B" | 15 | Systematic review; randomized, controlled trial; observational study | Low, very low |
| | | "High or frequent consumption of added sugars, particularly for infants and young children, is associated with increased risk of dental raries—Grade C" | - | Observational study | Very low |
| | | "Consumption of soft drinks is associated with increased risk of dental caries in children-Grade C" | - c | Observational study | Very low |
| | | Consumption of soft drinks is associated with increased risk of reduced bone strength—Grade C" | n | controlled trial; observational study | very low |
| Nordic Nutrition Recommendations | "Intake of added sugars should be kept below 10% of the energy intake" | ı | 14 | Systematic review; observational study | Low, very low |
| Evidence-based Guideline of the German Nutrition Society: Carbohydrate Intake and the Prevention of Nutrition-Related Diseases | "The consumption of sugar-sweetened beverages should be limited, because they increase the risk of obesity and diabetes" | "The available cohort and intervention studies regarding adults mainly show that a higher consumption of SSB is accompanied by an increased risk of obesity—Probable" "The majority of prospective cohort studies and meta analysis indicate an increased risk of type 2 diabetes with regular consumption of programs and power of the period of the studies and power of the period of the studies and power of the period of the studies and power of the studies and the studies and the studies and the studies and the studies are studies and the studies and the studies are studies and the studies and the studies are studies are studies and the studies are studies are studies and the studies are studies are studies are studies and the studies are studies | ۶ د د | Systematic review; randomized, controlled trial; observational study Systematic review; observational study | Low, very low Low, very low |

| Appendix Table 4–Continued | inued | | | | |
|---|---|---|---|---|---|
| Guideline Title | Overall Recommendation | Specific Recommendations, Including Strength (if Reported) | Citations Supporting Recommendation, n | Study Design | GRADE Evidence Quality (Certainty in Estimates of |
| Scientific Recommendations for Healthy Eating Guidelines in Ireland | "Healthy eating can be enjoyed with limited amounts of other foods' like biscuits, cakes, savoury snacks and confectionery. These foods are rich in calories, fat, sugar and salt so remember-NOT too MUCH and NOT too OFTEN" | 1 | ٥ | Randomized, controlled trial; narrative review or report | Very low |
| Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids | A maximal intake level of 25% or less of energy is suggested to prevent the displacement of foods that are major sources of essential micronutrients. | • | | Observational study | Very low |
| 2015-2020 Dietary Guidelines for Americans§ | "Consume less than 10% of calories per day from added sugars" | | 0 | | N A |
| Dietary Guidelines for the Brazilian Population | "Use oils, fats, salt, and sugar in small amounts for seasoning and cooking foods and to create culinary preparations" | ı | 0 | 1 | ∀ Z |

BMI = body mass index; GRADE = Grading of Recommendations Assessment, Development and Evaluation; NA = not applicable; SSB = sugar-sweetened beverage; WHO = World Health Organization.

* A systematic review on sugars and weight was conducted and referenced. However, authors did not look specifically at 10% reduction; only the effect of sugar on dental caries was cited for the final 2 of 3 recommendations.

That AMP reduct quality of evidence as "moderate"; however, in our independent assessment, we considered WHO's reasoning for rating up from low to be inappropriate.

Public Health England conducted its own systematic reviews that were unpublished.

§ A rigorous scientific report of unpublished systematic reviews was conducted but was not used to make recommendation.

| Annendiy Table 5 | Assessment o | of Individual Studios | Supporting Recomm | endations (GRADE) |
|--------------------|--------------|-----------------------|-------------------|--------------------|
| Abbelluix Tuble 5. | Assessment o | n maividuai studies | aubboruna kecomii | lendations (GRADE) |

| Study, Year (Reference) | Guidelines That Included the Study | GRADE | Reasons for Rating Up or Down |
|--|---|----------|--|
| Systematic reviews | | | |
| Forshee et al, 2008 (41) | Australia 2013, Nordic 2012 | Very low | Inconsistency, imprecision, publication bias |
| Gibson, 2008 (42) | Australia 2013 | Very low | Inconsistency, imprecision |
| Malik et al, 2006 (43) | Australia 2013 | Very low | Inconsistency, imprecision |
| Vartanian et al, 2007 (44) | Australia 2013, Germany 2012, Nordic 2012, Germany 2012 | Low | Inconsistency, imprecision |
| Wolff and Dansinger, 2008 (45) | Australia 2013 | Very low | Inconsistency, imprecision |
| Anderson et al, 2009 (46) | Australia 2013, Nordic 2012 | Very low | Inconsistency |
| Sonestedt et al, 2012 (47) | Nordic 2012 | Low | Inconsistency |
| Te Morenga et al, 2012 (33) | WHO 2015, Nordic 2012 | Low | Inconsistency, publication bias |
| Zhang et al, 2013 (48) | Nordic 2012 | Low | Indirectness, imprecision |
| Malik et al, 2010 (49) | Nordic 2012 | Very low | Inconsistency |
| Fogelholm et al, 2012 (50) | Nordic 2012 | Very low | Imprecision |
| Burt and Pai, 2001 (51) | Nordic 2012 | Very low | Inconsistency |
| Moynihan and Kelly, 2014 (32) | WHO 2015 | Very low | Inconsistency, imprecision |
| Mattes et al, 2011 (52) | Germany 2012 | Low | Inconsistency, imprecision |
| Nutritional Epidemiology Group, 2012 (53) | SACN 2015 | Very low | Inconsistency, indirectness, imprecision |
| SACN, 2011 (unpublished) | SACN 2015 | Very low | Inconsistency, imprecision |
| Randomized, controlled trials | | | |
| Sichieri et al, 2009 (22) | Australia 2013, Germany 2012 | Very low | Imprecision, indirectness |
| Chen et al, 2009 (21) | Germany 2012 | Very low | Imprecision, indirectness |
| Cohort studies | | | |
| Tucker et al, 2006 (23) | Australia 2013 | Very low | Indirectness, imprecision |
| Duffey et al, 2010 (24) | Nordic 2012 | Very low | Imprecision |
| Cohen et al, 2012 (25) | Nordic 2012 | Very low | Indirectness |
| Nissinen et al, 2009 (26) | Germany 2012 | Very low | Indirectness |
| Dhingra et al, 2007 (27) | Germany 2012 | Very low | None |
| Schulze et al, 2004 (30) | Germany 2012 | Low | Dose-response |
| Palmer et al, 2008 (29) | Germany 2012 | Low | Dose-response |
| Paynter et al, 2006 (28) | Germany 2012 | Very low | None |

GRADE = Grading of Recommendations Assessment, Development and Evaluation; SACN = Scientific Advisory Committee on Nutrition; WHO = World Health Organization.

CORRECTION

Disclosures from 2 authors (Drs. Johnston and Slavin) were explained in the Disclosures section of the article. The role of the funding source, ILSI, was also clarified in the article and in the Financial Support section.