CARBOHYDRATES: PUBLIC HEALTH GUIDELINES, SATIETY AND GASTROINTESTINAL TOLERANCE

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Dedication

This dissertation is dedicated to all of the food science and nutrition experts in my life who have served as professors, supervisors, mentors, role models and friends. Thank you for your guidance and inspiration.

Abstract

Consumer perception of carbohydrates is shifting, and not all carbohydrates are perceived in the same way. The 2016 Food and Health survey, conducted annually to assess factors impacting consumer food purchases, reveals that consumers are looking to increase their intake of certain carbohydrate foods, including whole grains, fiber and beans, while looking to decrease other carbohydrates sources, particularly added sugars.[1] Additionally, there has been increased interest in diets low in rapidly fermenting carbohydrates (FODMAPs) for the improvement of gastrointestinal symptoms.[2] Although all carbohydrates share the same basic chemical structure, different types of carbohydrates result in various physiological outcomes.[3] This body of work explores the rationale for consumer perception of various types of carbohydrates and examines the validity of these claims.

The first portion of this dissertation explores the changing perception of dietary sugars. Many public health agencies have made various recommendations encouraging decreased consumptions of non-intrinsic sugar, for a variety of reasons.[4–6] Additionally, the Food and Drug Administration has ruled that the Nutrition Facts Panel will be required to indicate the amount of added sugars contained within all labeled food products.[7] These dietary recommendations and regulatory changes will affect the food industry, health professionals and consumers. Our objective was to assess the scientific basis behind these recommendations and policies to determine if the evidence supporting these actions is sound.

We conducted a systematic review of public health guidelines providing dietary sugar recommendations across the globe.[8] The purpose of this chapter was to systematically review public health guidelines on sugar intake around the world and to assess consistency of recommendations, methodological quality of guidelines, and the quality of evidence supporting each recommendation. The search identified nine guidelines that offered 12 recommendations. Examination of the guidelines development process indicated limitations particularly in rigor of development, applicability, and editorial independence that should be considered when creating these dietary guidelines. Although each of the reviewed guidelines recommended limiting the consumption of foods containing non-intrinsic sugars, the specific recommendations were not consistent. The recommendations were based on various health concerns, including nutrient displacement, dental caries, and weight gain. The quality of evidence the guidelines cited in support making recommendations was low to very low based on a GRADE analysis of the supporting evidence.[8]

With the changes in consumer perceptions of processed foods, consumers are looking for whole foods that will fill their plates and provide health benefits. Pulse grains are a category of legumes, including beans, peas and lentils, which are not harvested for their oils. Due to the nutritious nature of pulse grains, rich in both protein and fiber, pulses have been promoted as a candidate to promote satiety and glycemic control at meals. In a crossover feeding study, participants consumed calorie-matched fruit smoothies prepared with either an ice cream base or pureed red lentils.[9] Self-reported satiety, blood glucose response, and ad libitum food intake at a secondary meal were all measured along with

breath hydrogen and methane and gastrointestinal tolerance. While there was no significant difference in satiety response, energy intake at the secondary meal or blood glucose response, the nutrient profile of the lentil smoothie was improved with increased protein and fiber and dramatically lower fat content. Both smoothies were generally well tolerated; however, there was a slightly elevated AUC for perceived gastrointestinal tolerance over 24 hours in the lentil smoothie. Overall, this study found that a substitution of lentils into a meal is not likely to improve satiety; however lentils are a good source of fiber and protein and can greatly improve nutritional content of the meal.[9]

While pulse grains generally have a positive consumer perception, there is a group of individuals who avoid legumes and other fermentable fibers due to an increase in gastrointestinal symptoms as indicated by the previous study. More specifically, there has been increased interest in a diet low in rapidly fermentable carbohydrates, known as FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) for individuals suffering from irritable bowel syndrome (IBS). While this diet has been shown to reduce symptoms in individuals with IBS and is growing in popularity, there are still many gaps in the literature that need additional research.[10] This dissertation describes two research trials examining the effects of high and low FODMAP foods on gastrointestinal tolerance in a healthy population.

While many fruits are allowable on a low FODMAP diet, consumption of all fruit juice is cautioned due to the large fructose load contained within a serving of juice. However, there is little research on the importance of fructose load for individuals following a low

FODMAP diet, potentially leading individuals following the low FODMAP diet to unnecessarily restrict their diet. The objective of this study was to determine if there was a difference in gastrointestinal (GI) tolerance between juice from a high FODMAP fruit (apple juice) and juice from a low FODMAP fruit (white grape juice) in healthy human subjects.[11] A double-blind randomized controlled crossover study was conducted with 40 healthy adults. Fasted subjects consumed 12 oz of either apple juice or white grape juice. Breath hydrogen measures were taken at baseline, 1, 2, and 3 hr. Subjective GI tolerance surveys were completed at the same time intervals and at 12 and 24 hr. Consumption of apple juice resulted in a greater mean breath hydrogen area under the curve at 23.3ppm·hr (13.0, 33.6) compared to white grape juice at 5.8 ppm·hr (-4.6, 16.1) ($p<0.001$). No differences in reported GI symptoms were seen between treatments.[11] Both juices were well tolerated and neither produced any severe symptoms in healthy adults, regardless of the high fructose load. White grape juice consumption resulted in only a small rise in breath hydrogen, which may suggest excluding foods only because of the high fructose load could be unnecessarily restrictive.[11]

The second study assessing the effects of low and high FODMAP foods on gastrointestinal tolerance assessed the gastrointestinal effects of three low FODMAP oral nutrition supplements (ONS) in healthy adults. A double-blind randomized controlled crossover study was conducted in 21 healthy adults (19-32 years).[12] Fasted subjects consumed one of four treatments at each visit, with a one week wash out period between visits. Each participant received all treatments. Treatments included three low FODMAP ONS formulas (A, B, and C) as well as a positive control consisting of 5g

fructooligosaccharides (FOS) mixed in lactose-free milk.[12] Breath hydrogen and subjective GI symptom questionnaires were collected at baseline and periodically following treatment consumption. The positive control resulted in higher breath hydrogen response compared to all three of the low FODMAP ONS beverages at 3 and 4 hours after consumption. There were no differences in GI symptom response between treatments. All treatments were well tolerated in healthy participants. These findings conclude that the low FODMAP formulas resulted in a lower breath hydrogen response compared to the positive control, and may be better tolerated in individuals with IBS.[12]

Although carbohydrates are made up of the same basic building blocks, different carbohydrates have varying public perceptions and physiological effects.[1,3] While there may be some evidence to support these public perceptions of carbohydrates, there remains a need for more research in the areas of dietary sugar, pulse grains, and low FODMAP diets.

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Chapter One

ARE RESTRICTIVE GUIDELINES FOR ADDED SUGARS SCIENCE BASED?

The text of this chapter is a reprint of the material as it appears in "Are restrictive guidelines for added sugars science based?" previously published by *Nutrition Journal*.[13] The content has been reformatted to meet university guidelines.

Summary

Added sugar regulations and recommendations have been proposed by policy makers around the world. With no universal definition, limited access to added sugar values in food products and no analytical difference from intrinsic sugars, added sugar recommendations present a unique challenge. Average added sugar intake by American adults is approximately 13% of total energy intake, and recommendations have been made as low 5% of total energy intake. In addition to public health recommendations, the Food and Drug Administration has proposed the inclusion of added sugar data to the Nutrition and Supplemental Facts Panel. The adoption of such regulations would have implications for both consumers as well as the food industry. There are certainly advantages to including added sugar data to the Nutrition Facts Panel; however, consumer research does not consistently show the addition of this information to improve consumer knowledge. With excess calorie consumption resulting in weight gain and increased risk of obesity and obesity related co-morbidities, added sugar consumption should be minimized. However, there is currently no evidence stating that added sugar is more harmful than excess calories from any other food source. The addition of restrictive added sugar recommendations may not be the most effective intervention in the treatment and prevention of obesity and other health concerns.

Introduction

Governments and health organizations worldwide have published dietary guidance for sugar intake.[14] Despite access to the same published literature, recommendations vary greatly and create confusion for health practitioners and consumers. Since 1980, Dietary Guidelines for Americans (DGA) has recommended we "avoid too much sugar", yet dietary advice has typically recommended foods high in sugar, such as fruits and dairy products. As a way to clarify the types of sugar to avoid, the terms added sugars and free sugars are used. Added sugar recommendations have been in existence since 2002, with recent recommendations becoming progressively more restrictive over the years.[14] This paper addresses current and proposed added sugar recommendations and assesses their practicality within the United States.

Definition of Added Sugars

No universally accepted definition for added sugars exist (Table 1-1). The Food and Drug Administration (FDA) classifies added sugars as, mono and disaccharides added to foods during production including sugars, syrups, fruit juice concentrates, honey, etc. This would not include sugars that naturally exist in foods, such as sugars in fruits or dairy products.[15] A common point of contention between institutions is whether or not fruit juice should be included as added sugars. The proposed revisions to the Nutrition Facts and Supplements Label published by the FDA in 2014 classifies fruit juice concentrate added to food products as added sugar, while juice not from concentrate as not added sugar. In comparison, the USDA recommendations do not specify that fruit juice from concentrate contributes to added sugar totals.[15,16]

In addition to various definitions for the term "added sugars", the World Health Organization (WHO) utilizes the term "free sugar". Free sugar is similar to added sugars, as it includes all sugars and syrups added to foods; however, free sugar also includes sugars naturally present in fruit juices and fruit juice concentrates.[4] Free sugar includes sugars naturally found in fruit juice that is consumed as a beverage as well as fruit juices added to food products. Assessing added sugar intake and compliance with recommendations would be extremely difficult without a clear and established definition of the term "added sugar" and, specifically, how fruit juice should contribute to added sugar values.

Function of Added Sugar

Added sugars are chemically identical to sugar that naturally occurs in food products.[14] The body cannot distinguish the source of the nutrient and processes the sugar in the same way. Sugar may be added to food products for many reasons, the most obvious reason being adding sweetness and enhancing the palatability of foods. Although this function of sugar is often opposed and criticized, many American consumers would not find a number of "healthy" foods palatable without added sugar. Some examples include cranberries, yogurt and oatmeal. Nutrition professionals often encourage clients to consume these foods as part of a healthy diet, even with some added sugar.[17]

Another function of sugar within food products is texture enhancement. Sugar produces a tender texture in baked products, and inhibits ice crystallization in frozen products. Sugar provides body to products and, when removed, has to be substituted with bulking agents to achieve a similar mouth feel.[18] Carmelization and maillard browning are both

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reactions specific to sugar and provide an appearance expected in food products. Sugar also plays a role in food safety by inhibiting the growth of microorganisms at high concentrations. By binding with water molecules, sugar can maintain moisture contents in products lengthening the shelf life.[18] Overall, it is important to remember that sugar functions in many capacities beyond just flavor.

Added Sugar Intake in the American Diet

Added sugar intake is on average 13% of total energy intake in adults and 16% in children, consistently decreasing with age.[19] Added sugar consumption has declined in all age groups from NHANES data taken in 2001-2004 to data from 2007-2010. Meanwhile, rates of obesity did not mimic the decline over the same time period.[20] According to NHANES data from 2009-2010, 47% added sugars in the American diet come from beverages, 31% from snacks and sweets, 8% from grains, and 14% from the categories of dairy, mixed dishes, condiments, fruits and fruit juice and vegetables combined.[20] While there is room for improvement in the American diet, this decrease in added sugar intake is encouraging and understanding the main sources of added sugars provides a direction to focus our efforts.

Added Sugar Recommendations in America

In 2002, the Institute of Medicine (IOM) Dietary Reference Intakes recommended that less than 25% of total energy should come from added sugars. The recommendation is based on the concept that foods containing high amounts of added sugars are typically high in calories and low in micronutrients.[21] The idea that added sugars are "empty calories" is a commonly cited reason that added sugar recommendations are necessary.

Diets containing a large amount of energy as "empty calories" can lead to micronutrient malnutrition or over consumption of calories. Consuming the daily recommendation of all nutrients within an individual's estimated energy requirement is challenging when the individual is consuming a large portion of his or her calories as empty calories. Repeated consumption of empty calories without compensation from other nutrients can lead to weight gain.

The current 2010 Dietary Guidelines for Americans, includes solid fats and added sugars (SoFAS) in their recommendation of 5-15% of total energy from solid fats and added sugars.[22] Minimizing SoFAS consumption is encouraged to reduce excess calorie consumption and to replace foods high in added sugars with foods lower in added sugars and greater nutrient density. SoFAS consumption above the recommendation is considered to be incompatible with the USDA Food Patterns, likely exceeding calorie limits or obtaining inadequate micronutrient intake.[22]

The USDA Food Patterns were created to assist the public in following Dietary Guideline recommendations, providing amounts of food from each food group to achieve optimal nutrient intake.[23] The USDA Food Patterns groups added sugars and solid fats together and recommends adult females and adult males to limit "empty calorie" intake to 120-250 calories per day and 160-330 calories per day, respectively, depending on caloric needs.[20] Consumption of empty calories is typically above the current recommendations in all age groups; almost 90% of Americans exceed the USDA food pattern recommendations.[20] The evolution of the concept of discretionary calories (2005 DGAs) to empty calories (2010 DGAs) is explained by Nicklas and O'Neil.[24] The authors also

explain that the reduction of solid fats and added sugars is to remove calories from the diet, not because solid fats and added sugars are linked to negative health outcomes.[24]

The World Health Organization not only cites the effects of excess calories, but also the impact that sugar can have on dental health. The current World Health Organization recommendation of fewer than 10% of total calories from free sugars was set in 2003.[25] However in 2015, WHO set a conditional recommendation suggesting that less than 5% of total energy should come from free sugars.[4] This conditional recommendation proposed by WHO is based on a positive association between free sugar intake and dental caries among children.[4] Sugar consumption has been positively associated with risk of dental disease. According to a meta-analysis published in 2014, there is moderate evidence indicating that a free sugar intake less than 10% of total calories was associated with decreased risk of dental caries.[26] Further decrease in caries was seen in Japanese surveys, taken between 1959 and 1960, when free sugar intake approached 5% of total calories.[27] The area surveyed had low fluoride exposure so may not be an accurate model to extrapolate to the good fluoride exposure in the United States, although the WHO states that all populations, regardless of fluoridation, could possibly see improvement in dental caries with decreased free sugar intake.[4,27]

Additionally, the sugar consumption data was calculated by looking at sugar consumption per capita, added sugar intake compared to incidence of dental carries for each individual was not known.[27] The limitations of the Japanese studies prevented the WHO from setting a strong recommendation to consume fewer than 5% of calories from free sugars.[4] However, because dental caries occur throughout the lifespan, consuming fewer free sugars is estimated to have a cumulative effect and result in decreased dental problems

later in life and no evidence of harm was seen in diets containing fewer than 5% energy from free sugars.[4]

Dietary Guidelines for Americans 2015

The release of the Scientific Report of the 2015 Dietary Guidelines Advisory Committee (DGAC) in February 2015 brought further attention to added sugars. The DGAC report placed a large focus on added sugars, making it one of the five "cross-cutting topics."[20] The Committee reexamined the evidence surrounding the potential health effects of added sugars. The DGAC assessed the evidence that added sugar negatively impacts the health risks for obesity, type II diabetes, cardiovascular disease and dental carries. The DGAC determined, based on the available evidence, there was a strong correlation between added sugars and negative health risks. Most of the cited evidence examines the association between sugar sweetened beverage (SSB) consumption and the health risk rather than the consumption of added sugar from variety of foods.[20] It is easier to count consumption of SSB with food frequency instruments used in epidemiologic studies than to estimate total added sugar intake since few databases included information on added sugars. While SSB consumption may be the best method available for added sugar estimates, it is not without its limitations including possible confounding variables within the population. According to a recent study of over 12,000 participants, individuals reporting to consume one or more SSB per day were significantly more likely to smoke, consume fewer fruits and vegetables and report a sedentary lifestyle.[28] No discussion of if these confounding variables were considered in the DGAC report.[20]

After an examination of the evidence and diet modeling, the DGAC suggested an appropriate intake of calories from added sugars to be between 4-6% and set a maximal intake of 10% total energy from added sugars.[20] After a period of time allowing for comments from the general public, the USDA and Department of Health and Human Services will assess evidence behind the recommendation from the USDA to set the Dietary Guidelines for Americans 2015 added sugar recommendation.[20]

With this suggested restriction on added sugars, the DGAC recognizes that the logical consequence of removing added sugars from the diet and food products would be replacing the added sugars with low calorie sweeteners. However, the DGAC report advises against this replacement due to the minimal evidence regarding long-term effect of low calorie sweeteners. Instead, the DGAC encourages the replacement of sugar-sweetened beverages with water and does not suggest a replacement in food products. Removal of sugar from products will change the taste, texture and shelf-life of products due to the functions of sugar previously discussed.[18] The sugar must be replaced with other ingredients and, if not low calorie sweeteners, what would be a better alternative? Evidence exists to support the use of low-calorie sweeteners in weight reduction[20] and many consumers utilize this approach to support weight loss. The FDA recognizes artificial and low-calorie sweeteners as safe for consumption, and the Academy of Nutrition and Dietetics advises that non-nutritive sweeteners can fit into a healthy diet.[29] Identifying alternative sweeteners or ingredients to produce comparable food and beverage products is essential in changing the consumption patterns in Americans. Taste is consistently the most important buying factor for most Americans, and without great tasting alternatives consumers are not likely to make dietary changes.[30]

Proposed Addition of "Added Sugar" to Nutrition Facts Panel

Currently, there is no easy way for consumers, researchers or health professionals to track added sugar consumption and assess compliance with recommendations. Very few databases exist that calculate added sugars, and, due to the various added sugar definitions, the information obtained from these databases may result in a range of added sugar values. In March 2014, the FDA proposed changes to the Nutrition Facts Panels to assist consumers in making more educated food choices that would lead to a healthy diet consistent with Dietary Guidelines for Americans. The recent proposal to update the Nutrition Facts Panel advocates for the addition of an "Added sugars" category below the "Sugars" category, that would provide a way to track and compare added sugars.[31] The proposed amendments to the food labels suggest displaying added sugar in grams. The DGAC report supports such changes to the food labels and recommends displaying added sugar values in grams, teaspoons and percent daily value.[20]

A supplemental proposed rule regarding the Nutrition Facts Panel was published in July of 2015. The FDA proposed to establish a less than 10% Daily Reference Value (DRV) and to include the percent Daily Value (DV) on the Nutrition Facts Panel.[32] The supplemental proposed rule cites the 2015 DGAC report as their basis for instituting an added sugar DRV. The proposed rule states that the 2015 DGAC showed a "strong association between a dietary pattern of intake characterized, in part, by a reduced intake of added sugars and a reduced risk of cardiovascular disease".[32] Traditionally, DRVs and %DVs have been established for nutrients where an average dietary requirement can be determined from available scientific evidence.[33] The data used to determine the <10% DRV for added sugar was based primarily on diet modeling conducted for the 2015

DGAC. No DRV is has been proposed for total sugars at this time due to lack of available evidence for a reference intake.[20,32]

The purpose of the FDA's changes to the Nutrition Facts Panel is to help consumers make choices leading to healthier diets, however; the addition of the "added sugar" category may not provide much novel knowledge to consumers. According to NHANES 2009-2010, nearly 80% of added sugars come from sugar-sweetened beverages (47%) and snacks and sweets (31%).[20] The proposed changes to the food labels would require food companies to invest their resources to calculate the added sugar in their products, when the majority of added sugar consumed comes from obvious sources of sugar. Just over 20% of added sugars consumed by Americans come from non-obvious forms where the consumer would benefit from the knowledge of added sugars on the food labels, if they choose to read the label.[20]

A study presented by the International Food and Information Council showed that the addition of the category "Added Sugars" to the Nutrition Facts Panel reduced the consumer comprehension of the food label. The percent of participants able to accurately identify the total grams of sugar dropped from 92% to 55% when the added sugars category was included, with more than half the participants adding added sugars with the sugar category.[34] A similar study was later conducted by the FDA, finding consistent results. Ability to accurately identify the grams of sugar per serving decreased from 81% to 65% when the label was updated to the proposed format.[35]

Other research supports that consumers are interested in added sugar labeling. Kyle & Thomas report that consumers believe Nutrition Facts labeling for added sugar will be

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more helpful than confusing[36] A study in European Union found that consumers expect

that a reduction in free sugars in a product will be linked to a reduction in the calorie

content of the food.[37] Nevertheless, a consumer study with cereals found that participants

rated cereals containing "fruit sugar" as healthier than cereals containing "sugar",

although there were no differences in nutrient content between the cereals.[38] Total sugar

analysis is challenging enough. When sugar content of commercial foods targeted to

infants and children was conducted by a blinded laboratory analysis of accepted chemical

methods, nutrient label data underestimated or overestimated actual sugar content

routinely. The authors suggest that more effort should be made to standardize methods

for sugar labeling of foods, especially foods targeted to children.[39]

Health Canada recently removed the added sugars category from their proposed nutrition

facts table and included a 20% DV for total sugar.[40] Consumer research by the Canadian

government found that information about carbohydrates and total sugars was confusing

when the table included added sugars. It also found the % DV approach to be useful and

easy to understand. They state:

> "*the proposal to declare the amount of added sugars was popular among
> consumers and health stakeholders (including health professionals). However,
> industry stakeholders questioned the scientific basis of requiring the declaration
> of added sugar given that the body metabolizes naturally occurring and added
> sugars in the same way. Similarly, the inability of analytical method to
> distinguish between naturally occurring and added sugars would contribute to
> significant compliance and enforcement challenges.*"

Because added sugars are not chemically different from intrinsic sugars, there is no way

to analytically determine the amount of added sugar in a food product.[14] Food

manufacturers would have to calculate the added sugars based on the recipe in order to

determine the added sugar content in each product every time the product is reformulated. Without a clear definition of added sugars the resultant labeling will likely be inconsistent. The FDA would require food companies to document, maintain and provide records on product composition to verify the published value of added sugars.[16] Due to competition within the food industry and the proprietary nature of the formulations, food manufacturers would be very resistant to release such information. Moreover, each of these steps will require additional time, money and an acquired skill set that smaller food companies may not have the resources to comply with.

Conclusion

Excess calorie consumption can lead to weight gain and increased risk of obesity and obesity-related co-morbidities.[20] Empty calories and added sugars play a role in this when consumed in abundance. Added sugars are low in nutrient density and calories from added sugars can add up quickly if the individual is not conscious of their diet. However, there is no evidence suggesting that excess calories from added sugars specifically are worse than excess calories from any other food source. Much of the evidence linking added sugars to chronic disease is done measuring sugar sweetened beverages rather than percent calories from all added sugars.[20] With nearly half of added sugar consumption in America being attributed to sweetened beverages, perhaps encouraging healthy beverage alternatives to sugar sweetened beverages should be the focus, rather than zeroing in on all added sugars.

Recommendations as low as 5% total energy from free sugars is likely too restrictive for most Americans to achieve.[41] Added sugars should be consumed at a minimum as they

are often a source for surplus calories in the American diet; however, stringent

recommendations and mandatory food labeling is likely not the most effective way to

reduce added sugar and excess calorie consumption. Education on healthy beverages,

snack choices and portion sizes may be a better starting point for reducing empty calorie

intake.

Table 1-1. Added sugar definitions and distinctions from various agencies

Food and Drug Agency (FDA) Proposed Nutrition Facts Label[16]	Mono- and disaccharides added to foods during production including: sugars, syrups, fruit juice concentrates, honey, etc.
United States Department of Agriculture (USDA) Choose MyPlate[15]	Sugars added during processing and preparation. Includes: sugars, syrups, honey, nectars, etc. Excludes: fruit juice and fruit juice concentrates
World Health Organization (WHO) Free Sugar Guidelines[4]	Mono- and disaccharides added to foods during processing or by the consumer during preparation. Includes: Sugars, syrups, honey, fruit juice and fruit juice from concentrate.
Scientific Report of the 2015 Dietary Guidelines Advisory Committee[20]	Sugars, syrups, isolated naturally occurring sugars (ex: fruit juice concentrate) and other caloric sweeteners

Chapter Two

TOTAL, ADDED, AND FREE SUGARS: ARE RESTRICTIVE GUIDELINES

ACHIEVABLE?

The text of this chapter is a reprint of the material as it appears in "Total, Added, and

Free Sugars: Are Restrictive Guidelines Science-based or Achievable? " previously

published by *Nutrients*.[41] The content has been reformatted to meet university guidelines.

Summary

Sugar consumption, especially added sugars, is under attack. Various government and health authorities have suggested new sugar recommendations and guidelines as low as 5% of total calories from free sugars. Definitions for total sugars, free sugars, and added sugars are not standardized, nor are there accepted nutrient databases for this information. Our objective was to measure total sugars and added sugars in sample meal plans created by the United States Department of Agriculture (USDA) and the Academy of Nutrition and Dietetics (AND). Utilizing the Nutrition Data System for Research (NDSR) nutritional database, results found that plans created by the USDA and AND averaged 5.1% and 3.1% calories from added sugar, 8.7% and 3.1% from free sugar, and 23.3% and 21.1% as total sugars respectively. Compliance with proposed added sugar recommendations would require strict dietary compliance and may not be sustainable for many Americans. Without an accepted definition and equation for calculating added sugar, added sugar recommendations are arbitrary and may reduce intakes of nutrient-rich, recommended foods, such as yogurt, whole grains, and tart fruits including cranberries, cherries, and grapefruit. Added sugars are one part of excess calorie intake; however, compliance with low added sugar recommendations may not be achievable for the general public.

Introduction

Sugar consumption, especially added sugar, has been indicated as a major cause of several chronic diseases prevalent in America including obesity, heart disease, diabetes and dental caries.[42] Results have been inconsistent in determining if increased added sugar consumption is associated with weight gain and obesity rates. Added sugars contain calories and are low in nutrients. The logic states that if added sugar consumption increases without compensation from other calorie sources, calorie intake will also increase which can result in weight gain.[42]

Debate continues on whether added sugars play any unique role in obesity. Bray and Popkin[43] argue that sugar-sweetened beverages are associated with several health problems and have effects beyond the calories they add to the diet. In contrast, Kahn and Sievenpiper[44] argue that there is no clear or convincing evidence that any dietary or added sugar has a unique or detrimental impact relative to any other source of calories on the development of obesity or diabetes. Added sugars provide 4 kcal/g just like any other digestible carbohydrate and are no more likely to cause weight gain than any other calorie source.[45] Unlike sodium or dietary fiber that have clear links to health outcomes, added sugar intake is not uniquely linked to negative health outcomes or chronic diseases.

Percent total energy from added sugar has decreased over the past fifteen years, returning to a value close to the typical American diet in the late 1970s.[42,46] Unfortunately, the rate of obesity has not followed the same downward trend, although rates have leveled off among most demographic subgroups. Confusion on definitions

for sugars, including total, added, and free will continue to challenge the research community. Additionally, recommendations to consume less than 10% of calories from added sugars, as suggested in recent reports will be impossible to adopt without agreement on definitions and accepted measures for total sugars, added sugars, and free sugars. Also, if these recommendations are not consistent with accepted dietary recommendations and food patterns, it will be impossible for government agencies and consumers to plan and consume diets that are within accepted guidelines for sugar intake.

Sugar

The Food and Drug Administration (FDA) defines sugars as, "the sum of all free mono and disaccharides" which would include glucose, fructose, galactose, lactose and sucrose and maltose.[44] Sugars can be found naturally in foods, including fruits and dairy products, in addition to those sugars that are added to foods during processing. No recommendations currently exist regarding total sugar intake in the United States. There is not sufficient evidence to set a quantitative value as a recommended intake or limit for total sugar intake at this time.[44]

Added Sugar

Added sugars are sugars that are not naturally found in the food product and are added during the production of the food.[15] Since USDA developed the added sugars definition, the added sugars term has been used in in the scientific literature. The 2000 Dietary Guidelines for Americans used the term to aid consumers in identifying beverages and foods that are high in added sugars.[47] Although added sugars are not

chemically different from naturally occurring sugars, many foods and beverages that are major sources of added sugars have lower micronutrient densities compared with foods and beverages that are major sources of naturally occurring sugars.[14] Currently, U.S. food labels contain information on total sugars per serving, but do not distinguish between sugars naturally present in foods and added sugars.

Calories from added sugars account for approximately 13% of total calories in American adults and 16% in adolescents, according to National Health and Nutrition Examination Survey (NHANES) data from 2005 to 2010.[19] As published by NHANES, the top sources of added sugar in Americans are sugar-sweetened beverages, desserts, sweetened fruit and candy.[16]

Added sugar has been defined by the FDA as, "sugars and syrups that are added to foods during processing or preparation" excluding sugars naturally found in foods, such as fruits or dairy products.[15] Other organizations and nutrient databases define added sugars slightly differently, resulting in a range of values. For example, in the FDA's proposed revisions to the Nutrition Facts Label, fruit juice concentrates are to be considered as added sugar, while the USDA does not consider any form of fruit juice as added sugar.[15,16] The World Health Organization (WHO) uses the term "free sugar" rather than "added sugar" in their sugar recommendations. Free sugar includes added sugars as well as sugars naturally present in fruit juices as well as fruit juice concentrates.[4] Without a universal and explicit definition, nutrition databases may use different equations to calculate added sugar resulting in a range of values, which could be very confusing to consumers.

The range of recommendations for added sugar consumption for Americans is broad and has trended down in recent years, as shown in **Table 2-1**. The rationale for establishing added sugar recommendations appears aimed at reducing the total calories in foods high in added sugars, driven by a belief that these food types contribute empty calories, with low nutrient density. Overconsumption of foods high in added sugars therefore may replace other, more nutrient dense foods, and result in nutrient deficiencies or overconsumption of calories.[14] The 2010 Dietary Guidelines for Americans (DGA) suggests that a diet containing more than 15% total calories from solid fats and added sugars cannot comply with a healthy diet within recommended calorie levels.[16] The most recent recommendation was drafted by the World Health Organization (WHO) and released in March 2015, proposing a conditional recommendation of no more than 5% of total energy intake contributing by free sugars.[4]

Most public health opinion leaders agree that added sugar should be consumed at a minimum to prevent excess intake of calories while taking in all necessary nutrients. The purpose of this paper is to determine the percent of total energy from total sugars and added sugars using meal plans designed by organizations responsible for dietary guidance. The objective is to determine if it is possible to meet the current and proposed recommendations following a recommended food pattern. Published meal plans from the USDA and the Academy of Nutrition and Dietetics were examined using current nutrient analysis software that calculates added sugar contents in food items.

Methods

Added sugar Database

Very few existing nutrient databases have information regarding added sugar contents in food products. Nutrition Data System for Research (NDSR) version 2014 includes added sugar estimations in its nutrient analysis and also includes food mixtures and commercial products so that it why it was chosen as the database for this work. NDSR contains a comprehensive nutrient database comprised of more than 18,000 food products including brand names. NDSR calculates added sugars in two separate ways: Added sugars by available carbohydrate, as well as added sugars by total sugars. Added sugars by available carbohydrates include all carbohydrates added as a caloric sweetener into the product as added sugars. This includes monosaccharides, disaccharides and polysaccharides. Added sugars by total sugars only includes monosaccharides and disaccharides that were added as caloric sweeteners as added sugars.[48] The method by which NDSR calculates the added sugar amounts is not public knowledge, however it likely leverages an equation that utilizes the ingredient list to reverse engineer the approximate amount of added sugar present in the product.

The USDA developed a database for providing estimated added sugar values in food products. This database utilizes the ingredient list and provided total sugar amounts to calculate the approximate added sugar value.[14] This database is no longer accessible to the general population and was removed from the USDA website in 2012 due to the constant changes in the formulation of food products.[49]

Table 2-2 provides a sample of common foods with the assigned added sugar values as determined by the NDSR software and the last version of the USDA added sugar database (2009–2010). Total sugar- USDA data was obtained from the National Nutrient Database for Standard Reference.[50] We also attempted to include information from the most recent (2011–2012) USDA database, the Food Patterns Equivalent Database (FPED), although it was difficult to use the information for recipes and complicated foodstuffs.

Nutrient Analysis

Meal plans created by the USDA and Academy of Nutrition and Dietetics (AND) were analyzed utilizing a nutrient database to assess total and added sugar content of daily consumption. Both meal plans were accessible online and utilized a multiday meal plan approach to help consumers plan and consume the recommended diet and modeling day-to-day variation. The meal plans were analyzed using Nutrition Data System for Research software version 2014, developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis, MN. The first seven days were selected from a "Sample 2-Week Menu" made available via USDA's ChooseMyPlate.gov website.[51] Corresponding food items were selected from the NDSR database. Some menu items referenced recipes that were made available from a corresponding cookbook.[52] These recipes were entered into the NDSR database allowing for the analysis of the precise recipe that was recommended in the menu. The Academy of Nutrition and Dietetics provides sample menus for client education through the Nutrition Care Manual®. The "1800-Calorie 5-Day Menu" was used as a

sample menu and analyzed.[53] Food from each of the five days was entered into and analyzed by NDSR.

Each day was analyzed individually populating total energy, total carbohydrate, total sugars, added sugars-by total sugars, and added sugars-by available carbohydrate. Percent of total energy from total sugars and percent of total energy from added sugars were calculated by multiplying the grams of total sugar and added sugar, respectively, by four and dividing by the total number of calories. Free sugars were estimated by adding the grams of sugar from fruit juice used as beverages, to grams of added sugar-by total sugars. Percent of total energy from free sugars was estimated by multiplying the calculated free sugars by four and dividing by total calories.

Results

The "Sample 2-Week Menu" made available by the USDA provides on average 23.3% energy from total sugar and 5.1% energy from added sugars-by total sugars. The "1800-Calorie 5-Day Menu" designed by AND provides on average 21.2% total energy from sugars and 3.1% energy from added sugar-by total sugar **(Figure 2-1).** It is possible to consume less than 5% of total calories from added sugar with strict compliance of these provided meal plans. However, the WHO's proposed recommendation of less than 5% of total energy from free sugars, includes fruit juices. The menu designed by the USDA uses juice as a beverage on several days, and the substantial difference between added sugar and free sugar is depicted in **Figure 2-2**. On average, the USDA sample menu provides 8.7% energy from free sugars, which is more than the WHO's recommended <5% of total energy. The AND meal plan does

not provide juice as a beverage option, so the AND meal plan remains below the WHO recommendations at 3.1% total energy from free sugars.

Discussion

It is possible to meet the stringent free sugar recommendation proposed by the WHO for consumers following a diet similar to the AND meal plan. The AND recommended daily menu provides 8 one-ounce servings of lean protein, 14 servings of carbohydrates (includes grains, dairy products and fruit), at least 3 servings of vegetables and 5 servings of fat. Besides fruit, a sweet snack is only provided twice throughout the 5-day menu. The listed desserts are sugar free gelatin and sugar free pudding. According to NHANES 2003–2004 data, the median vegetable intake (excluding fried potatoes) in adult men is less than 1.5 cups per day and the median fruit consumption was just over a half cup daily (0.61 cups). The most common fruit consumed by Americans was orange juice, which would contribute to free sugar consumption.[54] Additionally, about 24% of Americans consume at least one sugar sweetened beverage each day.[55] To comply with the AND meal plan, most Americans would have to at least double their fruit and vegetable consumption and eliminate all juice and sugar sweetened beverages from their daily routine. Following this meal plan would be very challenging for the average American as it is drastically different from the typical diet.

A recommendation of less than five percent free sugars or added sugars requires strict compliance to a diet, similar to the diets analyzed in this paper, and does not allow for indulgences. An individual with a 2000 calorie energy requirement could consume all

necessary daily nutrients and consume a 150 calorie can of soda within the 2000 calorie budget. The soda alone results in 7.5% energy from added sugar. It would seem doubtful for the American population to sustain a diet that does not allow for even small treats in their daily routine.

The meal plan provided by AND utilizes sugar-free products and artificial sweeteners to achieve a low quantity of added sugars. Not all consumers enjoy the taste of artificial sweeteners and while approved as safe by many regulatory bodies globally, may not be comfortable with the safety of synthetically derived food ingredients.[56] Survey results published in 2006 found a majority of consumers, 81%, prefer the taste of sugar compared to artificial sweeteners. Additionally, 64% of those surveyed were concerned regarding the potential health risks of consuming artificial sweeteners.[57] Achieving the recommended free sugar recommendation would not be possible if consumers are not willing to consume the sugar-free products or abstain from sweet treats.

Both of these analyzed menus provide an example of how to achieve low dietary intakes of added sugars and certainly represent a healthy diet to strive for. Following either of these diets would be an improvement from the current average American added sugar intake of 13% of total energy.[16] Because the menu designed by the USDA to comply with the MyPlate food guide exceeded the WHO's recommendation for free sugars, the WHO's proposed recommendation appears unrealistic at this time. Additionally, there is some question if consumers would possess the resources to assess their added sugar intake and comply with recommendations.

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Measuring Added Sugar

As noted earlier, most nutrient databases do not contain added sugar values. For those databases that do have the information, the values are not always consistent. **Table 2-2** compares the added sugar contents in the same food products between the USDA and NDSR databases. Some variation is expected, as the formulation of the food product identified may not be identical between databases. Additionally, the definition of "added sugar" and the method of calculations may differ between databases. For example, in looking at sweetened applesauce, one cup of applesauce has identical total sugar values between NDSR and the USDA database (36.09 g). However, NDSR identifies 21.2g as added sugars, while the USDA database only classifies 10.3 g sugar as added sugar. These types of disparities can make it challenging for consumers to understand and comply with recommendations. Without a standard definition and database to identify added sugar contents in food products, it is nearly impossible for dietitians and consumers to assess compliance.

As previously stated, NDSR distinguishes between added sugar- by total sugars and added sugar—by available carbohydrates based on the chemical structure of the carbohydrates in caloric sweeteners. Caloric sweeteners considered in the equation by NDSR include: sucrose, brown sugar, powdered sugar, honey, molasses, pancake syrup, corn syrup, high fructose corn syrup (HFCS), invert sugar, invert syrup, malt extract, malt syrup, fructose, glucose, galactose and lactose. Added sugar—by available carbohydrates includes all carbohydrates in the caloric sweeteners, not just mono and disaccharides.[48] In some foods, added sugar-by available carbohydrate content can be higher than the total sugar content in the product because

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oligosaccharides and polysaccharides do not contribute to total sugar, but would contribute to added sugar—by available carbohydrate. Corn syrup is likely the largest contributor to the increased value of added sugars—by available carbohydrate. Starches from corn are chemically broken down into sugars in corn syrup. However, not all of the starch is converted into glucose and fructose. Some oligosaccharides and polysaccharides remain in the syrups and would count as added sugars by available carbohydrate.[58] Foods in **Table 2-2** with considerable variation between added sugar contents include caramel-coated popcorn, ice cream, fruit flavored yogurt, soda, sports drinks and jelly. All of these products are typically manufactured with some inclusion of corn syrup.

Because the FDA's definition of sugar only includes monosaccharides and disaccharides, it is likely that the category of added sugars- by available carbohydrate will not be used in legislation. But this discrepancy does create another point of confusion for consumers.

FDA Proposed addition of "Added Sugar" to Food Labels

The FDA proposed changes to the Nutrition Facts and Supplement Facts label in March of 2014. The purpose of updating the Nutrition Facts label is to assist consumers in choosing foods that will help them to comply with a healthy diet and meet dietary recommendations. The FDA proposed many changes, including the addition of the category of "Added Sugars" listed beneath "Sugars" or "Total Sugars". The proposal from the FDA defines added sugars as sugars and syrups added during

the food manufacturing process. Fruit juice concentrates are considered added sugars, while fruit juice is not considered to be added sugar.[16]

The addition of an "added sugars" category on the food label would provide a tool for consumers to assess compliance with added sugar recommendations and compare food products. Added sugar values in nutrient databases would be more available, and ideally, a standardized equation would be used to calculate added sugar. The FDA hopes this addition will help consumers in making healthier choices and will cause food manufacturers to alter product formulations to decrease the amount of added sugars.[16]

Added sugar is chemically identical to sugars naturally found in the foods, therefore, food companies will have to utilize calculations to determine the amount of added sugar included in each food product. The FDA document anticipates requiring manufacturers to keep records verifying the amount of added sugars present in each step of processing for each food product.[16] Without a method to analytically test for added sugars, the food manufacturers would likely have to disclose their product formulations or other proprietary information to the FDA to confirm that the provided added sugar value is accurate. Food manufacturers would be resistant to provide this information, recognizing that the proprietary knowledge represented by their specific recipes give them an important edge over the competition.

The proposed food labels display added sugars in grams per serving. However, the majority of the added sugar recommendations are made in terms of percentage of total calories. In order to check personal compliance with added sugar recommendations,

consumers would have to convert total grams of added sugar to percent of total calories from added sugars. This begs the question; will consumers know what to do with the information? The FDA has considered presenting the added sugars value in calories from added sugars rather than grams presumably to help consumers better relate this value to the recommendations made by the various organizations.[16] This format would still require some calculations and conversions and may cause confusion due to the difference in units between sugars and added sugars. Both methods of presentation have clear limitations. The goal of the new Nutrition Facts label is to help consumers make better-informed decisions when purchasing food products, but the addition of added sugars on the label may be more confusing to the consumer.

A study conducted by the Turner Research Network, asked consumers to look at food labels and determine the total amount of sugar in the product. According to preliminary data, participants who were shown a label that only had "sugars" listed, 92% were able to accurately identify the total amount of sugar. When "added sugars" was added below the "sugars" category, only 55% accurately identified the amount of total sugar. Notably, 52% of participants thought that the "added sugars" were in addition to the total amount of sugars listed on the label.[59] The inclusion of the "added sugars" category appears to make interpreting the Nutrition Facts label more difficult and may actually be doing the opposite of what the FDA had hoped to do.

Conclusions

At this point in time, it would be difficult to measure compliance with added sugar recommendations. There is no universal definition for "added sugars", consumers do

not have an easily accessible method to calculate added sugar consumption, and various organizations utilize different units of measurements for their recommendations. Newly proposed recommendations provided by the WHO encourage limiting added sugar intake to less than 5% total energy intake from free sugars. A meal plan provided by the USDA, following MyPlate dietary guidelines, was unable to achieve such strict recommendations. Although a menu developed by the AND demonstrates that it is possible to achieve the WHO recommendations, it would be very difficult for the average American to follow such a restrictive diet for an extended period with no allowance for any indulgences. While it is important to minimize discretionary calories, it is also important to follow a diet that is sustainable for the individual. The proposed free sugar recommendation from the WHO is likely too restrictive and unachievable for most Americans.

Table 2-1. Current and proposed recommendations for added sugar intake for

Americans[4,14]

Institution	Recommendation
Institute of Medicine (2002)	<25% total energy intake from added sugars
World Health Organization- current recommendation (2003)	<10% total energy intake from **free** sugars
American Heart Association (2009)	No more than half of discretionary calorie intake from added sugars. 100 calories for females, 150 calories for males.
USDA- Dietary Guidelines for Americans (2010)	5-15% total energy from **solid fats and added sugars**
World Health Organization- proposed recommendation (2014)	Aim for <5% total energy intake from **free** sugars

Table 2-2. Approximate total and added sugar content of selected foods

Food	Common serving size	Serving size (g)	Total sugars	Added sugar-by total sugars (g)	Added sugars-by available carbohy-drate (g)	Total Sugars (g)-USDA	Added Sugars (g)-USDA	USDA FPED 2011-12
Grains								
Bagel, plain	1 medium (3.5' - 4")	105	5.3	0.0	0.0	8.9	5.07	5.1
Bread, white	1 medium slice	25	1.3	1.0	1.0	1.4	1.04	1.0
Bread, whole wheat	1 medium slice	28	2.9	1.4	1.9	1.2	1.50	1.2
Chocolate cake, frosted, prepared from mix	2" x 2" slice	40	23.5	23.4	26.4	16.0	14.90	15.6
Cereal, corn flakes	1 cup	28	2.9	2.7	2.9	2.7	2.55	2.3
Cereal, corn flakes, frosted	1 cup	40	15.5	15.2	17.6	14.2	15.25	13.9
Brownie	2" x 2" slice	43	17.5	17.2	17.3	15.7	15.66	15.4
Cookie, chocolate sandwich	1 cookie	12	4.9	4.1	4.1	4.9	4.76	4.8
Crackers, graham, plain	1 large rectangle	14	4.4	3.6	3.8	3.5	4.26	4.3
Doughnut, cake-type, frosted	3.25" diameter	67	21.4	20.8	21.1	17.9	14.97	16.6
Muffin, blueberry	3" diameter	113	16.7	12.6	12.7	35.6	29.10	32.7
Pie, apple, lattice crust	1/8 of 9" pie	162	26.5	18.7	18.7	25.4	17.35	17.4
Popcorn, caramel-coated	1 cup	35	19.7	19.4	23.0	18.6	18.32	18.2
Fruit								
Applesauce, sweetened	1 cup	246	36.1	21.2	21.3	36.1	10.33	13.0
Applesauce, unsweetened	1 cup	244	22.9	0.0	0.0	22.9	0.00	0.0
Blueberries, frozen, sweetened	1 cup	230	45.4	25.3	25.3	45.4	25.80	25.9
Cranberries, dried, sweetened	1/2 cup	60	39.0	39.0	39.1	39.4	32.63	32.6
Peaches, heavy syrup, canned	1 cup	262	48.8	33.5	33.5	48.8	36.20	36.2
Peaches, in juice, canned	1 cup	248	25.5	0.0	0.0	25.5	0.00	0.0
Raisins	1/2 cup	72.5	42.9	0.0	0.0	42.9	0.00	0.0
Dairy								
Cream substitute,	1/2 oz	14	0.7	0.7	1.9	4.6	1.59	1.6

liquid								
Milk, plain 1% milk fat	1 cup, 8 fl oz	244	12.7	0.0	0.0	12.7	0.00	0.0
Milk, chocolate, low-fat	1 cup, 8 fl oz	250	24.9	13.4	13.4	24.9	16.59	11.9
Yogurt, plain, low-fat	1 cup	245	17.2	0.0	0.0	17.3	0.00	0.0
Yogurt, vanilla, low-fat	1 cup	245	33.8	15.0	15.0	33.8	16.67	16.7
Yogurt, fruit-flavored, low-fat	1 cup	245	40.2	10.2	30.8	45.7	29.53	29.5
Ice cream, vanilla	1/2 cup	66	14.0	8.0	12.1	14.0	12.00	11.6
Sugar-sweetened beverages								
Cola, regular	1 can, 12 fl oz	368	33.0	33.0	35.2	33.0	33.08	39.6
Soda, lemon-lime	1 can, 12 fl oz	370	33.2	33.2	37.5	38.3	33.26	33.3
Fruit punch	8 fl oz	227	25.6	25.6	26.7	25.9	23.64	21.6
Sports drink, all flavors	8 fl oz	227	11.9	11.9	14.6	11.9	11.90	11.9
Other								
Candies, hard	1 piece	3	1.9	1.9	2.8	1.9	1.89	1.9
Gelatin	3.25 oz	92	12.5	12.5	13.1	12.4	12.40	12.4
Milk chocolate	1.55oz bar	43	22.1	20.2	20.2	22.1	18.89	18.0
Peanut butter, regular	2 Tbsp	32	3.0	1.6	1.6	3.4	1.68	1.7
Jelly	1 Tbsp	19	9.2	8.2	12.3	9.7	9.74	9.1
Total and added sugar values calculated from USDA Added Sugar database, USDA Food Pattern Equivalents Database (FPED) and NDSR database								

Figure 2-1. Average percent energy from total, added and free sugar from sample menus

designed by the USDA and AND
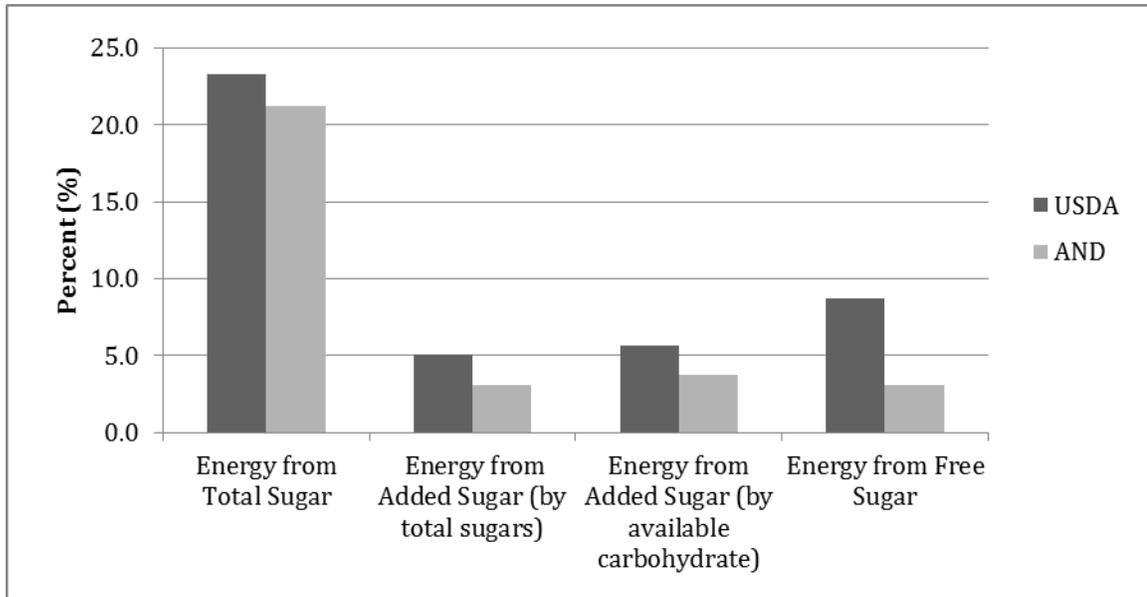
Figure 2-2. Percent energy from added sugar verses free sugar in the USDA sample

menu by day
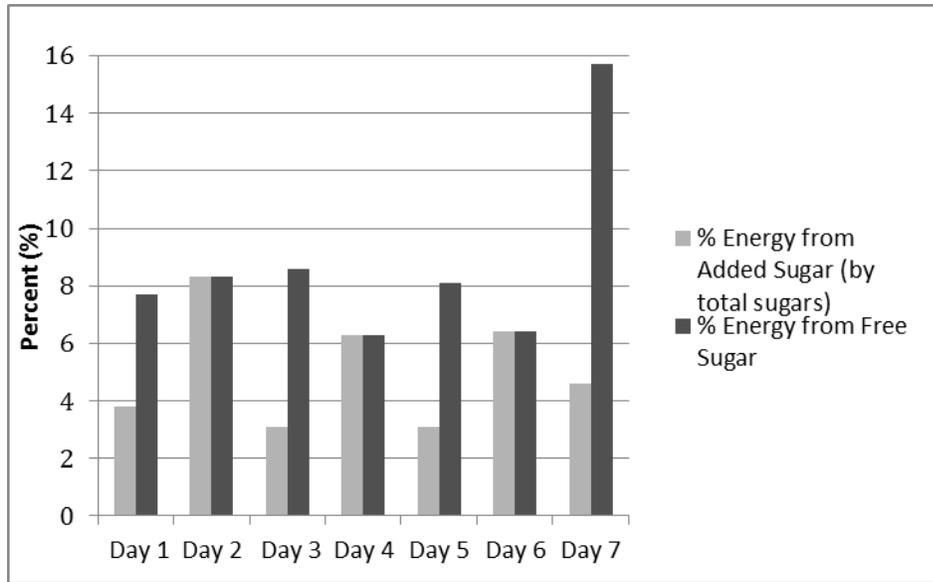
Chapter Three

THE SCIENTIFIC BASIS OF GUIDELINE RECOMMENDATIONS ON

SUGAR INTAKE: A SYSTEMATIC REVIEW

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Summary

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 nonquantitative 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.

Primary Funding Source: Technical Committee on Dietary Carbohydrates of the North American branch of the International Life Sciences Institute. (PROSPERO: CRD42015029182)

Background

The 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.[60] 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.[14] Dietary guidance addresses the types of sugars, especially sources of nonintrinsic sugars, such as added sugars and free sugars.[14] 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 syrup.[41]

As research continues to add knowledge, authoritative organizations have issued public health guidance based on the available evidence.[14] Recent guidelines have included both qualitative and quantitative recommendations that consistently focus on limiting and reducing sugar consumption, especially sources of nonintrinsic sugars.[14] For example, in 2015, the World Health Organization (WHO), the Scientific Advisory Committee on Nutrition (SACN), and the U.S. Department 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.

Methods

We registered the protocol for this systematic review in the PROSPERO database in November 2015 (registration number CRD42015029182).[61]

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 (Table 3-1, available at www.annals.org), as well as bibliographies of included studies. We consulted with 3 experts in the field of carbohydrates (Table 3-1) 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)

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instrument, which is composed of 23 items within 6 domains: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence (Table 3- 2, available at www.annals.org).[62] 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[63] 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.

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Data Synthesis and Analysis

Agreement for the full-text screening was calculated using the κ statistic and its 95% CI.[64] 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.[65] 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.[66] 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

Results

A total of 5315 records were screened, 26 records were considered potentially eligible for full-text screening, and 9 PHGs proved eligible (Figure 3-1). Eligible guidelines included 1 global guideline,[4] 2 international guidelines,[21,67] and 6 national guidelines.[5,6,68–71] 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,[68] the Australian National Health and Medical Research Council,[71] the Nordic Council of Ministers,[67] the German Nutrition Society,[69] the Food Safety Authority of Ireland,[70] and the Institute of Medicine[21] (Table 3-3).

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 3-3). Guidelines used variable terminology in sugar recommendations. For example, 2 guidelines used the term "free sugars",[4,5] 3 used the term "added sugars",[6,21,67] 2 made recommendations on sugar-sweetened beverages (SSBs),[5,69] and 3 referred to food and beverage sources of refined sugars.[68,70,71] 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.[21] 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 utilized the assessment to develop their recommendations,[4,5,69,71] and 5 did not.[6,21,67,68,70]

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.[72] 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 3-4) with 8 of 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.[72] The median score for this domain was 63.0% (IQR, 38.9% to 77.8%) (Table 3-4). Four guidelines scored below 60% in this domain.[5,21,69,70] 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.[72] The median score for this domain was low, at 47.2% (IQR, 24.0% to 69.4%) (Table 3-4). Three of the guidelines met the 60% threshold.[4,6,71] Four guidelines did not use systematic methods to search for evidence.[6,21,68,70] Four

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guidelines assigned strength to their recommendations,[4,6,69,71] but only the WHO guideline used the GRADE approach.[4] Three of the guidelines discussed external review by experts before publication.[4,6,71] 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.[72] The median score for this domain was 59.3% (IQR, 49.1% to 71.3%), with 4 guidelines meeting the 60% threshold (Table 3-4).[6,21,70,71] 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.[72] The median score for this domain was low, at 34.7% (IQR, 11.1% to 50.0%) (Table 3-4). Only 1 guideline met the 60% threshold.[71] 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 recommendations. Only 1 guideline[4] presented monitoring and auditing criteria.

Editorial Independence

Editorial independence relates to unbiased formulation of recommendations and competing interests.[72] This domain had the lowest median score (33.3% [IQR, 6.9% to

65.3%]), with only 2 guidelines meeting the 60% threshold (Table 3-4). 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 (Table 3-5, 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)[69] to 5.3 (Australian guideline)[71] (Table 3-4). All of the guidelines were categorized as "recommended with modifications."

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 (Table 3-6, 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,[6,68] 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 (Table 3-7, available at www.annals.org).[4,5,67,69,71] 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,[73,74] both on SSBs and body weight, informed 2 recommendations from the German and Australian guidelines[69,71] (Table 3-7). 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 (Table 3-7), all on SSBs and health outcomes (such as type 2 diabetes and body weight), informed 3 recommendations across the Nordic German, and Australian guidelines.[67,69,71] Evidence was considered very-low-quality for 6 studies[75–80] (75%) and low-quality for 2 studies (25%).[81,82] Three studies were downgraded for indirectness (37.5%), and 2 were downgraded for imprecision (25%). Two studies were rated up for a dose-response (25%).[81,82] 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[20] 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.[63] The WHO conducted 2 systematic 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[27] and free sugars, SSBs, fructose, sucrose, sweet foods, and added sugars for the body weight review.[83] Similar discrepancies were found in 5 additional guidelines (Table 3-3).

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[84]).

A PubMed search for reviews of dietary sugar guidelines done within the past 5 years identified only 1 other review. Although Hess and colleagues[14] 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 supporting 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

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and transparency with respect to the quality assessment. We believe that the use of GRADE reduces the likelihood of mislabelling 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[85–88] containing dietary sugar recommendations written by influential organizations (the American Academy of Pediatrics, the European Food Safety Authority, the American Heart Association, and the 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.[61] 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 around the world.[89] Based on 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.[4–6,21,67] 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,[6,21] 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 population-wide weight loss. To obtain this 100-calorie deficit, an approximated 100 calories of free sugars was subtracted from the previous sugar recommendation, 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.[67] 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.[90]

Table 3-1. 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
 5. 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

Table 3-2. AGREE II Instrument

Item, by Domain

Scope and purpose
    1. The overall objective(s) of the guideline is (are) specifically described.
    2. The health question(s) covered by the guideline is (are) specifically described.
    3. 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.
    9. The strengths and limitations of the body of evidence are clearly described.
    10. 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.

Table 3-3. Identified Guidelines and Corresponding Sugar Recommendations

Guideline, Year (Reference)	Guideline Title	Funding	Qualitative Recommendation	Quantitative Recommendation*	Basis for Recommendation	Methods Used to Determine Recommendation	Sugar Definition in Public Health Guidelines	Types of Sugar in Relevant Evidence
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"	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
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	"Reduced intake of free sugars throughout the life course"	"In both adults and children, WHO recommends reducing the intake of 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	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,	Sucrose, added sugar, total sugars, free sugars, SSBs, fructose, and sweet foods

		WHO Regional Office for Europe		"intake"				syrups, fruit juices, and fruit juice concentrates
Public Health England/SACN, 2015 [5]	Carbohydrates and Health	Unclear	"The definition for free sugars be adopted in the UK"; "The consumption of sugars-sweetened beverages should be minimized in both children and adults"	"The population average intake of free sugars should not exceed 5% of total dietary energy for age groups from 2 years upwards"	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
Ministry of Health of Brazil, Secretariat of Health Care, Primary Health Care Department, 2014 [68]	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"	–	Excess energy intake	Consensus	No definition	Not applicable; did not assess the literature

National Health and Medical Research Council, 2013 [71]	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"	–	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
Nordic Council of Ministers, 2012 [67]	Nordic Nutrition Recommendations	Nordic Council of Ministers	–	"Intake of added sugars should be kept below 10% of the energy intake"	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
German Nutrition Society, 2012 [69]	Evidence-based Guideline of the German Nutrition Society	Unclear	"The consumption of sugar-sweetened beverages should be limited"	–	Excess energy intake	Systematic review	Not applicable	Sweets, SSBs, fructose, and glucose

| Food Safety Authority of Ireland, 2011 [70] | 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" | – | Dental caries | Diet modeling | Not applicable | Total sugar |

| Institute of Medicine, Food and Nutrition Board, 2002 [21] | 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 | – | "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" | 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 data.

Table 3-4. Public Health Guideline Domain Scores on the AGREE II Instrument

Guideline, Year (Reference)	Intraclass Correlation Coefficient*	Score, %						Combined Overall Rating	Systematic Method†
		Scope & Purpose	Stakeholder Involvement	Rigor of Development	Clarity of Presentation	Applicability	Editorial Independence		
Carbohydrates and Health [5]	0.966	81.5	37.0	47.2	48.1	0	0	3.7	Yes
Guideline: 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 [67]	0.913	83.3	63.0	50.0	53.7	15.3	33.3	4.7	Yes
Dietary Guidelines for the Brazilian Population [68]	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 [69]	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 [70]	0.964	70.4	40.7	10.4	72.2	58.3	0	4.0	No
Australian Dietary Guidelines [71]	0.870	92.6‡	77.8	69.4	66.7	61.1‡	77.8	5.3‡	Yes
Dietary Reference Intakes [21]	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.

* 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.

Table 3-5. COI Reporting Across Guidelines

Guideline	COI Process Reporting	Groups Requiring COIs (Number of Members)	COI Reporting		
			Affiliation	**Financial**	**Intellectual**
Australian Dietary Guidelines	Unclear	Dietary guidelines working committee (11)	Yes	No	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	No	No
		Public consultation contributors; 2 rounds	No	No	No
Dietary Guidelines for the Brazilian Population	No	Listening workshop (59), evaluation workshop (29), working group for consideration of public consultation (10)	Yes	No	No
		Public consultation contributors	No	No	No
Nordic Nutrition Recommendations	No	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)	No	No
		Public consultation contributors	No	No	No
Scientific Recommendations for Healthy Eating Guidelines in Ireland	No	Steering committee (11)	Yes (except for contract researcher)	No	No
		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)	No	No	No
		Nutrition and novel foods subcommittee	Yes	No	No
Evidence-based Guideline of the	No	Authors of publication	Yes	No	No

German Nutrition Society					
DRI/Institute of Medicine	No	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)	No	No	No
		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), independent reviewers (18)	Yes	No	No
		Organizations, including industry (15)	NA (these are organizations, not people)	No	No
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	No*	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	Yes	No	No

		(918 [number of comments accounted for; comments may be by person or group or organization]), public consultation contributors 2014 meeting (53), public consultation 2015 meeting (73)			
		Invited expert speakers (32), staff, contract, and/or technical support (20), national service volunteer evidence abstractors (28)	No	No	No
Carbohydrates and Health (SACN)	No	Membership of Scientific Advisory Committee on Nutrition: Carbohydrates Working Group (12), observers (4), observers carbohydrates working group (1), external consultants carb working group (5)	Yes	No	No
		Membership of Scientific Advisory Committee on Nutrition (16)	Yes (but unclear affiliation for 2 members)	No	No
		Secretariat nutrition committee (15), secretariat carb working group (12), public consultation contributors (unspecified)	No	No	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	No	No
		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."

Table 3-6. Assessment of the Supporting Evidence for Each Recommendation (GRADE)

Guideline Title	Overall Recommendation	Specific Recommendations, Including Strength (if Reported)	Citations Supporting Recommendation, *n*	Study Design	GRADE Evidence Quality (Certainty in Estimates of Effect)
Sugars Intake for Adults and Children (WHO)*	–	"Reduced intake of free sugars throughout the life course—Strong Recommendation"	0	–	NA
		"In both adults and children, WHO recommends reducing the intake of free sugars to less than 10% of total energy intake—Strong Recommendation"	1	Systematic review	Low†
		"WHO suggests further reduction of the intake of free sugars to below 5% of total energy intake—Conditional Recommendation"	1	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"	1	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"	1	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 caries—Grade C"	1	Observational study	Very low
		"Consumption of soft drinks is associated with increased risk of dental caries in children—Grade C"	1	Observational study	Very low
		"Consumption of soft drinks is associated with increased risk of reduced bone strength—Grade C"	3	Randomized, controlled trial; observational study	Very low
Nordic Nutrition Recommendations	"Intake of added sugars should be kept below 10% of the energy intake"	–	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"	6	Systematic review; randomized, controlled trial; observational study	Low, very low
		"The majority of prospective cohort studies and meta analysis indicate an increased risk of type 2 diabetes with regular consumption of sugar sweetened beverages—Probable"	5	Systematic review; observational study	Low, very low

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"	–	6	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.	–	7	Observational study	Very low
2015–2020 Dietary Guidelines for Americans§	"Consume less than 10% of calories per day from added sugars"	–	0	–	NA
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"	–	0	–	NA

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.

† The WHO rated the 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.

Table 3-7. Assessment of Individual Studies Supporting Recommendations (GRADE)

Study, Year (Reference)	Guidelines That Included the Study	GRADE	Reasons for Rating Up or Down
Systematic reviews			
Forshee et al, 2008[91]	Australia 2013, Nordic 2012	Very low	Inconsistency, imprecision, publication bias
Gibson, 2008 [92]	Australia 2013	Very low	Inconsistency, imprecision
Malik et al, 2006 [93]	Australia 2013	Very low	Inconsistency, imprecision
Vartanian et al, 2007 [94]	Australia 2013, Germany 2012, Nordic 2012, Germany 2012	Low	Inconsistency, imprecision
Wolff and Dansinger, 2008 [95]	Australia 2013	Very low	Inconsistency, imprecision
Anderson et al, 2009 [96]	Australia 2013, Nordic 2012	Very low	Inconsistency
Sonestedt et al, 2012 [97]	Nordic 2012	Low	Inconsistency
Te Morenga et al, 2012 [83]	WHO 2015, Nordic 2012	Low	Inconsistency, publication bias
Zhang et al, 2013 [98]	Nordic 2012	Low	Indirectness, imprecision
Malik et al, 2010 [99]	Nordic 2012	Very low	Inconsistency
Fogelholm et al, 2012 [100]	Nordic 2012	Very low	Imprecision
Burt and Pai, 2001 [101]	Nordic 2012	Very low	Inconsistency
Moynihan et al, 2014 [27]	WHO 2015	Very low	Inconsistency, imprecision
Mattes et al, 2011 [102]	Germany 2012	Low	Inconsistency, imprecision
Nutritional Epidemiology Group, 2012 [103]	SACN 2015	Very low	Inconsistency, indirectness, imprecision
SACN, 2011 (unpublished)	SACN 2015	Very low	Inconsistency, imprecision
Randomized, controlled trials			
Sichieri et al, 2009 [74]	Australia 2013, Germany 2012	Very low	Imprecision, indirectness
Chen et al, 2009 [73]	Germany 2012	Very low	Imprecision, indirectness
Cohort studies			
Tucker et al, 2006 [75]	Australia 2013	Very low	Indirectness, imprecision
Duffey et al, 2010 [76]	Nordic 2012	Very low	Imprecision
Cohen et al, 2012 [77]	Nordic 2012	Very low	Indirectness
Nissinen et al, 2009 [78]	Germany 2012	Very low	Indirectness
Dhingra et al, 2007 [79]	Germany 2012	Very low	None
Schulze et al, 2004 [82]	Germany 2012	Low	Dose-response
Palmer et al, 2008 [81]	Germany 2012	Low	Dose-response
Paynter et al, 2006 [80]	Germany 2012	Very low	None

Figure 3-1. Summary of evidence search and selection
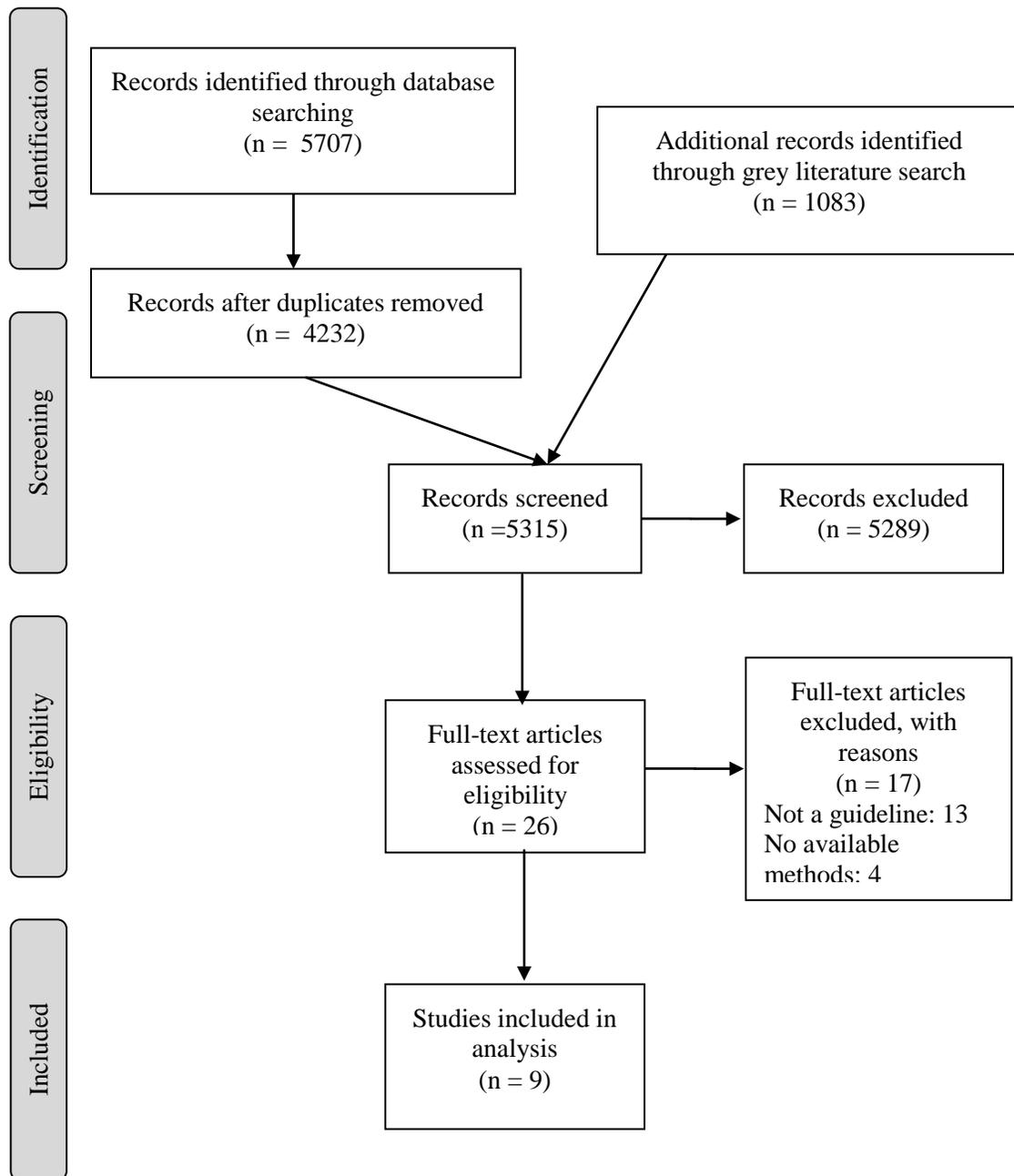
Chapter Four

HOW TO TALK TO CONSUMERS ABOUT "ADDED SUGAR"

The text of this chapter is a reprint of the material as it appears in "How to Talk to Consumers about 'Added Sugar'" previously published by *Today's Dietitian*.[104] The article has been reprinted with the permission of Today's Dietitian ©. Great Valley Publishing, Co. The content has been reformatted to meet university guidelines.

Background

The nutrition facts panel (NFP) is being updated for the first time since its introduction in the early 1990s.[7] The most talked about change will be the inclusion of added sugar information to the label. There has been a lot of controversy regarding the addition of the added sugar line on the NFP, with food and nutrition professionals questioning if providing consumers with added sugar values will help them to make healthier food choices, or create more confusion. Regardless of where you stand on the issue, the law has been passed and by July 26, 2018, most food companies will be required to have the updated label on their product.[7] This is an exciting time for registered dietitians (RDs) and registered dietitian nutritionists (RDNs) as it is an opportunity to educate consumers on how to correctly read the new NFP and, more importantly, how to make well-informed food choices.

What Are Added Sugars, and Why Are They Being Added to the NFP?

According to the FDA's final rule, added sugars are defined as free monosaccharides and disaccharides that are added during the processing or preparation of the food. Additionally, sugars that are packaged as isolated sources of sugars will be labeled as added sugars.[7] Added sugars include ingredients like sugar, brown sugar, honey, maple syrup, agave, high fructose corn syrup, concentrated fruit or vegetable juices, nectars, etc.[7] While added sugars are chemically identical to sugars naturally found in foods like fruits and dairy products, they provide an isolated calorie source without other beneficial nutrients.[20] With more than one third of American adults categorized as obese,[105] sources

of empty calories, such as added sugars, are being targeted to decrease calorie consumption. Major sources of added sugars in the American diet include sugar-sweetened beverages, snacks and sweets, and grain products.[20]

Added sugar content is being added to the NFP in hopes that with the new information, consumers will be able to make better food choices.[16] The new NFP will list added sugars in grams per serving, as well as the percent daily value (%DV) contained within one serving of the food. The %DV is calculated by dividing the grams of added sugar in one serving of the food by 50g of added sugar (representing 10% of total daily calories in a 2000 calorie diet). The daily value of added sugar was based on the 2015-2020 Dietary Guidelines for Americans which, for the first time, set a quantitative limit for added sugar consumption of less than 10% total calories consumed.[6] The recommendation is based on food pattern modeling and intake data indicating that it is challenging to meet all nutrient needs in diets containing more than 10% of calories from added sugars.[6] This recommendation was made for the general population, and may not be appropriate for all individuals. After looking at a patient's energy intakes and expenditures, RDs can determine a more individualized goal for their patient. The goal is not to eliminate all added sugars from the diet, but rather to minimize the consumption of empty calories and not to exceed their energy needs.

Function of Sugar

With the addition of added sugars to the NFP, consumers may be confused or concerned to find added sugars in products like whole grain bread, tomato sauce and salad dressings.

Because these foods do not taste sweet, it may come as a surprise to consumers that they contain added sugars. However, sugar has a variety of functions beyond adding sweetness.[106] Sugar aids in the fermentation process of yeast leavened breads, and some fermented foods. Sugar influences the texture of food products, providing body and bulk to many products, creating a soft, tender texture in baked products and a smooth texture in frozen products. Sugar is essential to Maillard browning and caramelization reactions to produce the expected appearance and flavors in many foods including breads and baked products. Sugar can enhance the shelf life of many products by binding water, preventing a product from becoming stale. Extended shelf lives decrease food waste, food costs and limit environmental impact of shipping food more frequently. Sugar has a preservative effect, inhibiting microbial growth in jams, jellies and preserves, and extending shelf life of baked goods, so it also decreases food waste. Sugar can protect the color, shape, nutrients and phytonutrients of fruits and vegetables during the freezing and canning process. Sugar can round flavors of tart, bitter or acidic foods. This helps to balance flavors and soften strong flavors and contributes to mouth-feel. This can help consumers enjoy nutrient dense foods that they may not have otherwise chosen.[106]

Understanding the multifunctional characteristics of sugar provides some clarity on why it is so challenging for food manufacturers to remove or decrease the added sugar in products. Much research and development is needed to find the right ingredients to mimic the appearance, texture and taste of the same product that was made with sugar. "Low sugar" or "no added sugar" solid foods typically have long lists of ingredient. Unlike liquid or semisolid foods, the calorie reduction may be inconsequential because

carbohydrate, protein or fats at either 4 or 9 calories, not water, must be added to get the number of grams needed for the serving size.[106]

RDs will be a resource for the public and media as they search for answers about added sugars. This can be a great opportunity to educate the public about the functions of added sugars in their foods. Consumers can make more educated food decisions with increased ingredient knowledge and awareness.

Reading the New NFP

The added sugar line will be located within the carbohydrate category on the NFP. The sugar line will now be titled "Total Sugars" and the added sugar information will be indented below the Total Sugar line written as "Includes Xg Added Sugars" with a %DV included on the right side of the panel.[107] The total sugars line reflects all the sugar in the product per serving, and is the sum of sugars naturally contained within the food and those that have been added. The indented added sugar line merely reflects the grams of added sugar per serving. Studies have shown that many consumers are inclined to add the added sugars to the total sugars, so RDs must help consumers understand how to correctly interpret the updated NFP.[34,35]

If the product contains less than 1g of added sugar per serving, the label can read "Includes 0g Added Sugars", but must have the phrase "not a significant source of added sugars" on the bottom of the NFP.[7] If there is less than 0.5g of added sugar per serving, the label can read 0g added sugar without any additional phrase at the bottom of the

label.[7] This may create some confusion for consumers who read the ingredient list and may see a source of added sugar listed as an ingredient in a product that has 0g added sugars. RDs should inform patients and clients that the product may still use a small amount of sugar, but that the amount is insignificant in the serving size listed. However, consumers must be aware that a product with no added sugar does not mean the consumer can eat as much as they would like. Consumers should still pay attention to the calories and serving sizes to remain within their energy needs.

Another major change to the NFP will be updated serving sizes. The new serving sizes will more appropriately represent the amount consumers are generally eating in one sitting, rather than the amount consumers should be eating in one sitting.[107] Because added sugars are related to portion sizes, nutrition educators will need to update their serving size knowledge when educating consumers on appropriate sugar contents for certain product categories. Education on appropriate portion sizes of different foods will also help consumers maintain their calorie goals.

In the upcoming years before all food manufacturers are required to display the updated label format, the grocery store will contain a combination of old and new labels. This may prove to be challenging when consumers are comparing labels and deciding which products to purchase. RDs will need to educate patients and clients how to effectively read and compare the two labels during this time.

Helping Consumers Make the Right Choice

The FDA decided to include added sugars on the NFP to aid consumers in making more informed food choices and ultimately improve the nutrient intake profile of Americans.[31] However, making food choices based on one nutrient alone leads to an unbalanced diet and is generally ineffective. Many nutrient dense foods contain added sugars for functionality, or to enhance palatability. Foods like breakfast cereals, whole grain bread, flavored milk, flavored yogurt, cranberry juice and oatmeal are commonly prepared with added sugars, but that does not negate the fact that these products are high in essential nutrients. In fact, consumption of ready-to-eat cereal, a major target for added sugar criticism, is associated with a more nutritionally complete diet.[108] If the added sugars were removed, many consumers may choose to omit these nutrient dense foods from their diets leading to unintended consequences. For example, a study found that when schools removed chocolate milk as a beverage option with school lunch, the students purchased less milk, threw away more milk, and purchased fewer school lunches.[109] As dietitians, we need to educate consumers to look at the nutrient profile of a food, learn how to balance the intake of nutrients with added sugars when making food choices, and decide when the addition of added sugars are worthwhile.

Without consumer education, the negative portrayal of added sugars in the media may lead consumers to make unfavorable substitutions to avoid substantial amounts of added sugars. For example, a switch from a bowl of breakfast cereal with skim milk to a bagel with cream cheese could be more detrimental to that consumer, especially if he or she does not consume dairy foods for the remainder of the day. While the bagel and cream cheese will have less added sugars, it is likely higher in calories and lower in important

nutrients, such as calcium and vitamin D. By educating consumers to look at the entire nutrient package of the food, rather than just focusing on the added sugar content, dietitians can empower consumers to make healthy substitutions to their diet.

On a physiological level, eating is an opportunity to consume nutrients and energy to help our body function. But on a human level, eating is an enjoyable social experience. Added sugars and occasional indulgences can fit into a healthful diet as long as the consumer is making other nutrient dense food choices and is not exceeding his or her calorie needs. Added sugar labeling is just one tool consumers can use to improve their diet. Education on making nutrient dense food choices, appropriate portion sizes, and reading NFPs are fundamental to helping consumers consume a nutrient rich diet while remaining within their calorie needs.

Conclusion

It is the job of all RDs to be well informed of the changes to the NFP, especially in regards to added sugar labeling. The media, patients, friends and neighbors will be looking to RDs as they try to understand the upcoming changes and apply the new information when making food choices. As always, dietitians should provide consumers with the scientific evidence, allowing them to make informed decisions. Added sugars are a source of calories, but many products containing added sugars can also be nutritious. Consumers need to look at the entire nutrient composition of the food product as a part of their daily intake to decide whether or not they should add the product to their shopping cart. While some foods with added sugars like soda or candy might be an occasional

indulgent choice, foods that make important nutrient contributions such as sweetened fruits, whole grain breads and cereal products, and flavored yogurts can fit into consumers' pantries and balanced diet patterns.

Chapter Five

WHERE DRY BEANS FIT IN 2015 DIETARY GUIDELINES FOR AMERICANS

The text of this chapter is a reprint of the material as it appears in "Where Dried Beans

Fit in 2015 Dietary Guidelines for Americans" previously published by *Dry Bean

Quarterly*.[110] The content has been reformatted to meet university guidelines.

Summary

The 2015 Dietary Guidelines Advisory Committee (DGAC) recently released its report and most found the report supportive of a more vegetarian intake, which should bode well for dry beans.[20] Yet the changes in subcommittee structure from the 2010 DGAC made it difficult to see if the advancing scientific findings on dry beans were added to the Nutrition Evidence Library (NEL). Also, confusion on where dry beans fit in the USDA food guidance system continues to concern dietitians who would prefer more clear dietary rules for increasing consumption of dry beans and peas.

Advancing Science

The relationship between intake of dry beans and health outcomes was considered in the 2010 DGAC.[111] For all questions, the body of evidence was limited because of few published studies on this topic. Since that time, more research has been published, including meta-analyses of the relationship between intake of dry beans and measures of food intake.[112] The developing literature base is limited by the lack of accepted terminology for the dry beans and peas group. USDA has traditionally called the group "dry beans and peas" most likely to differentiate it from green beans and peas—which fit in the vegetable group. Actually, USDA says dry beans and peas can be in both the vegetable group and the protein group. The MyPlate.gov food guidance system that is based on the 2010 DGAC states that a serving of dry beans and peas can be counted as either a vegetable or a protein, but not both.

The 2015 DGAC report is confusing since it recognizes the health benefits of dry beans, but the report omits "pulse" crops (dry beans, peas, lentils, and chickpeas) from the description of foods in the protein group. The report defines protein foods as a "broad group of foods including meats, poultry, fish/ seafood, soy, nuts, and seeds." Pulses/dry beans are not mentioned.[20]

The recommendations state that a diet high in plant-based foods promotes good health. And pulses are among the plant-based foods specifically mentioned elsewhere in the report. It is likely that the exclusion of pulses from the protein group is an oversight and the 2015 Dietary Guidelines for Americans, expected out later this year, will include

pulses in the protein group. It is not known whether MyPlate.gov will also be modified, so the place where pulses fit on the plate may change, as well.

Agreement on Nomenclature and Measurement

Although pulses have the unique ability to be both a vegetable and a protein source in dietary guidance, this flexibility may actually be a detriment to increasing consumption of beans. USDA has continued to keep the group name as dry beans and peas, a descriptor that has little appeal or understanding for consumers. "Pulse" is the descriptor generally used in recent scientific literature, although "legume" is also often used. The lack of a broadly accepted name for this group of foods will continue to make it difficult to agree on where pulses fit on the plate and how many servings to recommend for different age groups.

Domestic and Global Consumption

Global consumption of pulses is rising, but in the U.S. consumption remains low. An analysis of NHANES data for 1999–2002 found that on any given day, only 7.9% of U.S. adults aged 19 years or older consume dry beans (excluding soybeans) and peas.[113] Consuming ½ cup per day of dry beans or peas was associated with increased intake of fiber, protein, folate, zinc, iron, and magnesium, with decreased intakes of saturated fat and total fat.[114] There is an inverse association between high pulse consumption and body weight, according to NHANES cross-sectional data.[113]

To determine the relationship between intake of a food group and health outcomes, it is important that subjects in prospective cohort studies consume enough of the food to divide subjects into quintiles of intake. Since pulse consumption is so low, little information is available from these trials to link pulse consumption to positive health outcomes.

New Studies on Pulses and Health Outcomes

Recent published feeding studies find that pulses are protective against diabetes[115] and metabolic syndrome.[116] Li, et al,[112] conducted a systematic review and meta-analysis of acute feeding trials on dietary pulses, satiety, and food intake. Nine trials met the eligibility criteria. Dietary pulses produced a 31% greater satiety incremental area under the curve (AUC) without affecting second meal intake. Data were limited by small sample sizes, narrow participant characteristics, and significant unexplained heterogeneity among the available trials.[112]

Pulses are of interest in dietary guidance because they include a wide range of vitamins, minerals, and phytochemicals; they are low in fat; and they are high in protein and dietary fiber. The importance of dietary fiber and other non-digestible carbohydrates in gut health is gaining recognition.[117]

Pulses are often not consumed because of concern about gastrointestinal intolerance and flatulence.[118] The fermentation of non-digestible carbohydrates in the gut produce more than gas; the short chain fatty acids produced lower fecal pH and provide an important

energy source for the intestinal cells. Also, fiber feeding studies, with fiber blends that include pea fiber, find that this fermentation increases bifidobacteria and lactobacillus, considered healthier microbiota.[119] Pulses are much higher in dietary fiber than other accepted fiber sources, whole grains, vegetables, and fruits. More research is needed on the gastrointestinal effects of pulses in health and disease.

Conclusion

Pulses are an important food source. Their nutrient composition, including protein, fiber, fermentable carbohydrate, vitamins, minerals, and phytochemicals, makes them a versatile food source that is under-consumed in most populations.[120] Although inclusion in both the vegetable and protein group in U.S. dietary guidance appears to be an advantage, the lack of clarity on how many servings of pulses to include in the diet for different ages is more likely a barrier to increased consumption. Although pulses are an important protein source, they are underutilized in programs such as school lunch, WIC, and SNAP. No doubt that acceptance of one name for this group of foods—perhaps pulses—would make it easier to identify and promote consumption of dry beans and peas.

Chapter Six

SATIETY, GASTROINTESTINAL TOLERANCE, BREATH HYDROGEN AND

GLYCEMIC EFFECTS OF LENTILS IN A CALORIE MATCHED FRUIT

SMOOTHIE

The text of this chapter is a reprint of the material as it appears in "Satiety Effects of

Lentils in a Calorie Matched Fruit Smoothie" previously published by *Journal of Food*

Science.[9] The content has been reformatted to meet university guidelines.

Summary

The food environment is changing, with consumers being more health conscious and concerned about the wholesomeness of their food than ever before. Consumers are looking for nutritious whole food alternatives to fill their plates and stomachs. Pulse grains, rich in both protein and fiber, may be the ideal candidate to promote satiety at meals. In a crossover feeding study, participants consumed calorie-matched fruit smoothies prepared with either an ice cream base or pureed red lentils. Self-reported satiety, blood glucose response, and ad libitum food intake at a secondary meal were all measured along with breath hydrogen and methane and gastrointestinal tolerance. While there was no significant difference in satiety response or energy intake at the secondary meal, the nutrient profile of the lentil smoothie was improved with increased protein and fiber and dramatically lower fat content. Blood glucose response was not statistically different between the two treatments. Both smoothies were generally well tolerated; however, there was a slightly elevated AUC for perceived gastrointestinal tolerance over 24 hours in the lentil smoothie. No difference in breath hydrogen or methane response was seen between treatments. The substitution of lentils into a meal is not likely to improve satiety; however lentils are a good source of fiber and protein and can greatly improve nutritional content of the meal.

Introduction

As the obesity epidemic continues to be a major public health problem worldwide, many are searching for ways to combat weight gain and support weight loss. With consumers shifting away from processed foods, individuals are looking for whole food products with the ability to elicit satiety and potentially aid in weight management.

Satiety is the state of fullness an individual experiences following a meal. Hormonal and neural signals provide feedback to the brain regarding the composition of nutrients and volume consumed. The signaling mechanisms alter the body's perceived hunger and fullness influencing food intake.[121] Foods with the ability to enhance satiety could decrease caloric intake and postpone the recurrence of hunger, potentially resulting in overall reduced calorie consumption and weight loss over time.

Protein is the most satiating macronutrient. Amino acids in the small intestine stimulate the secretion of hormones that are linked to satiety, including cholecystokinin (CCK), glucagon-like peptide 1 (GLP-1) and peptide YY (PYY).[122] The consumption of high protein diets over time has been shown to enhance satiety and is consistent with weight loss.[122]

Fiber consumption has also been shown to result in increased satiety.[123,124] Fiber can influence satiety and appetite regulation in several ways. The gelling effect seen in soluble viscous fibers can increase gastric distention and slow the rate of gastric emptying into the intestine, increasing perceived fullness. Additionally, the fermentation

of fiber in the colon increases the release of satiety related hormones.[117] Increased consumption of fiber may contribute to reversed obesity trends.[117]

With both protein and fiber contributing to satiety, a product rich in both protein and fiber could potentially result in an additive effect resulting in a greater satiety impact than either nutrient could produce on its own. Pulse grains are legumes including peas, beans and lentils that are not harvested for their oils.[125] Pulse grains are inexpensive and sustainable products, naturally rich in both protein and fiber, making them an ideal addition to meals to increase satiety, reducing overall calorie intake, and over time, lead to weight loss.[126]

Research exploring the effects of pulse grains on satiety is minimal, and few studies have looked at the combined satiating properties of fiber and protein. Mollard et al.[116] compared ad libitum consumption of four different pulses to pasta in energy consumption at the ad libitum pulse meal and at a pizza meal consumed four hours later. The lentil treatment resulted in a significantly lower energy intake at ad libitum pulse meal compared to chickpeas and pasta. No decreased intake was seen among treatments at the ad libitum pizza meal.[116] Nilssen et al[127] assessed the effects of brown beans compared to white bread in 16 male participants. The brown bean treatment resulted in a lowered glucose and insulin response, suppressed hunger hormones, while breath hydrogen and fatty acids were increased.[127] These two studies suggest that pulse grains may impact satiety potentially resulting in decreased caloric intake.

This study investigated whether a smoothie containing ½ cup of pureed red lentils has more satiating potentially than a more traditional dairy-based fruit smoothie made with ice cream.

Methods

The study design and all aspects of the study was reviewed and approved by the University of Minnesota Institutional Review Board Human Subjects Committee. This randomized crossover study compared the effects of two different smoothies as a lunch meal on satiety, glycemic response and gastrointestinal tolerance. Visits were scheduled at least two weeks apart and female participants were only scheduled during their follicular phase of their menstrual cycle.

Subjects

Healthy men and women 18- 65 years old with a BMI between 18.5 and 27kg/m^2 were recruited through posters placed around the University of Minnesota campus as well as surrounding community areas. Interested individuals were asked to complete a screening questionnaire to identify inclusion and exclusion criteria. Restrained eaters (score > 11 on the dietary restraint factor of the Three Factor Eating Questionnaire), smokers, non-regular breakfast or lunch consumers, vegetarians, individuals regularly consuming 4 or more servings of high fiber foods per day and individuals with diseases or conditions that may influence the results of the study, including digestive diseases, were excluded from the study. Exclusions also included women who were pregnant or lactating or have

irregular menstrual cycles, individuals with recent weight fluctuation and individuals on medications that may influence results; individuals who had recently taken antibiotics were scheduled at least three months following the completion of the antibiotic treatment.

Forty subjects (20 men and 20 women) were enrolled into the study based on power calculations of 80% power with $\alpha=0.05$ calculated from the differences in visual analog scale (VAS) scores.

Procedure

Subjects were asked to consume breakfast on the days of their visit and were asked to fast for four hours prior to arrival on their study appointments. Subjects were asked to record their intake for 24 hours prior to their arrival to check for extreme differences in intake prior to study visits that may affect intake. Dietary records were analyzed with the Nutrition Data System for Research (NDSR, version 2014, Nutrition Coordinating Center, Minneapolis, MN). Subjects were asked to refrain from alcohol, excessive fiber consumption, fiber supplements and excessive exercise the day prior to their study visits.

Subjects arrived at testing site at 11:30am and were seated in a quiet testing room where they remained for the remainder of the visit, approximately 4 hours. Informed consent was obtained from each participant. Subjects were weighed at the beginning of each visit to assess for weight changes between visits that may influence their results. Baseline blood glucose, breath hydrogen, gastrointestinal tolerance and visual analog scale (VAS)

questionnaires were taken prior to treatment consumption. Treatments were consumed at 12:00pm and subjects were given 10 minutes to consume the smoothie and 8oz of water.

Additional VAS measures were completed at 15, 30, 45, 60, 90, 120 and 180 minutes from baseline. Five additional questions were asked through the VAS software at 30 minutes regarding palatability of the treatment meal. Researchers measured blood glucose at baseline, 30, 60 and 180 minutes post treatment. Breath hydrogen measures were taken at baseline, 60 and 180 minutes. Following the completion of all 180 minute measures, an ad libitum pizza meal was provided. Each subject was provided with an entire DiGiorno Original Rising Crust Four Cheese pizza (1860kcals) and ad libitum water. Subjects were told to "eat until you are comfortably full". Subjects were given 15 minutes to eat the pizza meal. Pizza was weighed before and after consumption to determine calories consumed at the ad libitum meal.

Treatment

The treatment was delivered in a fruit smoothie form to allow for sufficient blinding to participants. A treatment dose of one half cup of cooked red lentils was selected to be consistent with the recommended serving size of beans and lentils. Red lentils (Bob's Red Mill, Milwaukie, OR) were prepared according to package directions and pureed using a hand blender to achieve a smooth consistency. Pureed lentils were measured out into half cup portions and were frozen individually. Frozen lentils were thawed in the refrigerator one day prior to the study visit.

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Control smoothies were matched with a substitution of a half cup of vanilla ice cream
(Breyers Natural Vanilla, Unilever, Englewood Cliffs, NJ) in place of the lentils, as a
calorie and volume controlled replacement. Recipes used are detailed in Table 6-1. Ice
cream is a common ingredient in smoothies and can be a source of added fat and sugar.
By replacing the ice cream with the same amount of lentils, the nutritional value of the
smoothie is substantially improved. Nutrient comparison of the tested smoothies is shown
in Table 6-2. All smoothies were assembled and prepared just before serving.

Study outcomes

Visual Analog Scales (VAS)

Satiety was measured using a validated 100mm VAS questionnaire. The VAS asked the
subjects four questions regarding their satiety, hunger, fullness and prospective food
consumption. Subjects indicated their current status by placing a mark on a 100mm line.
Questions included: How hungry do you feel? Not hungry at all (0mm) → I have never
been more hungry (100mm); How satisfied do you feel? I am completely empty (0mm)
→ I cannot eat another bite (100mm); How full do you feel? Not full at all (0mm) →
Totally full (100mm); How much food do you think you can eat? Nothing at all (0mm)
→ A lot (100mm).

Palatability of the smoothies were assessed at the 30 minute time point with 5 questions
assessing visual appeal, smell, taste, aftertaste, and overall pleasantness. Responses for

visual appeal, smell, taste and overall pleasantness were rated on a scale of good (0mm) →bad (100mm). Aftertaste was rated on a scale of much (0mm) → none (100mm).

Ad libitum secondary meal intake

One DiGiorno Original Rising Crust Four Cheese pizza was prepared for each subject (1860kcals) and cut into various sized pieces. Each pizza was weighed prior to consumption. Subjects were allotted 15 minutes and asked to eat until they were "comfortably full". After 15 minutes, the remaining pizza was weighed and energy intakes were calculated.

Gastrointestinal tolerance

Gastrointestinal tolerance was determined through a seven question survey assessing each of the following symptoms: gas or bloating, nausea, flatulence, diarrhea or loose stools, constipation gastrointestinal rumbling, gastrointestinal cramping. Each symptom was rated as either: none, mild, moderate or severe.

Colonic fermentation

Breath hydrogen values were measured utilizing the BreathTracker DM (QuinTron Instrument Company, Milwaukee, WI). Subjects were asked to breath into a sample collection bag. After calibration, 20ml exhaled air was removed from the collection bag and injected into the BreathTracker. Samples were analyzed in duplicates to increase accuracy of results.

Glycemic response

Blood glucose was measured using the Bayer Contour Next EZ glucometer (Bayer HealthCare LLC, Mishawaka, IN). Researchers collected the blood samples using sterile techniques. The first drop of blood was wiped away and the second drop of blood was collected for measurement.

Statistical Analysis

Area under the curve for VAS scores, gastrointestinal symptom score, breath hydrogen and methane and blood glucose was measured using the trapezoidal rule, and was adjusted to reflect each subject's baseline measurement. All other endpoints were compared using 2-sample t-tests. Statistical significance was achieved at $P < 0.05$.

Results

Subject demographics

Forty subjects (20 males and 20 females) were recruited, one female subject dropped out following the first visit resulting in a subject population of 39 subjects (20 males, 19 females). Mean age for males was 22.5 ± 0.8 years, and mean age for females was 21.9 ± 1.1 years. Mean BMI was within the normal range, 23.6 ± 0.5 for males and 21.6 ± 0.4 for females (Table 6-3).

Visual analogue scales

There were no significant differences in mean AUC for any of the satiety measures (hunger, satisfaction, fullness and prospective food intake). Average satiety scores over time are shown in Figure 6-1 through 6-4 and Table 6-4.

The control smoothie was considered significantly more palatable than the treatment smoothie in the aspects of visual appeal, taste, aftertaste and overall pleasantness. However, both smoothies were well liked, scoring in the positively in all areas of palatability. Taste, smell, visual appeal and overall pleasantness on average rated below 20 on a scale of 0mm (good) to 100mm (bad). The aftertaste of both of smoothies was the area that could be most improved upon, scoring neutrally with 46mm for the treatment smoothie and 57mm for the control smoothie, on the range of 0mm (much aftertaste) to 100mm (no aftertaste). (Table 6-4 and Figure 6-5)

Ad libitum secondary meal intake

No significant difference in energy intake was seen at the secondary pizza meal. Energy intake at secondary meal was 1034 ± 45 kcals and 1065 ± 49 kcals for treatment and control smoothie respectively ($P= 0.31$).

Gastrointestinal tolerance

No severe symptoms or side effects were reported following the consumption of either treatment. The cumulative sum for all GI symptoms over time was significantly different between the treatment and control smoothies ($P = 0.04$). The mean sum of GI symptoms over time was 8.12 ± 0.22 for the treatment smoothie and 7.75 ± 0.15 for the control

smoothie with possible sums ranging from 7-28. Reports of gastrointestinal cramping were occurred more often following the treatment smoothie than the control smoothie (P = 0.02). No other symptoms were significantly different between treatments (Table 6-4).

Colonic Fermentation

No significant difference was seen between treatments in breath hydrogen or methane response over time (P= 0.28 and P=0.60 respectively).

Glycemic Response

No significant difference in blood glucose AUC between treatments (P= 0.32) with mean AUC of 97 ± 1.76 for the treatment smoothie and 99 ± 1.62 for the control smoothie.

Discussion

The findings of this study suggest that the high protein and fiber lentil-based smoothie has a similar satiety response to a traditional dairy based smoothie. No significant differences were seen in any of the subjective satiety ratings or energy intake at a secondary meal. The addition of ½ cup of purred lentils to a smoothie in place of ice cream does not result in enhanced satiety or reduced intake at a later meal.

While previous research has indicated that meals high in protein and fiber provide enhanced satiety,[122,128] this study is complicated by the practicality of working with whole foods. We chose not to formulate the control smoothie with isolated nutrient sources because that is not something a typical consumer would do. Instead, we used a

more traditional smoothie base, ice cream, containing the same number of calories as the lentils. The control smoothie had a significantly greater fat content compared to the treatment smoothie and, although thought to be less than the other macronutrients, fat does have some satiating properties as well.[129] A study by Bertenshaw et al[130] found a thick, creamy beverage to have a stronger satiety effect compared to a juice-like beverage. The increased creaminess of the control smoothie may have contributed to the effects of perceived satiety. Another factor impacting satiety is the food form of the smoothies. Studies have shown that food form is important to satiety and that liquids result in weaker satiety responses than solid foods.[131] The satiating effects of lentils may be greater in a solid form. Additionally, it is possible that the caloric load of the treatments (305 calories) was not adequate enough to provide substantial and sustained satiety over the three hour monitoring period.

 While the treatment smoothie was just as satiating as the control smoothie, it is important to note that the treatment smoothie had a significantly more desirable nutrient profile (Table 6-2). The treatment smoothie contained more 11.4 grams of protein, 13.2 grams of fiber and less than one gram of fat, while the control smoothie contained 4.5 grams of protein, 3.6 grams of fiber and 7 grams of fat. With only 4% of men and 13% of women meeting their recommended fiber intake[20] (25g for women, 38g for men), dietary changes to increase fiber consumption are encouraged.[132] Adding lentils into smoothies may be an easy way to increase fiber and legume consumption.

Although there were no severe symptoms reported following either treatment, the lentil smoothie resulted in a higher composite gastrointestinal symptom score and gastrointestinal cramping score compared to the control smoothie. Increased perceived gastrointestinal symptoms following consumption of pulse grains, including lentils, is not uncommon. Veenstra et al[133] found increased reported gastrointestinal symptoms in participants consuming 100g lentils daily. However, as with the current study, the symptoms were not severe and do not merit concern or avoidance of lentils.

Participants of our study were low fiber consumers, which likely contributed to the increased reports of gastrointestinal symptoms. Frequent and consistent consumption of legumes has been shown to reduce the occurrence of perceived gastrointestinal symptoms.[134] Overall, while the lentil treatment did result in significantly greater gastrointestinal symptoms, this should not deter individuals from consuming lentils and other legumes.

Another finding of interest was the lack of difference in blood glucose response between the lentil and control smoothie. The lentil-based smoothie contained 14% more carbohydrates compared to the control smoothie; therefore, the similar blood glucose response may indicate improved glycemic response following the treatment smoothie. This finding is consistent with several studies showing significantly lower blood glucose response of lentils compared to other carbohydrate-controlled treatments.[116,127,135,136]

Conclusion

In conclusion, this study suggests that there is no difference in acute subjective satiety measures or energy consumption at a secondary meal in a plant based high protein, high fiber smoothie compared to a traditional, higher fat, dairy-based smoothie. Both smoothies produced a very similar physiologic response, and while the control smoothie was significantly more palatable, both smoothies were well liked. The lentil-based smoothie produced a significantly greater gastrointestinal symptom score, with an increase seen specifically in gastrointestinal cramping. However, both smoothies were generally well tolerated and no severe symptoms were reported. Further studies are needed to determine if there is a difference in blood glucose response between treatments in a carbohydrate controlled experiment. Additional studies using lentils as a meal component in other meal types should be conducted to determine their true effect on satiety.

Acknowledgements

Table 6-1. Recipe comparison between treatment and control smoothie

Lentil Smoothie	Control Smoothie
½ cup pureed red lentils	½ cup vanilla ice cream
60 g banana	60 g banana
2 oz light yogurt	2 oz light yogurt
1/3 cup frozen blueberries	1/3 cup frozen blueberries
4 oz pomegranate juice	4 oz pomegranate juice

Table 6-2. Nutrient comparison between lentil smoothie and control smoothie

	Total Kcal	Total Fat (g)	Carbohydrates (g)	Fiber (g)	Sugar (g)	Protein (g)
Lentil Smoothie	305.5	0.7	65	13.2	30.3	11.4
Control Smoothie	305.9	7	57	3.6	43.6	4.5

Table 6-3. Subject demographic characteristics

	Men (n=20)	Women (n=19)
Age (years)	22.5 ± 0.8	21.9 ± 1.1
BMI (kg/m2)	23.6 ± 0.5	21.6 ± 0.4
Weight (lbs)	169.9 ± 4.7	130.2 ± 3.6
Values presented as mean $\pm$ SE		

Table 6-4. Summary of Results

	Lentil Smoothie	Control Smoothie	P value[†]
Fullness [a]	0.41 ± 0.03	0.40 ± 0.03	0.71
Hunger [a]	0.51 ± 0.03	0.52 ± 0.03	0.55
Satisfaction [a]	0.41 ± 0.03	0.40 ± 0.03	0.91
Prospective consumption [a]	0.59 ± 0.03	0.61 ± 0.03	0.54
Ad libitum meal intake (kcals)[b]	1034 ± 45	1065 ± 49	0.31
Visual appeal [b]	19 ± 3	11 ± 2	0.01*
Smell [b]	18 ± 2	13 ± 2	0.06
Taste [b]	17 ± 2	6 ± 1	0.00*
Aftertaste [b]	46 ± 4	57 ± 4	0.02*
Pleasantness [b]	19 ± 2	8 ± 1	0.00*
GI Tolerance- composite [a] symptom score	8.12 ± 0.22	7.75 ± 0.15	0.04*
Gas or bloating [a]	1.33 ± 0.07	1.24 ± 0.06	0.18
Nausea [a]	1.03 ± 0.02	1.05 ± 0.03	0.47
Flatulence [a]	1.32 ± 0.8	1.22 ± 0.06	0.17
Diarrhea [a]	1.04 ± 0.02	1.02 ± 0.01	0.31
Constipation [a]	1.07 ± 0.04	1.03 ± 0.02	0.24
Gastrointestinal rumbling [a]	1.22 ± 0.05	1.15 ± 0.03	0.12
Gastrointestinal cramping [a]	1.09 ± 0.04	1.02 ± 0.01	0.02*
Breath hydrogen [a]	5.96 ± 0.96	7.29 ± 1.26	0.28
Breath methane [a]	1.86 ± 0.77	2.21 ± 0.81	0.60
Blood glucose response [a]	97 ± 1.76	99 ± 1.62	0.32

[a] Mean baseline adjusted AUC $\pm$ SE
[b] Mean $\pm$ SE
*Indicates a significance at $P < 0.05$
[†] P value indicated for paired t-tests

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Figure 6-1. Subjective hunger ratings over time
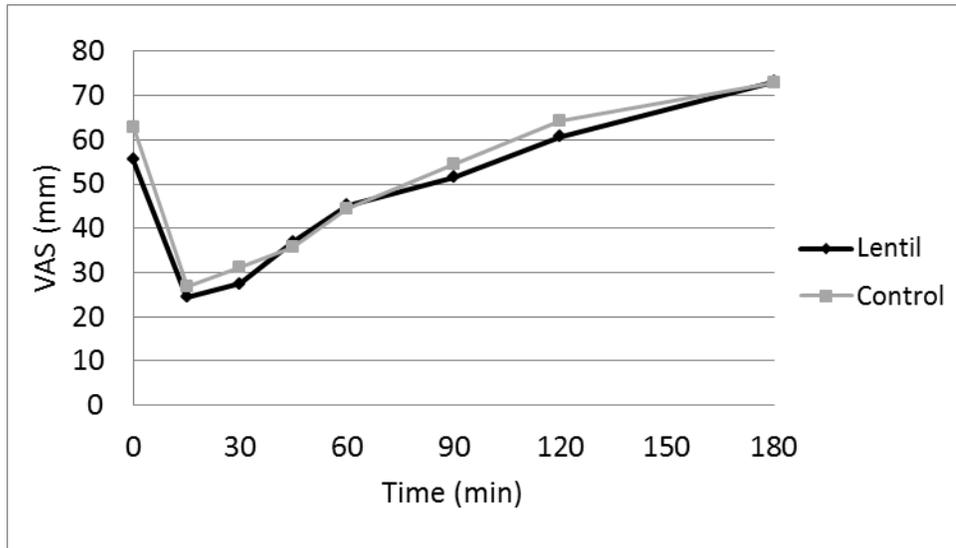
Figure 6-2. Subjective satisfaction ratings over time
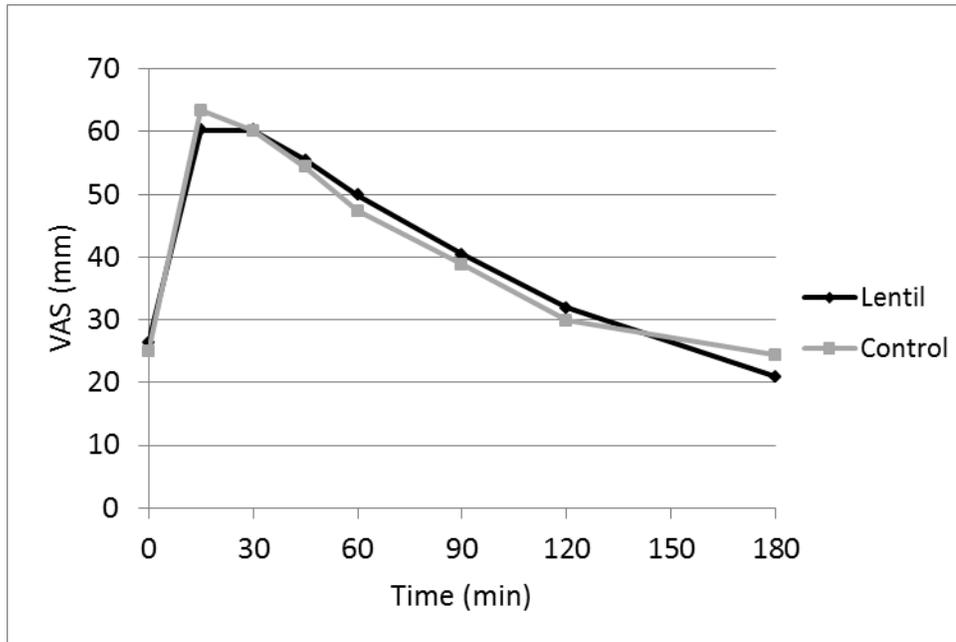
Figure 6-3. Subjective fullness ratings over time
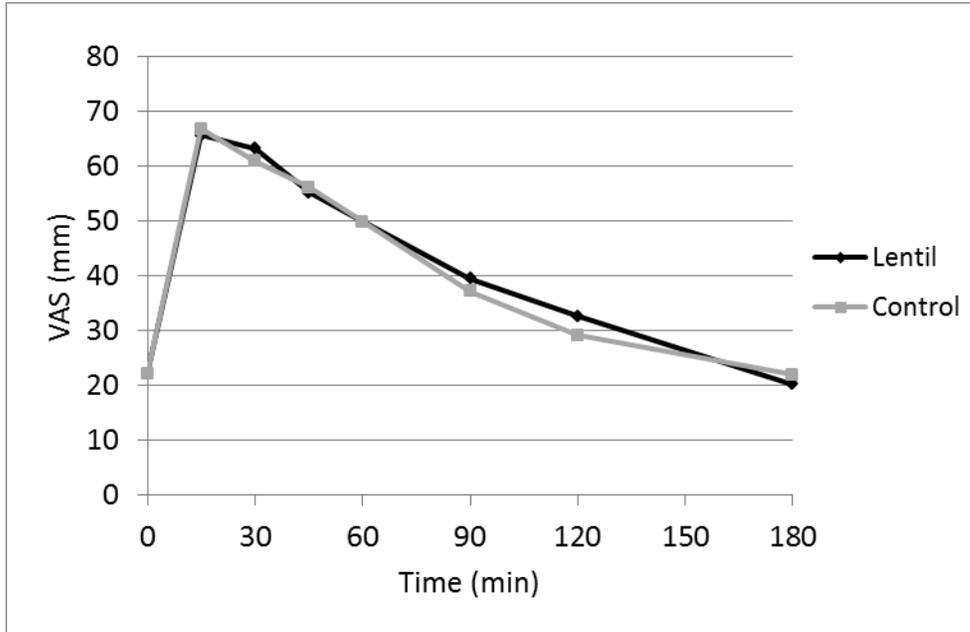
Figure 6-4. Subjective prospective consumption ratings over time
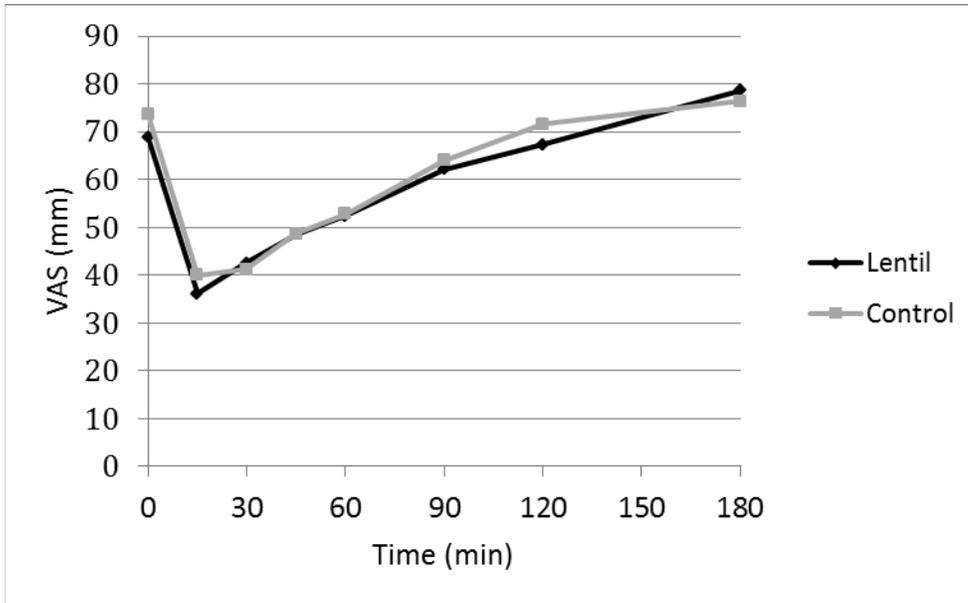
Figure 6-5. Palatability ratings of lentil and control smoothies
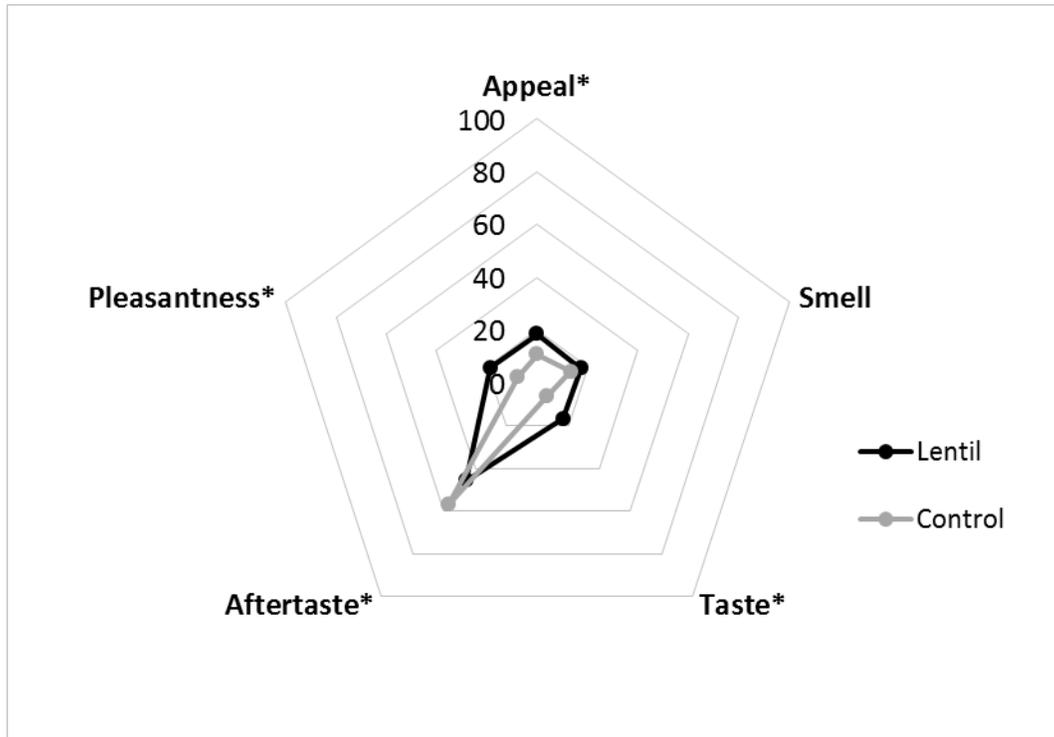
*Indicates a significance at $P < 0.05$

Chapter Seven

LOW FODMAP DIETS IN IRRITABLE BOWEL SYNDROME: A LITERATURE

REVIEW

Summary

Low FODMAP diets have been gaining popularity in recent years, as individuals experiencing gastrointestinal distress search for a diet to alleviate their symptoms. Diets low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPS) have been identified as a diet that could potentially reduce symptoms for individuals diagnosed with irritable bowel syndrome (IBS). It has been hypothesized that limited intakes of FODMAPs reduce luminal distention, thus reducing the symptoms of irritable bowel syndrome. Clinical trials of this diet have indicated mostly positive results. However, there are still aspects of the diet that require further research.

Background

Irritable bowel syndrome (IBS) is a prevalent gastrointestinal (GI) condition affecting approximately 11% of the global population.[137] According to Rome III diagnostic criteria, patients diagnosed with IBS experience reoccurring abdominal pain three or more days per month over the past three months, with at least two of the following symptoms: pain reduction occurring after a bowel movement, symptoms occurring with a change in bowel movement frequency, and change in stool consistency.[138] Currently, there are no biomarkers used to definitively diagnose the condition, so the disease is diagnosed following a clinical assessment of symptoms.[137] Because the pathophysiology of IBS is not well understood, there are no direct targets for pharmacotherapies in the treatment of the condition.[139,140] While there is a wide variety of medications used to treat the symptoms of IBS, a survey of IBS sufferers revealed that only 14% of patients reported complete satisfaction with their conventional treatment regimen.[141]

The role of dietary components in the treatment of IBS has been explored, and recently there has been increasing interest in a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs).[10] FODMAPS are poorly absorbed in the intestine, osmotically-active, and rapidly fermented in the colon. These physiological properties result in luminal distention which can lead to pain, bloating, abdominal distention and even motility changes.[10] Therefore, it has been hypothesized that the exclusion of all FODMAPs in the diet will reduce the symptoms of IBS.[142]

FODMAPs are prevalent in Western diets, occurring in each of the major food groups. The main carbohydrates that are to be avoided include fructans and galactans, lactose, fructose in excess of glucose or large quantities of fructose, and polyols.[10] Many common foods have been analyzed and categorized as either a high FODMAP food or a low FODMAP food (Table 7-1). Researchers at Monash University have established cutoff values for some FODMAP components based on symptom reports from patients with IBS (Table 7-1).[142] It has been recommended that FODMAP intake be limited to less than 0.5g per eating occasion, and low FODMAP diets should not exceed 3g total FODMAPs per day.[142] These cutoffs have not yet been confirmed by clinical trials in patients with IBS. Additionally, these limits and cut-off values pose a challenge as FODMAP content is not provided on nutrient fact panels, limiting consumers to incomplete lists of high FODMAP foods to avoid.

Low FODMAP diets are intended to be short term diets during which individuals avoid all high FODMAP foods for 6-8 weeks (elimination phase).[143] Following the elimination phase, the diet is to be slowly liberalized, reintroducing one FODMAP containing food at a time with strict symptom monitoring.[143] Very little research exists on the reintroduction phase of the FODMAP diet. The low FODMAP diet should be conducted under the supervision of a dietitian to ensure appropriate diet education and implementation.[10,144] Diet liberalization to the point of adequate symptom control should be done quickly to reduce the risk of adverse changes to the microbiota.[145]

Efficacy of a low FODMAP diet

Clinical studies of the low FODMAP diet have indicated substantial symptom improvement in a large subset of patients with IBS. The first study demonstrating the effectiveness of the low FODMAP diet was a retrospective study of 62 patients, ranging from 17 to 81 years of age, diagnosed with IBS and fructose malabsorption.[142] Patients were referred for outpatient dietary advice for their condition. Patients saw a dietitian for an initial symptom assessment and a one- hour education session on the diet. Change in symptoms and dietary compliance was measured at a follow up interview conducted 2-40 months following the initial education session (median follow up at 14 months).[142] General compliance to the diet was seen in 77% of the participants. Seventy-four percent of the patients saw a significant reduction in GI symptoms following the initial diet education session. Rate of symptom reduction increased to 85% in an exclusive analysis of participants who reported strict compliance to the low FODMAP diet.[142]

A double blind, quadruple-arm randomized controlled trial was conducted with 25 patients diagnosed with IBS and fructose malabsorption who had previously reported symptom improvement while following a low FODMAP diet.[146] Patients were provided with low FODMAP meals and snacks for the entirety of the study. In addition to the low FODMAP diet, patients received four treatment beverage to consume for two weeks each, with a two-week washout period between treatments. The treatments included beverages containing fructose, fructans, fructose and fructans, and glucose. Participants completed symptom questionnaires throughout each treatment and washout period.[146] Inadequate symptom control was reported by 70% of the patients during the fructose treatment, 77% of the fructan treatment and 79% of the fructose and fructan treatment

compared to only 14% of the glucose treatment.[146] While this study shows that fructose and fructans both individually and in combination can cause GI symptoms in patients with IBS and fructose malabsorption, the sources are highly isolated and do not mimic a typical diet, which may limit the applicability of this study.

A clinical trial in the United Kingdom examined the effectiveness of the low FODMAP diet compared to standard dietary advice given to patients with IBS attending outpatient visits with a dietitian.[147] Eighty-two participants received either standard diet education based on the UK National Institute for Health and Clinical Excellence (NICE) guidelines or a low FODMAP diet education. Symptom questionnaires were completed at baseline as well as at a follow up appointment completed 2-6 months after the initial diet education.[147] A significantly greater portion of participants from the low FODMAP group reported improvement in bloating, abdominal pain and flatulence. Eighty-six percent of those receiving the low-FODMAP education saw improvement in the composite symptom score, compared to only 49% receiving the standard education. Overall, participants in the low FODMAP group were significantly more satisfied with their change in symptoms.[147]

In 2014, Halmos et al. published a randomized crossover study comparing a low FODMAP diet to a standard Australian diet in patients diagnosed with IBS and matched healthy controls.[148] Thirty-eight participants were randomized to a treatment diet for 21 days, with a 21 day washout period before beginning the alternate treatment. Meals and snacks were provided by the research institute. Participants were asked to rate perceived

symptoms on a visual analogue scales daily throughout all phases of the study.[148]
Clinically significant symptom improvement was seen in 70% of the IBS patients while
following the low FODMAP diet. Overall, the IBS participants saw significant reduction
in overall symptoms, bloating, abdominal pain and flatulence during the low FODMAP
treatment compared to the typical Australian diet. Healthy participants reported no
change in GI symptom scores during either treatment.[148]

A single-blind study of 75 IBS patients in Sweden randomly assigned participants to
follow a low FODMAP diet or a diet typically recommended for patients with IBS for
four weeks.[149] The typically recommended diet focused on avoiding large meals,
decreased fat intake, and avoidance of insoluble fibers, caffeine and "gas-producing
foods". Participants received advice on following their assigned diet from a dietitian and
received a brochure with information on the diet. Food was not provided to study
participants, and compliance was assessed through a four-day food diary at the
conclusion of the trial.[149] Symptom severity was significantly reduced in both the low
FODMAP and typical IBS diet group, with no significant difference in symptom scores
between the two groups following the 4 week trial. While this study does the support the
ability of the low FODMAP diet to reduce symptoms in participants with IBS, it does not
show that it is significantly more effective than traditional dietary advice for IBS
patients.[149]

Each of these clinical trials shows significant GI symptom improvement in participants
with IBS while following a low FODMAP diet. These studies provide important evidence

to support the use of a low FODMAP diet as a dietary intervention for individuals struggling with functional GI disorders. While the body of evidence is overwhelmingly positive, it is important to note that some individuals with diagnosed IBS experience no symptom improvement while following the diet, and the diet should be evaluated on a case by case basis.[144] Additionally, there is little evidence of diet effectiveness following diet liberalization.

Measures of Gastrointestinal Tolerance

The overall goal of the low FODMAP diet is to reduce GI distress in individuals with functional bowel disorders. The acceptability of foods in the low FODMAP diet mainly relies on analytical measures.[142] However, to fully understand the effects of a particular food item, GI tolerance should be assessed. GI tolerance is generally measured through subjective symptom questionnaires. Currently, there are no validated questionnaires measuring acute GI symptom response in either healthy or IBS populations. Many of the validated questionnaires assess changes in symptoms over long periods of time or are specific to a disease or condition.[150–153] FODMAPs are rapidly fermented, so gastrointestinal changes should be assessed in frequent intervals over a period of hours to days. Common GI symptoms, including nausea, bloating, flatulence, abdominal pain, cramping, diarrhea and constipation, should be measured individually as well as a part of a composite symptom score, as individuals may experience GI distress as a variety of symptoms.[154] Symptom questionnaires can provide good insight into the GI response of

the test product; however, they are subjective and it can be difficult to control for outside factors that may impact the way the participant perceives their symptoms.[154]

Hydrogen breath tests can also be used to assess the acute GI response of a particular food or substance.[155] Unabsorbed carbohydrates are fermented by bacteria in the colon, producing hydrogen. The hydrogen is absorbed through the intestinal membrane, into the blood, and travels to the lungs. The hydrogen is then released during exhalation.[155] The breath samples are collected and analyzed by a modified gas chromatograph, measuring hydrogen, methane and carbon dioxide.[156] Large amounts of hydrogen may be indicative of carbohydrate malabsorption, and thus GI intolerance. A 20 ppm increase in breath hydrogen measured from baseline to peak is generally regarded as a clinically significant marker of intolerance.[155] Breath methane is also measured during hydrogen breath tests, as about 15-30% of the population have the microorganism, *Methanobrevibacter smithii*, which converts hydrogen to methane.[155] Existing research suggests that breath methane values are not significantly impacted by low FODMAP diets.[143]

Individuals with IBS produce more hydrogen compared to healthy individuals regardless of the FODMAP content of the meal.[157] Healthy and IBS participants were asked to consume either a low FODMAP diet (9g of FODMAPs) or a high FODMAP (50g of FODMAPs) diet with breath hydrogen tests conducted hourly throughout the day.[157] Compared to the low FODMAP diet, the high FODMAP diet produced a greater hydrogen production in both populations, with significantly greater hydrogen production in the IBS group compared to the healthy group.[157] The low FODMAP diet (9g of

FODMAPs/day) did not produce a clinically significant increase in breath hydrogen in either group, even though the participants consumed more than the recommended daily limit of FODMAPS (3g).[142,157]

Nutritional Significance

Low FODMAP diets appear to be an effective dietary intervention for many individuals with uncontrolled IBS. As consumer's self report their improved health outcomes as a result of following this diet, its awareness and popularity will increase. While this diet is well tolerated, it is complex and the broad availability of convenient food solutions are limited today. With a growing consumer demand for low-FODMAP products, some food companies will react to this opportunity as a new growth direction for their product offerings and develop low FODMAP options for meal choices to supplement consumers' diet, helping them meet their daily nutrient needs. Oral nutrition supplements (ONS) may also grow in demand, providing a good source of nutrition and serve as a convenient and healthy alternative to solid food for individuals who are malnourished or have limited diets.

While interest in low FODMAP diets is clearly growing today, there are still large gaps in the literature that need to be explored, particularly in the lack of established cutoff levels of polyol and lactose allowable in food products. Additionally, the established cutoffs for all FODMAP components should be reevaluated based on randomized controlled trials measuring acute GI tolerance of varying quantities of the FODMAP to determine acceptable limits.

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Table 7-1. Established FODMAP limits and examples of high-FODMAP food sources

FODMAP	Established limits [a]	Examples of food sources determined to be high in FODMAP content [b]
Excess fructose	<0.5g fructose in excess of glucose per 100g; or more than 3g fructose per serving	Apples, pears, honeydew melon, water melon, honey, high-fructose corn syrup, fruit juice and dried fruits
Lactose	No established limit	Milk, yogurt, ice cream and soft cheeses
Oligosaccharides (fructans and galactans)	<0.2g fructans per serving; no specific guidelines for galactans	Garlic, onions, peas, broccoli, cabbage, wheat and rye, chickpeas, lentils and red beans
Polyols	No established limit	Sorbitol, mannitol, xylitol, isomalt, etc.

[a] Adapted from Shepherd et al., 2006
[b] Adapted from Gibson et al., 2010

Chapter Eight

WHITE GRAPE JUICE ELICITS A LOWER BREATH HYDROGEN

RESPONSE COMPARED TO APPLE JUICE IN HEALTHY HUMAN

SUBJECTS: A RANDOMIZED CONTROLLED TRIAL

The text of this chapter is a reprint of the material as it appears in "White grape juice elicits a lower breath hydrogen response compared to apple juice in healthy human subjects: A randomized controlled trial" previously published by the *Journal of the Academy of Nutrition and Dietetics*.[11] The content has been reformatted to meet university guidelines.

Summary

Background: Diets low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPS) are used to manage symptoms in individuals with irritable bowel syndrome. While effective at reducing symptoms, the diet can be complex and restrictive. Additionally, there are still large gaps in the literature and many foods with unclear effects in the GI tract, like fruit juice. While many fruits are allowable on a low FODMAP diet, consumption of all fruit juice is generally cautioned due to the large fructose load contained in juice, regardless of the glucose concentration. Very little research exists regarding the importance of limiting fructose load during a low FODMAP diet; therefore, individuals following a low FODMAP diet may be unnecessarily restricting their diets.

Objective: Determine if there is a difference in gastrointestinal (GI) tolerance between juice from a high FODMAP fruit (apple juice) and juice from a low FODMAP fruit (white grape juice) in healthy human subjects. Provide insight into the role of juice in a low FODMAP diet.

Methods: A double-blind randomized controlled crossover study was conducted with 40 healthy adults. Fasted subjects consumed 12 oz of either apple juice or white grape juice. Breath hydrogen measures were taken at baseline, 1, 2, and 3 hr. Subjective GI tolerance surveys were completed at the same time intervals and at 12 and 24 hr. Breath hydrogen and GI symptoms were assessed with area under the curve analysis. Significance was determined with a two-sided t test with a p-value <0.05.

Results: Consumption of apple juice resulted in a greater mean breath hydrogen area under the curve at 23.3ppm·hr (13.0, 33.6) compared to white grape juice at 5.8 ppm·hr (-4.6, 16.1) (p<0.001). No differences in reported GI symptoms were seen between treatments.

Conclusions: Both juices were well tolerated and neither produced any severe symptoms in healthy adults. White grape juice consumption resulted in only a small rise in breath hydrogen, which may suggest excluding foods only because of the high fructose load could be unnecessarily restrictive. The results of this study suggest that the fructose to glucose ratio is likely more important than the total fructose load of the food when considering the acceptability of a food on a low FODMAP diet. More research is needed in individuals with IBS to determine if white grape juice and other juices from low FODMAP fruits could be additional beverage options for individuals following a low FODMAP diet.

Introduction

The role of dietary interventions in the treatment of irritable bowel syndrome (IBS) has been explored, and recently there has been increasing interest in a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs).[10] FODMAPS are poorly absorbed in the intestine, osmotically-active, and rapidly fermented in the colon. These physiological properties result in luminal distention which can lead to pain, bloating, abdominal distention and even motility changes.[10] The particular carbohydrates of concern include fructose, lactose, fructans, galactans and polyols. By removing high FODMAP foods from the diet, many patients experience a reduction in IBS symptoms. Clinical trials assessing the efficacy of a low FODMAP diet have shown symptom improvement in 70-86% of patients with IBS.[142,147,148]

The consumption of fructose in excess of glucose (free fructose), as well as the consumption of large quantities of fructose, regardless of the glucose content, is to be avoided while following a low FODMAP diet. Fructose can be absorbed alone through carrier-mediated diffusion, using GLUT-5 transporters; however, this transporter has a low capacity.[158] As a result, when consumed in large quantities, some fructose may not be absorbed resulting in gastrointestinal (GI) distress.[158] When fructose is consumed in combination with glucose, the fructose absorption is much more efficient. Absorption is most effective when fructose and glucose are consumed in equal quantities.[158] Truswell et al shows a combination of 25g fructose with 25g glucose to have no significant rise in breath hydrogen in healthy subjects, and had a significantly lower breath hydrogen

response compared to the consumption of 25g fructose, despite the higher total sugar content.[159]

The original guidelines of the low FODMAP diet as described in Shepherd et al states that foods allowable on the low FODMAP diet should not contain more than 0.5g fructose in excess of glucose per 100g serving.[142] Shepherd et al also recommends limiting fructose consumption to 3g per eating occasion, regardless of the glucose content or serving size.[142] These cutoff values were chosen based on physiological principals of fructose absorption, and are still used as guidelines for the low FODMAP diet.[10,142] Clinical trials assessing the physiologic capacity of fructose absorption in patients following a low FODMAP diet have not been conducted to confirm these cutoff values. Additionally, the importance of avoiding foods with high fructose loads during low FODMAP diets has not been established.[10]

The consumption of fruit juice is generally not recommended while following a low FODMAP diet, due to the high fructose load of fruit juices. While many fruits are allowed on the low FODMAP diet, the juices of those fruits are still discouraged. When consumed in appropriate amounts, 100% fruit juice can be a healthy beverage option delivering necessary nutrients and phytochemicals in a year-round, cost effective manner.[160] Individuals following a low FODMAP diet are already restricted in the types of fruits they can consume; by further restricting all 100% fruit juices it becomes even more challenging to meet the daily recommended fruit intake.

The objective of this study is to examine the GI tolerance and breath hydrogen response of 100% juice from a low FODMAP fruit, grapes, compared to juice from a high FODMAP fruit, apples in healthy adults. We hypothesized that white grape juice would be better tolerated and would result in a lower breath hydrogen response compared to apple juice. This study may provide important insight into the absorption of juice and the potential to offer some juices as a healthy beverage option to individuals following a low FODMAP diet.

Materials and Methods

Study Design

The study was reviewed and approved by the University of Minnesota Institutional Review Board, Human Subjects Committee. The protocol for this study was registered on ClinicalTrials.gov in September 2015 (Clinical Trials ID: NCT02565472). This study was a double-blind, randomized controlled, crossover trial with two visits. The treatment order was randomized over the two visits, and each subject received one treatment at each visit with at least one week washout period between the two visits. Treatments were coded prior to arrival at the research facility and code was not broken until after the statistical analysis was complete.

Subjects

This study was conducted with healthy human subjects, with no history of gastrointestinal disorders. While this is not the target population for a low FOMDAP diet,

it is important to determine the GI effects of juice in a healthy population because there is minimal research in the area. Additionally, conducting research in a healthy population provides evidence to support future research in individuals with gastrointestinal disorders. Subjects were recruited with flyers posted around the University of Minnesota campus. Individuals who expressed interest in the study were asked to complete a screening questionnaire to determine if they met the participant criteria. Individuals were eligible for the study if they were between the ages of 18 and 65 years old, had a BMI between 18.5 kg/m^2 and 29.5 kg/m^2 and could provide written informed consent. Applicants were excluded if they were smokers, high fiber consumers (consuming three or more high fiber foods per day), non-regular breakfast and lunch consumers, were enrolled in a concurrent or recent dietary intervention trial, or had recent weight fluctuations of more than 10 pounds in the past three months. Participants were also excluded if they had a history of past or existing GI diseases or surgeries, used enemas, laxatives, proton pump inhibitors or antibiotics within the past three months, or had any allergies to any of the treatments. Informed consent was obtained from each participant prior to the beginning of the study.

Treatments

Treatments included apple juice (Mott's LLP, Plano, TX) as well as white grape juice (Welch Foods Inc, Concord, MA). Treatments were both provided as 12 oz servings to control for volume of juice consumed rather than calories or fructose consumed. The

juices were analytically measured by Covance Laboratories (Madison, WI) for sugar composition provided in Table 8-1.

Hydrogen breath tests

Hydrogen breath tests are a marker of bacterial fermentation within the GI tract. Unabsorbed carbohydrates are fermented by bacteria in the colon, producing hydrogen. The hydrogen is absorbed through the intestinal membrane, into the blood, and travels to the lungs. The hydrogen is then released during exhalation.[155] Breath samples were measured with the Breath Tracker SC (QuinTron Instrument Company, Milwaukee, WI), a gas chromatograph, which measures breath hydrogen, methane and carbon dioxide to correct for atmospheric contamination. Subjects exhaled into a mouthpiece with a sample bag collecting the end expiratory air. Following calibration, 20ml of exhaled air was removed from the sample bag and injected into the Breath Tracker SC. Samples were run in duplicates, and corrected values were averaged for more accurate results.

Following consumption, large amounts of hydrogen may be indicative of carbohydrate malabsorption, and thus GI intolerance. Because baseline values vary among individuals, a 20 ppm increase in breath hydrogen measured from baseline to peak is generally regarded as a clinically significant marker of intolerance.[161] Breath methane is also measured during hydrogen breath tests, as about 15-30% of the population have *Methanobrevibacter smithii*, a microorganism that converts hydrogen to methane.[155] Existing research suggests that breath methane values are not significantly impacted by low FODMAP diets.[157]

Gastrointestinal symptom questionnaires

Acute GI tolerance of the two treatments was determined through the repeated completion of GI symptom questionnaires. The questionnaire used in this study was based on the GI symptom questionnaire validated by Bocenschen et al., but was modified to fit the symptoms of interest for this study.[151] The survey asked subjects to rate the intensity or frequency of the following symptoms: gas or bloating, nausea, flatulence, diarrhea or loose stools, constipation, gastrointestinal rumbling and gastrointestinal cramping. Each symptom could be rated as either none, mild, moderate, quite a lot, severe, very severe, or unbearable.

Study procedures

Subjects received pre-study diet instructions to follow for the 24 hours prior to each of the two study visits. Subjects were asked to follow a low fiber diet, avoid the consumption of apple and pear juice, sugar alcohols, alcoholic beverages and excessive exercise for the day prior to each study visit. Participants were instructed not to eat or drink anything (except for water) after 7:00pm the night before each visit.

Subjects arrived to the testing facility at the University of Minnesota following a 12 hour fast, where they remained for three hours to complete the study visit. Upon arrival, subjects completed their baseline hydrogen breath tests, as well as their baseline GI symptom questionnaire. Subjects were given 10 minutes to drink the provided beverage. Hydrogen breath tests were taken again at 60, 120 and 180 minutes post treatment

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consumption. GI symptom questionnaires were completed at 0.5, 1, 1.5, 2, 3, 12, and 24 hours post treatment consumption. The subjects returned to complete their second within seven to ten days following the initial visit.

Statistical analysis

An independent statistician, blinded to the treatments, conducted the statistical analysis of the results. Baseline-corrected area under the curve (AUC) was calculated using the trapezoidal rule, and was corrected to account for each subject's baseline measurement. Breath hydrogen and GI symptom response were compared using mixed-effects models. Means were compared using paired t-tests. Statistical significance was determined at *P* < 0.05.

Results

Subject demographics

Forty healthy adults (20 males, 20 females) were recruited and completed this study. The average age of participants in the study was 22.7 years, with an average BMI of 23.4 ± 2.8 kg/m^2 (Table 8-2). No differences between treatment order was observed.

Breath hydrogen

The apple juice treatment resulted in a significantly greater breath hydrogen AUC than the white grape juice (Figure 8-1). The mean breath hydrogen AUC (95% CI) for apple juice (23.3(13.0, 33.6) ppm·hr) is higher than that of the white grape juice (5.8(-4.6, 16.1)

ppm·hr; *P*= 0.001). The mean breath hydrogen concentrations (95% CI) were significantly different between apple juice and white grape juice two hours post consumption (28.8(22.3, 35.3) ppm and 19.6(13.1, 26.1) ppm respectively; *P*= 0.003) as well as three hours post consumption (21.7(17.6, 25.8) ppm and 14.4(10.3, 18.4) ppm respectively; *P*= 0.005). The mean breath methane AUC (95% CI) for apple juice was 3.6(-0.1, 7.2) ppm·hr compared to white grape juice at 3.2 (-0.4, 6.9) ppm·hr. There was no significant difference between treatments in breath methane response (*P*= 0.90).

Gastrointestinal symptom response

No symptoms were reported as severe, very severe or unbearable at any time point following either treatment. The difference between the total symptom score AUC of the two juice treatments were not statistically significant. Additionally, there were no significant differences in the AUC of any of the individual symptoms following the consumption of the treatment (Table 8-3).

Discussion

Overall, both apple juice and white grape juice were well tolerated by healthy adults. No severe GI symptoms were reported during the 24 hours following consumption of either juice treatment. This result was expected, as a 12 oz dose of juice is a realistic and readily consumed serving size among healthy adult populations. However, the significantly higher breath hydrogen response of apple juice compared to white grape juice may suggest that there is a difference in carbohydrate absorption between the two juices that

does not elicit GI symptoms in a healthy population. The difference in fructose to glucose ratio is likely the cause of the difference in breath hydrogen response.

Fructose is known to be absorbed through carrier-mediated diffusion utilizing the GLUT 5 transporter on intestinal epithelial cells. The estimated free-fructose absorptive capacity for healthy individuals is between 25 and 50g fructose.[162] When fructose is consumed in conjunction with glucose, the absorptive capacity increases.[159,163,164] While the mechanism by which glucose enhances fructose absorption is not completely known, it has been hypothesized that glucose transport causes a direct stimulation of fructose transport, possibly through the upregulation of the GLUT 2 transporter to the brush boarder.[165] GLUT 2 can transport both fructose and glucose and is known to exist on the basolateral membrane of intestinal cells.[165] Recruitment to the apical side of intestinal epithelial cells has been seen in rodent models.[166–168]

This study found that apple juice produced a much greater breath hydrogen response compared to white grape juice in a healthy adult population. Ong et al measured the breath hydrogen response of both healthy and IBS subjects following a low FODMAP and high FODMAP diet.[157] The breath hydrogen increase following a high FODMAP meal was more exaggerated in the IBS subjects, but the healthy subjects also had a significantly greater breath hydrogen response following the high FODMAP meals, with no difference in GI symptoms.[157] The low FODMAP diet maintained low breath hydrogen levels in both healthy and IBS subjects.[157] The findings from Ong et al supports

the lack of GI symptoms in a healthy population, even with evident breath hydrogen differences.[157]

While hydrogen breath tests are simple, noninvasive way to assess the GI response of particular foods or substances, the tool does have limitations. The hydrogen breath test is designed to measure the effects of specific substrates like glucose, fructose and lactose to diagnose small intestine bacterial overgrowth, fructose malabsorption and lactose malabsorption.[155] While the tool can measure the gas produced following the consumption of specific foods or diets, there is not a well-established cutoff value to determine when a food or diet is not well tolerated.[161] As a result, the hydrogen breath test has been coupled with a GI symptom questionnaire to produce a more complete assessment of GI tolerance. Additionally, although subjects were 12 hours fasted and instructed to follow a low fiber and polyol lead in diet, it is possible that there was fermentation occurring in the colon from previous meals at the time of measurements. Subjects were responsible for their own food choices the day prior to study visits, and if not compliant with the lead in diet, this could falsely elevate the breath hydrogen values.[161] To account for this potential limitation, the area under the curve was corrected for baseline values.

Another alternative method to measure fructose absorption is the $^{13}CO_2$ breath test.[169] This test uses carbon 13-labeled fructose to determine how much fructose is absorbed, metabolized and released as CO_2 in the breath. This measurement tool is not completely effective because unabsorbed fructose that is fermented in the colon is also released as

CO_2 in the breath, and the two processes cannot be separated with this tool.[169] While the hydrogen breath test also has limitations, it is considered the best methodology for assessing fructose malabsorption.[170]

The two juice treatments were provided in matched volumes rather than matched calories, or matched carbohydrate contents. Although one could justify controlling for any one of those factors, we chose to match for volume because consumers quantify and measure beverage intake based on volume rather than calories or grams of fructose. Further, differences in caloric density and sugar profile of the two treatments are characteristic among the juices. Controlling for one or the other may limit the practicality of the study. The treatment dose of 12oz was selected based on typical beverage portion sizes.[171]Although the white grape juice treatment has more fructose than the apple juice treatment and greatly exceeds the established fructose load cutoff of 3g per serving for a low FODMAP food, the baseline to peak rise of breath hydrogen following white grape juice consumption was very small (3.9ppm). Apple juice has a high fructose load, a high fructose to glucose ratio, and contains sorbitol (polyol). Each of these factors likely contributed to colonic fermentation as evidenced by the greater breath hydrogen response. The individual effects of each of the FODMAP components cannot be separated and assessed. The addition of a water control group would have been beneficial to compare the effects of each treatment to a continued fasting state. The lack of such control group is a limitation of the study design. However, the goal of this study was to assess the effects of juices that are readily available on the market, at practical doses.

Additional research should be conducted on the additive and comparative effects of products containing various FODMAP components.

This study was conducted in a healthy population, so the results cannot be applied to individuals with IBS who may be following a low FODMAP diet. However, this study does suggest that the fructose to glucose ratio may be a more important factor for carbohydrate malabsorption than the total load of fructose in the product. More research should be conducted to determine the importance of limiting the fructose load of foods during a low FODMAP diet. Additional studies should also be carried out to determine if juices from fruits allowable on low FODMAP diets may be allowable beverage options for individuals following a low FODMAP diet. Juices with similar fructose to glucose ratios to white grape juice (1.2), like orange juice (1.17) and red grapefruit juice (1.06),[172] may also be well tolerated.

Conclusion

The consumption of white grape juice resulted in a significantly lower breath hydrogen response compared to apple juice. Both juices were well tolerated in healthy subjects according to GI symptom questionnaires. While this study was not conducted in participants with IBS, it still provides important information regarding the gastrointestinal tolerance of juices with varying FODMAP contents. Findings from this study should inform future research assessing the physiological effect of fruit juice consumption in individuals with IBS.

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Acknowledgments

Table 8-1. Sugar composition of juice treatments used in a randomized controlled trial comparing the gastrointestinal tolerance of apple juice and white grape juice in healthy adult subjects

	Fructose to glucose ratio	Fructose (g/12 oz)	Glucose (g/12 oz)	Sucrose (g/12 oz)	Total sugar (g/12 oz)	Sorbitol (g/12 oz)
Apple juice	2.6	23.4	8.9	5.7	38.0	1.5
White grape juice	1.2	28.4	24.1	0.0	52.5	0.0

Table 8-2. Demographics of healthy adults participating in a randomized controlled trial

assessing the gastrointestinal tolerance of white grape juice and apple juice (n=40)

	Mean ± SD	Range
Age (years)	22.7 ± 4.2	19- 34
BMI (kg/m^2)	23.4 ± 2.8	19.1-28.1

Table 8-3. Area under the curve gastrointestinal symptom measurements in healthy

adults participating in a randomized controlled trial comparing the gastrointestinal

tolerance of apple juice and white grape juice

	Apple Juice (n=40)	White Grape Juice (n=40)	*P* value
Sum of all symptoms (points·hr)	0.8 (-1.4, 3.0)	2.4 (0.2, 4.6)	0.29
Gas or Bloating (points·hr)	0.9 (-2.4, 4.2)	1.2 (-2.1, 4.5)	0.90
Nausea (points·hr)	-0.2 (-1.8, 1.3)	-0.3 (-1.8, 1.3)	0.95
Flatulence (points·hr)	1.9 (-0.9, 4.7)	4.0 (1.2, 6.7)	0.25
Diarrhea (points·hr)	0.3 (-0.7, 1.3)	1.1 (0.1, 2.1)	0.22
Constipation (points·hr)	0.3 (-0.5, 1.0)	0.7 (-0.03, 1.5)	0.41
GI Rumbling (points·hr)	-4.8 (-9.2, -0.4)	-2.8 (-7.2, 1.6)	0.45
GI Cramping (points·hr)	-0.9 (-3.4, 1.6)	-1.2 (-3.7, 1.3)	0.86

Results presented as Mean AUC (95% CI)

Figure 8-1. Breath hydrogen response of healthy adults (n=40) participating in a randomized controlled trial to determine differences in gastrointestinal tolerance following consumption of apple juice and white grape juice
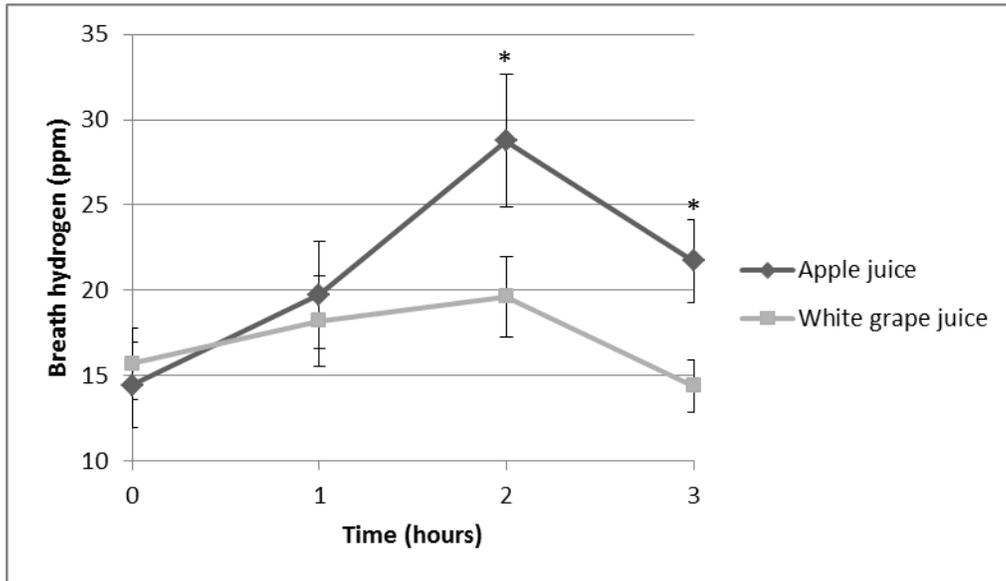
* Indicates significance at 0.05

Error bars indicate standard error of the sample mean

Chapter Nine

GASTROINTESTINAL TOLERANCE OF LOW FODMAP ORAL NUTRITION SUPPLEMENTS IN HEALTHY HUMAN SUBJECTS: A RANDOMIZED CONTROLLED TRIAL

The text of this chapter is a reprint of the material as it appears in "Gastrointestinal tolerance of low FODMAP oral nutrition supplements in healthy human subjects: A randomized controlled trial" previously published in *Nutrition Journal*.[12] The content has been reformatted to meet university guidelines.

Summary

Background: There has been increasing interest in utilizing a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) for the treatment of irritable bowel syndrome (IBS), a functional gastrointestinal disease. While studies have indicated that this diet can be effective at symptom reduction, it is a restrictive diet and patients may find it challenging to find low FODMAP products to meet their nutrient needs. The primary objective of this study was to assess the gastrointestinal (GI) tolerance of three low FODMAP oral nutrition supplements (ONS) in healthy adults.

Methods: A double-blind randomized controlled crossover study was conducted in 21 healthy adults (19-32 years). Fasted subjects consumed one of four treatments at each visit, with a one week wash out period between visits. Each participant received all treatments. Treatments included three low FODMAP ONS formulas (A, B, and C) as well as a positive control consisting of 5g fructooligosaccharides (FOS) mixed in lactose-free milk. Breath hydrogen was measured at baseline, 1, 2, 3, and 4 hours post treatment consumption. Subjective GI symptom questionnaires were completed at baseline, 0.5, 1, 1.5, 2, 3, 4, 12, 24 and 48 hours following treatment consumption. Mean breath hydrogen concentrations and baseline corrected area under the curve for both breath hydrogen and GI symptoms were analyzed and compared between treatments. Significance was determined at $P < 0.05$.

Results: The positive control resulted in higher breath hydrogen response compared to all three of the low FODMAP ONS beverages at 3 and 4 hours after consumption. There were no differences in GI symptom response between treatments.

Conclusions: All treatments were well tolerated in healthy participants. The low FODMAP formulas resulted in a lower breath hydrogen response compared to the positive control, and may be better tolerated in individuals with IBS. More research should be conducted to better understand the GI tolerance of low FODMAP ONS in individuals with IBS.

Trial registration: The protocol for this study was registered on ClinicalTrials.gov in January 2016 (Clinical Trials ID: NCT02667184).

Background

Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal (GI) disorder impacting 11.2% of individuals worldwide.[173] The disease presents as various GI symptoms including abdominal pain and changes in stool consistency and frequency.[138] While many medications and therapies exist to treat the symptoms of IBS, no cure currently exists.[139] Recently, clinical research has focused on diet as a treatment for IBS, since food can be related to symptom expression in many patients.[174] Diets low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) are recommended treatment options in Australia and the United Kingdom to manage the symptoms of IBS.[175,176] FODMAPs are not readily absorbed in the small intestine causing fluid to be pulled into the intestinal lumen, and the remaining carbohydrates to be fermented in the colon causing gas production.[10] By removing the carbohydrates with these properties from the diet, patients often see a reduction in symptoms. Halmos et al. reported clinically significant symptom improvement in 70% of participants with IBS while following a low FODMAP diet.[148]

The main advantage to following a low FODMAP diet is that it can greatly improve symptoms; however, the diet can also be very restrictive. There are not many ready-to-eat options for consumers, and almost all meals and snacks must be prepared at home. Low FODMAP diets should be initiated with the guidance of a registered dietitian (RD), to ensure the patient has the knowledge and skills to create a nutritionally complete diet.[10] Without such guidance, restrictive diets, like the low FODMAP diet, may leave

consumers focused on only a few foods that they know are well tolerated. Limited diets may result in nutrient deficiencies.[177,178] While well tolerated, the low FODMAP diet is complex and the broad availability of convenient food solutions are limited today. Oral nutrition supplements (ONS) are liquid beverages formulated to improve the nutrient consumption of those individuals with either minor nutritional gaps or specific disease conditions. While several types of ONS already exist on the market, it is very difficult to find an ONS that is low in FODMAPS. Low FODMAP ONS may grow in demand, providing a good source of nutrition and serve as a convenient and healthy alternative to solid food for individuals who suffer from IBS and struggle to meet their nutritional needs with conventional foods.

While previous studies have assessed the effects of enteral nutrition formulas with varying FODMAP contents,[179–181] no prior studies have examined the acute gastrointestinal tolerance of ONS beverages that have been formulated to be low in FODMAPs. Therefore, in this pilot study, our aim was to examine the gastrointestinal tolerance of three low FODMAP formulated ONS (A, B and C) in 21 healthy human subjects. We compared the three low FODMAP ONS to an isocaloric, positive control consisting of lactose-free milk mixed with 5g of fructooligosaccarides. We hypothesized that the consumption of the low FODMAP ONS would produce a lower breath hydrogen response compared to the positive control. Additionally, we hypothesized that the subjective reports of gastrointestinal symptoms would be lower following the consumption of the low FODMAP supplements compared to the positive control.

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Methods

Study Design

The study was reviewed and approved by the University of Minnesota Institutional
Review Board, Human Subjects Committee. The protocol for this study was registered
on ClinicalTrials.gov in January 2016 (Clinical Trials ID: NCT02667184). The study
design was a randomized, controlled, crossover study with 21 subjects (11 males, 10
females). The study consisted of four visits, assessing the effects of three low FODMAP
ONS and one positive control, with a seven day washout period between each visit.
Participants received each of the four treatments only once. Treatments were randomized,
coded and blinded to both participants and researchers. Treatment codes were not
revealed until following the statistical analysis.

Subjects

Subjects were recruited via flyers displayed around the University of Minnesota campus
in Saint Paul and Minneapolis. Prior to enrollment, interested individuals were screened
to determine if he or she met all of the eligibility criteria. Eligible participants were
between the ages of 18 and 65 with a BMI between 18.5 and 29 kg/m^2 with the ability to
provide written, informed consent after review of study protocol and procedures.
Exclusion criteria included the use of enemas, laxatives, proton pump inhibitors, or
antibiotics within the past 3 months, history of past or current gastrointestinal conditions,
high fiber consumption, use of tobacco products and regularly skipping breakfast and/or

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lunch. Applicants with recent weight fluctuations of more than 10 pounds, known

allergies to any ingredients in the treatments, or recent participation in another dietary

intervention trial were excluded. Subjects meeting all of the inclusion and exclusion

criteria were enrolled in the study. Informed consent was obtained from each participant

before the commencement of the study.

Treatments

We tested three different ONS beverages that were all formulated to be low in FODMAP

concentration, formulas A, B and C. Each of the low FODMAP formulas contains less

than 0.5g FODMAPs per serving (8 ounces). The positive control beverage was 8 ounces

of lactose-free whole milk with 5 grams of fructooligosaccharides (FOS) and 2.7 grams

of sucrose added to match for calories (Table 9-1). Serving size was determined based on

the typical serving size of ONS beverages. FOS is a prebiotic fiber that is commonly

added to enteral formulas for putative GI benefits.[182,183] The positive control contained a

known FODMAP dose of 5 grams, exceeding the recommended daily limit of FODMAPs

(3 grams).

The low FODMAP supplements contain 3 grams of fiber, sourced from partially

hydrolyzed guar gum and gum acacia. These fibers are slowly fermented and have been

shown to be well tolerated in clinical studies.[184,185] Daily consumption of partially

hydrolyzed guar gum has been shown to improve GI symptoms in IBS patients.[186]

Hydrogen breath tests

Carbohydrate that is not absorbed by the GI tract is fermented by bacteria in the GI tract. The fermentation process results in hydrogen production as a byproduct, which is then absorbed by the intestine, transferred through the blood to the lungs where it is expired. Approximately15-30% of the population contains *Methanobrevibacter smithii*, a microorganism that convert hydrogen to methane, which would then be absorbed and expired.[155] Hydrogen breath tests measure hydrogen and methane expired from the lungs to quantify the amount of fermentation occurring in the gut.[157] A breath hydrogen increase of 20ppm is generally indicative of symptom induction.[161]

Participants were instructed to breathe into breath collection bag, and 20 ml of the end expiratory air was removed and tested. The samples were analyzed using the Quintron GaSampler System (Quintron Instruments, Milwaukee, WI). Samples were analyzed for hydrogen and methane content in duplicate and averaged to improve accuracy.

Gastrointestinal symptom questionnaires

GI tolerance of the four beverages was established through the continual completion of GI symptom questionnaires. Bonnema et al observed reported GI symptoms in healthy participants over a two day period following an oligosaccharide treatment.[187] For this reason, we instructed participants to complete GI symptom questionnaires for 48 hours after treatment consumption. We used a modified version of the GI symptom questionnaire validated by Bocenschen et al.[151] Participants were asked to evaluate the perceived intensity or frequency of their symptoms. Symptoms measured included gas or bloating, nausea, flatulence, diarrhea or loose stools, constipation, gastrointestinal

rumbling and gastrointestinal cramping. Participants could report each symptom as none, mild, moderate, quite a lot, severe, very severe, or unbearable. Symptom scores for each time period were added to create a composite GI symptom score.

Study procedures

Prior to the first visit, enrolled subjects received instructions to follow a low-fiber diet and avoid sugar alcohols and other sources of FODMAPs such as apples, pears, etc for 24 hours before each visit. Participants were also asked to avoid excessive exercise during the 24 hours prior to each test visit. Participants were instructed to begin fasting at 7:00pm the night before the test visit, not eating or drinking anything other than water before arriving to the testing facility.

Treatments were blinded to both investigators and subjects. Treatment order was randomly assigned by the research statistician. Treatments were portioned into opaque cups with lids and straws by a researcher with no other role in the study to conceal any visual differences between treatments from researchers and participants.

Upon arrival to the research facility, subjects completed their first breath test and GI questionnaire at baseline, prior to treatment consumption. Subjects were then given their treatment beverage and were instructed to consume the entire portion within 10 minutes. Additional subjective GI questionnaires were completed at the following time points: 30, 60, 120, 180, and 240 minutes, as well as at 12, 24, and 48 hours after consumption of the test beverage. Breath hydrogen was measured at 60, 120, 180, and 240 minutes after

ingestion of the treatments. Participants were able to return to leave the testing facility and continue with their normal daily routine after the completion of their 240 minute breath hydrogen measurement. Participants were scheduled for three return visits no sooner than one week apart. The same procedures were repeated at each visit.

Statistical analysis

Subjective GI symptoms and breath hydrogen were expressed as a change from baseline and will be compared using a baseline corrected area under the curve (AUC). Breath hydrogen measures were also compared at each individual time point. Repeated measures analysis of variance (ANOVA) was performed to evaluate whether the means were significantly different among the four treatments. If the overall F test was significant, pairwise comparisons were conducted to assess which means differ from which other means. *P*-values for pairwise comparisons were adjusted with Tukey-Kramer adjustment to account for multiple comparisons. All analysis was performed using Statistical Analysis Software (version 9.3, SAS Institute Inc., Cary, NC). A two-sided p-value < 0.05 was considered statistically significant.

Results

Subject demographics

Twenty-two subjects (11 males, 11 females) were recruited and enrolled in the study. One female subject was dropped from the study after the first visit due to the initiation of

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antibiotics. The 21 subjects who completed the study and were included in statistical analysis had an average age of 21.9 ± 3.7 years and average BMI of 23.3 ± 2.4 kg/m^2.

Hydrogen breath tests

There was no difference in baseline breath hydrogen measures between treatments (*P*= 0.86). Baseline breath hydrogen levels for all treatments were elevated, suggesting that the lead in diet insufficiently restricted fermentable carbohydrates prior to the study visits. None of the three low FODMAP ONS produced an increase in breath hydrogen production in the four hours following consumption. However, the positive control did produce an increase in breath hydrogen of 9 ppm baseline to peak (Figure 9-1). The breath hydrogen AUC was statistically different between the positive control and Low FOMDAP B (10.6 vs -15.6 respectively) and the positive control and Low FODMAP C (10.6 vs -17.26) formulas after pairwise comparisons (P= 0.040 and 0.026 respectively). Additionally, the mean breath hydrogen level was statistically different between the positive control and each of the three low FODMAP ONS at three and four hours post consumption (Table 9-2).

Gastrointestinal symptom questionnaires

No symptoms were reported as "severe", "very severe" or "unbearable" by any of the participants following any of the treatments. Overall, each of the treatment beverages was well tolerated by the healthy participants. There were no significant differences in AUC responses of any of the individually measured symptoms or the composite GI symptom

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score between treatments. Differences in AUC measures were analyzed at both the first four hours post consumption as well as 48 hours post consumption (Table 9-3).

Discussion

The lack of a positive breath hydrogen response following the consumption of the low FODMAP ONS demonstrates that these products are not rapidly fermented in the colon. There was a significant difference in breath hydrogen concentration at 3 and 4 hours post-consumption between each of the three low FODMAP formulas and the positive control. This finding was expected as the ONS were formulated with ingredients that are known to be well tolerated and easily digested, while the positive control was made with FOS a rapidly fermentable prebiotic fiber. The positive control did produce a positive breath hydrogen response over the four hour time period; however, the 9 ppm increase (baseline to peak) was not large enough to elicit a symptomatic response in the healthy participants. Bonnema et al. observed similar findings when providing fibers to healthy subjects, as the 5g dose of FOS did not elicit significantly greater GI symptoms compared to control.[187] While a 10g dose of FOS has been shown to produce GI symptoms in healthy individuals, a 5g dose was a more realistic dose for a typical ONS.[187]

This study was conducted in healthy human subjects as opposed to subjects suffering from IBS. While the findings of this study provide insight into the effects of gastrointestinal tolerance of these low FODMAP formulas without confounding effects from GI disorders, it does not explain the effects of the supplements in individuals with IBS. Findings published by Magge et al. suggest that healthy individuals and individuals

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with IBS have similar breath hydrogen responses to low and high FODMAP diets.[143] Breath hydrogen levels remained low after consuming low FODMAP foods, and rose after consuming high FODMAP foods in both groups. The increase in breath hydrogen after consuming high FODMAP products was more exaggerated in individuals with IBS.[143] Furthermore, while healthy individuals had no difference in GI symptoms, the participants with IBS did report more GI symptoms following the high FODMAP diet.[143] Based on these reported findings, we would anticipate that the low FODMAP formulas would be well tolerated in individuals with IBS, although this study should be repeated in an IBS population to confirm.

Unfortunately, the four-hour time period used to measure the breath hydrogen response of the treatments was not enough to see a definite peak for the positive control. As a result, the full effect of the positive control on breath hydrogen is still unknown. However, the distinct difference in response between the low FODMAP and high FODMAP beverages is still evident. Additionally, a water control treatment would have allowed for a comparison between the various treatments to a continued fasting state. However, this would have required a 16 hour fast for participants which may have other unintended effects on gastrointestinal symptoms.

Another limitation of this study was the elevated baseline breath hydrogen levels seen throughout the study. Although subjects were asked to follow a low fiber, low polyol diet the day prior, and to fast for 12 hours prior to each visit, this was not completely effective at achieving a low baseline breath hydrogen level. Future studies should

consider providing a low FODMAP diet to participants on the days prior to study visits to improve upon these baseline measures. There were no significant differences in baseline measures between treatments and the AUC measurement was corrected for baseline measures, so this limitation likely had little impact on the overall findings of this study. This study did not test participants to ensure recruitment of hydrogen producing subjects. This is another limitation of this study and should be corrected in future research.

Because these beverages are low FODMAP, they could be incorporated into the diet of an individual who is following the elimination phase of the low FODMAP diet. This phase can be restrictive, and individuals may struggle to find ready-to-consume low FODMAP snacks to carry with them. ONS are also used for patients unable to meet their nutrient needs with food alone. Patients suffering from IBS, or those experiencing other digestive sensitivities, may benefit from the use of a low FODMAP ONS during times of inadequate calorie intake, or when the diet is very limited.

Conclusion

Overall, the three low FODMAP formulas were well tolerated by healthy human subjects as evidenced by the lack of increased breath hydrogen production and the absence of subject reported GI symptoms. This study provides evidence to support the use of a low FODMAP ONS as an option for individuals following a low FODMAP diet. More research should be conducted in the future using participants with IBS to assess the tolerance of low FODMAP ONS in the population of interest.

Acknowledgments

Table 9-1. Nutrient compositions of the treatment beverages

Formula	Calories	Carbohydrates (g)	Fiber (g)	Protein (g)	Fat (g)
Low FODMAP A	170	19	3	15	4
Low FODMAP B	180	22	3	15	4
Low FODMAP C	170	19	3	15	4
Lactose-free Milk + 5g FOS and 2.7g sucrose	170	16	5	8	8

Table 9-2. Pairwise comparisons of breath hydrogen measures at 3 and 4 hours post

treatment consumption

Treatment	vs. Treatment	Difference of means (3 hours)	*P* value (3 hours)	Difference of means (4 hours)	*P* value (4 hours)
Positive Control	Low FODMAP A	12.2381	0.0009*	16.5714	<.0001*
Positive Control	Low FODMAP B	9.5000	0.0143*	15.3810	<.0001*
Positive Control	Low FOMDAP C	11.2619	0.0026*	14.6429	<.0001*
Low FODMAP A	Low FODMAP B	-2.7381	0.8051	-1.1905	0.9696
Low FODMAP A	Low FOMDAP C	-0.9762	0.9885	-1.9286	0.8860
Low FODMAP B	Low FODMAP C	1.7619	0.9380	-0.7381	0.9924

* Indicates significance at 0.05

Table 9-3. Area under the curve measurements of gastrointestinal symptoms following

consumption of low FODMAP ONS beverages and positive control

	Positive Control	Low FODMAP A	Low FODMAP B	Low FODMAP C		
Symptom	Mean	Mean	Mean	Mean	SE	*P* value
Baseline- 4 hours post consumption						
Gas/bloating	0.25	-0.08	0.61	-0.21	0.37	0.40
Nausea	0.24	-0.06	0.08	-0.23	0.23	0.79
Flatulence	0.24	-0.20	0.13	0.27	0.33	0.77
Diarrhea/loose stools	0.00	-0.18	0.02	0.00	0.09	0.36
Constipation	0.24	-0.18	0.02	0.05	0.09	0.29
GI rumbling	0.21	-0.12	-0.15	0.04	0.45	0.93
GI cramping	-0.08	0.07	-0.07	-0.08	0.14	0.82
Composite GI symptom score	0.61	-0.71	0.61	-0.17	0.82	0.61
Baseline- 48 hours post consumption						
Gas/bloating	-2.42	-5.89	4.03	-5.83	3.73	0.21
Nausea	-6.07	-4.25	-0.77	-4.42	3.94	0.81
Flatulence	-1.02	-4.49	2.99	1.23	4.04	0.59
Diarrhea/loose stools	2.67	-1.13	0.50	0.95	1.79	0.52
Constipation	0.02	-1.42	1.36	0.05	1.32	0.54
GI rumbling	-4.26	-9.64	-11.20	-5.77	5.81	0.82
GI cramping	-2.18	0.07	-1.69	-1.32	2.02	0.88
Composite GI symptom score	-10.92	-26.24	-4.82	-13.40	9.91	0.48

Figure 9-1. Breath hydrogen response following consumption of low FODMAP ONS

beverages and positive control in healthy adults
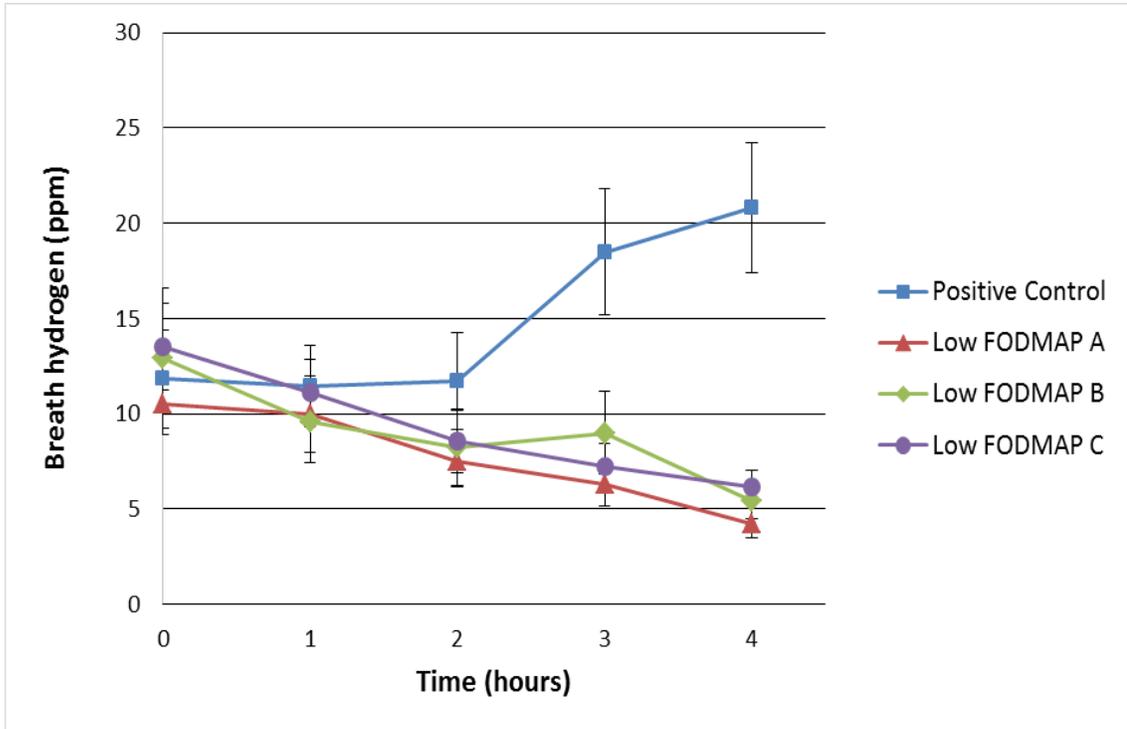
Appendix A. Dietary Restraint Questionnaire: Adopted from the Three Factor Eating Questionnaire

Now I'm going to give you a short questionnaire about your eating patterns. Please respond with the answer that applies to you on most eating occasions.		Score
1. When I have eaten my quota of calories, I am usually good about not eating any more	T (+1) F	
2. I deliberately take small helpings as a means of controlling my weight	T (+1) F	
3. Live is too short to worry about dieting	T F (+1)	
4. I have a pretty good idea of the number of calories in common food	T (+1) F	
5. While on a diet, if I eat food that is not allowed, I consciously eat less for a period of time to make up for it	T (+1) F	
6. I enjoy eating too much to spoil it by counting calories or watching my weight	T F (+1)	
7. I often stop eating when I am not really full as a conscious means of limiting the amount that I eat	T (+1) F	
8. I consciously hold back at meals in order to not gain weight	T (+1) F	
9. I eat anything I want, any time I want	T F (+1)	
10. I count calories as a conscious means of controlling my weight	T (+1) F	
11. I do not eat some foods because they make me fat	T (+1) F	
12. I pay a great deal of attention to changes in my figure	T (+1) F	
13. How often are you dieting in a conscious effort to control your weight? Rarely Sometimes Usually (+1) Always (+1)		
14. Would a weight fluctuation of 5 lbs affect the way you live your life? Not at all Slightly Moderately (+1) Very Much (+1)		
15. Do your feelings of guilt about overeating help you to control your food intake? Never Rarely Often (+1) Always (+1)		
16. How conscious are you of what you are eating? Not at all Slightly Moderately (+1) Very Much (+1)		
17. How frequently do you avoid "stocking up" on tempting food?\ Almost never Seldom Usually (+1) Almost always (+1)		
18. How likely are you to shop for low calorie foods? Unlikely Slightly likely Moderately likely (+1) Very likely (+1)		
19. How likely are you to consciously eat slowly in order to cut down on how much you eat? Unlikely Slightly likely Moderately likely (+1) Very likely (+1)		
20. How likely are you to consciously eat less than you want? Unlikely Slightly likely Moderately likely (+1) Very likely (+1)		
21. On a scale of 0 to 5, where 0 means no restraint in eating and 5 means total restraint what number would you give yourself?		

(0) Eat whatever you want, whenever you want it (1) Usually eat whatever you want, whenever you want it (2) Often eat whatever you want, whenever you want it (3) Often limit food intake but often "give in" (+1) (4) Usually limit food intake, rarely "give in" (+1) (5) Constantly limiting food intake, never "giving in" (+1)	
Total Score	
Exclude if score 11 or higher	

Appendix B. Satiety and Palatability Visual Analogue Scales (100 mm)

How hungry do you feel?

I am not
hungry at all ————————————————————— I have never
been more
hungry

How satisfied do you feel?

I am
completely ————————————————————— I cannot eat
empty another bite

How full do you feel?

Not at all ————————————————————— Totally full
full

How much do you think you can eat?

Nothing at ————————————————————— A lot
all

Please assess the smoothie regarding its:

Visual appeal

Good ————————————————————— Bad

Smell

Good ————————————————————— Bad

Taste

Good ————————————————————— Bad

Aftertaste

Good ————————————————————— Bad

Overall Pleasantness

Good ————————————————————— Bad

Appendix C. Gastrointestinal Tolerance Questionnaire Used in the Pulse Study

Please rate the level of the following symptoms you have experienced on the scale below.

1. Gas or bloating	☐ None	☐ Mild	☐ Moderate	☐ Severe
2. Nausea	☐ None	☐ Mild	☐ Moderate	☐ Severe
3. Flatulence	☐ None	☐ Mild	☐ Moderate	☐ Severe
4. Diarrhea or loose stools	☐ None	☐ Mild	☐ Moderate	☐ Severe
5. Constipation	☐ None	☐ Mild	☐ Moderate	☐ Severe
6. Gastrointestinal cramping	☐ None	☐ Mild	☐ Moderate	☐ Severe
7. Gastrointestinal rumbling	☐ None	☐ Mild	☐ Moderate	☐ Severe

Appendix D. Gastrointestinal Wellbeing questionnaire for Juice and Oral Nutritional Supplement Studies

This questionnaire is designed to assess any gastrointestinal symptoms experienced since consuming the test beverage.

Please make a mark on the circle under each title according to the intensity or frequency of the gastrointestinal symptoms you are experiencing at this time.

	None	Mild	Moderate	Quite a lot	Severe	Very Severe	Unbearable
Gas or bloating	○	○	○	○	○	○	○
Nausea	○	○	○	○	○	○	○
Flatulence	○	○	○	○	○	○	○
Diarrhea or loose stools	○	○	○	○	○	○	○
Constipation	○	○	○	○	○	○	○
Gastrointestinal rumbling	○	○	○	○	○	○	○
Gastrointestinal cramping	○	○	○	○	○	○	○

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