2021

Added Sugar Consumption And Prediabetes In U.S. Adults: A Cross-Sectional Analysis Of The National Health And Nutrition Examination Survey, 2013-2018

Nadia Markie Sneed
University of Alabama at Birmingham

ADDED SUGAR CONSUMPTION AND PREDIABETES IN U.S. ADULTS: A CROSS-SECTIONAL ANALYSIS OF THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2018

by

NADIA MARKIE SNEED

SHANNON MORRISON, COMMITTEE CHAIR
ANDRES AZUERO
AMY GOSS
JACQUELINE MOSS
GREG PAVELA

A DISSERTATION

Submitted to the graduate faculty of The University of Alabama at Birmingham,
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

BIRMINGHAM, ALABAMA

2021

ADDED SUGAR CONSUMPTION AND PREDIABETES IN U.S. ADULTS: A CROSS-SECTIONAL ANALYSIS OF THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2018

NADIA MARKIE SNEED

NURSING

ABSTRACT

Prediabetes is a modifiable risk factor for type 2 diabetes (T2D) that effects 88-million U.S. adults. Added sugar is linked to the risk for prediabetes through direct and indirect mechanisms that promote hepatic and whole-body insulin resistance. Added sugar is overconsumed and totals ~13% of American's daily caloric intake, with consumption highest for non-Hispanic Blacks and Hispanic minority populations also disproportionality affected by prediabetes and T2D. The effects of total added sugar on prediabetes have been mixed; however, total added sugar intake has primarily been examined using added sugar proxies (e.g., sugar-sweetened beverages, fructose), likely increasing systemic measurement error and limiting findings. Thus, it remains unclear if total added sugar consumption increases the risk for prediabetes in U.S. adults and/or if the prediabetes disparities observed in non-Hispanic Blacks and Hispanics are due to greater added sugar consumption, or if total added sugar imparts unique negative metabolic consequences in these groups. Therefore, the purpose of this dissertation was to examine associations between total added sugar consumption and prediabetes using a nationally representative U.S. adult sample (≥20 years) from the 2013-2018 National Health and Nutrition Examination Survey. This purpose was accomplished through the development of three manuscripts: 1) a principle-based concept analysis that evaluated the concept of added sugar in the context of T2D risk (i.e., prediabetes); 2) a cross-

sectional, correlational study that examined the associations between prediabetes awareness and total added sugar consumption; and 3) a cross-sectional, correlational study that examined the associations between total added sugar consumption and risk for prediabetes.

This research will advance nursing and health science through the examination of added sugar's association with prediabetes in U.S. adults. Manuscript one revealed that added sugar is an immature concept warranting further investigation. Manuscript two revealed that prediabetes awareness was not associated with reduced consumption of added sugar. Manuscript three revealed that total and percent intakes of added sugar do not increase the risk of prediabetes, even for different racial/ethnic groups. More research from prospective cohort and experimental studies are needed to confirm these findings.

Keywords: prediabetes, type 2 diabetes risk, added sugar, prediabetes awareness, dietary guidelines, national health and nutrition examination survey

DEDICATION

To

Andrew and Quinn

ACKNOWLEDGMENTS

Andrew- the fact that we were both able to accomplish major academic, career, and family goals within the past four years is a testament of our ability to achieve anything together. At times it felt impossible, but we somehow made it work even when the odds seemed against us. I could not have accomplished this goal without your support and encouragement. Thank you for always being my better half.

Quinn, my little PhD baby- you are my pride and joy. I hope my love of learning cultivates a desire within you to always ponder, ask questions, discover, and explore so you can use your talents to make our world better. Dream big my sweet girl and follow your passions! You will always have my love and support.

Dr. Morrison- for all the times I asked if we were there yet, I think it's safe to say "yes, we made it"! THANK YOU for your constant support, guidance, and dedication.

To my committee- each of you has provided continual support and guidance during this journey. THANK YOU for guiding me through this process!

Colleen, Jessica, and Macy- I would have 100% given up if it had not been for you three. Together, we conquered the good, the bad, and the ugly. From Starbucks, to the Hoover Library, to our Zoom "writing hours" (i.e., social hour) your friendship has kept me going. I can't wait for the next chapter of life- it's gonna be GOOD!

Mom, Dad, and Tasha- My achievements are a reflection of your continual love and support. Thank you for always being there when it has mattered the most.

TABLE OF CONTENTS

Page

LIST OF TABLES

Tables *Page*

PREDIABETES AWARENESS IS NOT ASSOCIATED WITH LOWER CONSUMPTION OF SELF-REPORTED ADDED SUGAR IN U.S. ADULTS: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2016

TOTAL ADDED SUGAR CONSUMPTION IS NOT ASSOCIATED WITH RISK FOR PREDIABETES AMONG U.S. ADULTS: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2018

LIST OF FIGURES

Figure *Page*

INTRODUCTION

INFLUENCES OF ADDED SUGAR CONSUMPTION IN ADULTS WITH TYPE 2 DIABETES RISK: A PRINCIPLE-BASED CONCEPT ANALYSIS

TOTAL ADDED SUGAR CONSUMPTION IS NOT ASSOCIATED WITH RISK FOR PREDIABETES AMONG U.S. ADULTS: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2018

LIST OF ABBREVIATIONS

ADA	American Diabetes Association
AMPM	Automated Multiple-Pass Method
BMI	body mass index
CDC	Centers for Disease Control and Prevention
CI	confidence interval
FPED	Food Patterns Equivalents Database
G	grams
HFCS	high fructose corn syrup
H(g)bA1c	hemoglobin a1c
HHS	Health and Human Services
HOMA-IR	homeostatic model assessment of insulin resistance
IFG	impaired fasting glucose
IGT	impaired glucose tolerance
IRB	Institutional Review Board
KCAL	kilocalories
NCHS	National Center for Health Statistics
NCI	National Cancer Institute
NHANES	National Health and Nutrition Examination Survey
OLS	ordinary least squares

OR	odds ratios
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SAS	Statistical Analysis Software
SD	standard deviations
SSBs	sugar-sweetened beverages
T2D	type 2 diabetes
U.S.	United States
USDA	United States Department of Agriculture
WHO	World Health Organization
WWEIA	What We Eat in America

INTRODUCTION

CHAPTER 1

Added sugar consumption among U.S. adults has significantly increased in recent decades (i.e., 120 pounds/year in 1994 to >150 pounds/year in 2000) paralleling current obesity and diabetes epidemics (Bray & Popkin, 2014; Johnson et al., 2017). In addition, added sugar consumption has transitioned from mainly table sugar (i.e., sucrose) added directly to foods/beverages to products mainly comprised of fructose and high fructose corn syrup (HFCS) primarily in the form of sugar sweetened beverages (SSBs) and ultra-processed foods (Bray & Popkin, 2014; Johnson et al., 2017; Juul et al., 2018). For example, in the 1960's and 1970's, SSBs accounted for one-third of all added sugar intake; however, by 2000, consumption of SSBs nearly doubled in children and adults (Bray & Popkin, 2014; Slining & Popkin, 2013).

Highly processed foods were introduced into the American diet in the early 20th century primarily as ready-to-eat cereals, snacks (e.g., sweet/savory products, confectioneries, ice creams), and SSBs (Monteiro et al., 2013; Slining & Popkin, 2013) but dietary fat consumption remained the greatest percentage of daily macronutrient intake. During the 1950s and 1960s, cardiovascular disease (CVD) rose dramatically and dietary fat, particularly saturated fat, was theorized to be the primary driver of CVD. As such, the American Heart Association (AHA) signaled for a reduction in fat consumption. Fat provides food with flavor. Thus, in response to the AHA recommendation to reduce fat consumption, food manufactures replaced much of the fat in their products with added

sugar and additives to maintain food palatability (Hite et al., 2010; Monteiro et al., 2013). A significant shift in dietary practices from a diet high in fat to a carbohydrate rich pattern of consumption occurred (i.e., 24% less fat and 31% more carbohydrate) between 1965 and 2011 (Cohen et al., 2015; United States. Congress. Senate. Select Committee on Nutrition and Human Needs., 1977). Today, ultra-processed foods and SSBs account for 75% of total added sugars found in the U.S. diet (Juul et al., 2018; U.S. Department of Health and Human Services and U.S. Department of Agriculture [HHS and USDA], 2015). Unfortunately, after four decades, the shift in macronutrient consumption from a diet higher in fat and lower in carbohydrates to a diet lower in fat and greater in carbohydrate did not significantly reduce CVD prevalence. Rather, this shift mirrors the obesity and metabolic disease epidemics observed in the U.S. today (Bray & Popkin, 2014; Cohen et al., 2015).

In response to the AHA's suggestion for changes in macronutrient consumption, the U.S. Departments of Agriculture and Health and Human Services published revised dietary guidelines that recommended reduced fat consumption (i.e., 45% to ≤ 30% percent total daily calories) and increased carbohydrate consumption, inclusive of added sugars (i.e., 39% to 55-60% percent total daily calories) (Cohen et al., 2015; Hite et al., 2010; Kritchevsky, 1998). In 2015, U.S dietary guidelines recommended added sugar consumption not exceed 10% of total daily calories for all populations (i.e., independent of preexisting obesity status or preexisting cardiovascular and/or metabolic disease). Today, despite dietary recommendations to consume <10 % calories from added sugar (i.e., < 200 calories per day based on a 2,000-calorie diet), the average American consumes ~13% of their total daily calories exclusively from added sugars. This accounts

for roughly 270 calories per day with other macronutrient intake remaining constant (HHS and USDA, 2015). Added sugars provide few to no essential nutrients and are associated with weight gain and increased caloric intake beyond recommended daily calorie limits (e.g., 1,800 to 2,000 calorie diet) (Bhargava & Amialchuk, 2007; Bray & Popkin, 2014; Te Morenga et al., 2012). Thus, persons that exceed added sugar consumption recommendations also tend to consume greater total calories and are more likely to be overweight/obese (Te Morenga et al., 2012). For example in adults, minority populations (i.e., non-Hispanic Black and Hispanics) consume the greatest quantities of added sugar as compared to non-Hispanic Whites (i.e., 17.5%, 15.8%, and 14.6% total daily calories, respectively) (Bowman et al., 2017) Likewise, these groups are more overweight and exhibit greater rates of obesity as well as metabolic disease and CVD in comparison to non-Hispanic Whites (Gaillard, 2018; Yang et al., 2014; Zhu et al., 2019). Whether or not the greater rates of chronic disease observed in these populations are a consequence of higher obesity prevalence, greater added sugar consumption, added sugar/obesity interaction, or if race imparts a unique metabolic disparity is unknown.

Approximately 88 million U.S. adults have prediabetes. Among individuals with prediabetes, only 15% are aware of their condition (i.e., 13.5 million) (Centers for Disease Control and Prevention [CDC], 2020). Prediabetes is characterized by a state of insulin resistance and/or glucose intolerance that precedes the onset of T2D (Tabak et al., 2012). However, evidence from landmark clinical trials has demonstrated that progression from prediabetes to T2D may be delayed and in some cases prevented with lifestyle modifications (Knowler et al., 2002). These modifications include caloric restriction with emphasis on reduced total sugar and saturated fat intake, increased

consumption of fruits and vegetables in addition to physical activity of at least 150 minutes per week (Diabetes Prevention Program Research Group, 2002; Knowler et al., 2002; Pan et al., 1997). Evidence suggests that being aware of having T2D, and in some cases prediabetes, may results in dietary changes such as reductions in total calories, total sugar, carbohydrates, and fat (Bardenheier et al., 2014; Kristal et al., 1990; Owei et al., 2019). However, it is unclear if individuals aware of having prediabetes actively engage in dietary-risk reduction behaviors that include reducing their intake of added sugar.

A plethora of epidemiological studies suggest consumption of added sugar, specifically fructose-containing sugars (e.g., sucrose, HFCS), directly and indirectly alter normative energy metabolism (Barrio-Lopez et al., 2013; de Koning et al., 2011; Dhingra et al., 2007; Montonen et al., 2007; Schulze et al., 2004). It is hypothesized that the fructose component of added sugar alters lipid and carbohydrate metabolism as a consequence of unregulated hepatic fructose metabolism. Dysregulated fructose metabolism promotes greater hepatic lipid and circulating low density lipoprotein/ triglyceride concentrations associated with hepatic and whole-body insulin resistance (Maersk et al., 2011; Stanhope et al., 2009; Teff et al., 2009). Thus, dysregulated fructose metabolism has been directly linked to worsened insulin resistance and subsequently risk for prediabetes and occurs independent of overweight/obesity status or caloric intake (Aeberli et al., 2011; Aeberli et al., 2013; Maersk et al., 2011; Stanhope et al., 2015). However, an indirect pathway has been hypothesized through which added sugar intake increases the risk of prediabetes via mechanisms of body weight/fat gain (Khan & Sievenpiper, 2016). As such, the causal role of added sugar on metabolic health continues to be debated (Stanhope, 2016).

While added sugar is considered a primary driver of metabolic conditions such as prediabetes, newer evidence suggests metabolism of added sugar may also differ between liquid and solid sources (Stanhope, 2016; Sundborn et al., 2019). Added sugar consumed in liquid form (e.g., SSBs) results in large quantities of fructose being digested and then transferred to the liver for processing. This influx is thought to overload the liver prompting greater metabolic dysregulation resulting in insulin resistance and increased prediabetes risk (Stanhope, 2016). A similar effect has not been observed with consumption of added sugars from solid sources (i.e., candy), likely due to slower rates of digestion (DiMeglio & Mattes, 2000; Stanhope, 2016; Sundborn et al., 2019). This topic remains largely understudied as the vast majority of research has operationalized total added sugar using proxy measures such as SSBs (Bray & Popkin, 2014; Hu, 2013). As such, whether total added sugar consumption, from all dietary sources, is associated with prediabetes risk remains unknown.

Recent studies have indicated that consuming at or above recommended intake levels of added sugar (≥10% of total daily calories) increases the risk of metabolic conditions, including prediabetes (Stanhope, 2016). Experimental research have suggested that consuming 10% - 25% calories from added sugars promotes dyslipidemia, increased visceral adiposity, decreased insulin sensitivity, and hepatic insulin resistance (Aeberli et al., 2011; Aeberli et al., 2013; Lewis et al., 2013; Perez-Pozo et al., 2010; Stanhope et al., 2015; Stanhope et al., 2009). However, whether total added sugar consumption influences metabolic health in a dose-dependent manner is unclear. Several scientific organizations (e.g., World Health Organization, Institutes of Medicine, AHA, U.S. Dietary Guidelines Advisory Committee) provide recommendations for upper limits

of added sugar consumption ranging from 5% to 25% of total daily calories. The goal of these recommendations is to encourage healthy eating patterns to reduce diet-related chronic conditions such as obesity, CVD, and diabetes in the general public. As such, these recommendations were not intended for the management of metabolic conditions in at risk populations (Institutes of Medicine, 2005; Johnson et al., 2009; HHS and USDA, 2015; World Health Organization [WHO], 2016). Moreover, it is unknown at what percent intake the risks of prediabetes occurs or if the metabolic effects of added sugar differ between normal weight, overweight, and/or obese individuals. In addition, it is unknown whether consumption of added sugar (total and/or differing percent intakes) imparts a unique metabolic disparity in minority populations (i.e., non-Hispanic Black and Hispanic) or if the greater prevalence of metabolic disease in these groups is a consequence of widespread rates of obesity (Zhu et al., 2019). Thus, studies comparing differences in added sugar consumption using current upper limits (i.e., <10%), median intake levels (10-15%), and above average intake levels (>15%) are needed to determine what percent intakes may contribute to prediabetes in U.S. adults, and whether the effects of percent intake differ by obesity status and/or race/ethnicity in the most vulnerable groups (i.e., non-Hispanic Blacks and Hispanics).

In order to address the aforementioned knowledge gaps, additional evidence from observational and experimental studies is needed. As such, the purpose of this chapter was to discuss the 1) background and significance; 2) research problem statement; 3) purpose; 4) specific aims and hypotheses; 5) guiding theoretical framework; 6) design and methods; and 7) terminology of this dissertation study.

Problem Statement

Prediabetes, a state of decreased insulin sensitivity and impaired glucose tolerance, is a precursor to T2D and 85% of individuals with prediabetes are unaware of their condition (American Diabetes Association [ADA], 2020; National Center for Chronic Disease Prevention and Health Promotion, 2020). Yet, evidence suggests lifestyle changes can slow the progression or thwart the onset of T2D (ADA, 2019a, 2019c; Tabak et al., 2012). Moreover, individuals aware of having prediabetes or T2D have been shown to engage in dietary-risk reduction behaviors such as reducing their intake of total calories, carbohydrates, total sugars, and dietary fats compared to unaware individuals (Okosun & Lyn, 2015; Owei et al., 2019). Yet, the parallel rise in metabolic disease prevalence (i.e., prediabetes and T2D) and increased added sugar consumption over the past four decades has suggested that added sugar is a primary driver of impaired energy metabolism (Allister & Stanhope, 2016; Bray & Popkin, 2014). Current dietary recommendations suggest limiting added sugars to <10% total daily calories; however, these recommendations are based on lower quality evidence from mostly observational data (HHS and USDA, 2015). Thus, the following remain unclear: 1) whether being aware of one's prediabetes status influences consumption of added sugar, 2) whether added sugar consumption influences prediabetes risk via total intake from all dietary sources and in a dose-dependent manner based on percent intakes, 3) if overweight/obesity status influences the metabolic consequences of added sugar consumption and mediates the risk of prediabetes, and 4) whether the metabolic effects of total and differing percent intakes of added sugar on prediabetes risk differ by race and ethnicity.

Background and Significance

Health and government institutions were under rising pressure to stem the rising CVD epidemic that began in the 1950s – 1960s. By 1961, data from epidemiological and medical research labelled dietary saturated fats and cholesterol as a major contributor of heart disease leading to drastic recommendations by the AHA to reduce their intake. The U.S. dietary guidelines followed suit in 1977 encouraging Americans to reduce fat consumption from 45% of daily energy intake to ≤ 30% (Cohen et al., 2015). In order to achieve caloric balance, an increase in carbohydrate consumption was encouraged in lieu of fat. Between 1965 to 1977, carbohydrate consumption rose from 39% to 55-60% of total daily calories (Cohen et al., 2015; Kritchevsky, 1998). As such, the call for decreased fat consumption prompted food companies to change how their products were manufactured. Since fat serves as a food additive to enhances flavor and palatability, food companies substituted fat with highly processed added sugars (including HFCS), a trend that continues (Fitch & Keim, 2012; Monteiro et al., 2013). Today, a majority of all foods and beverages (75%) consumed in the U.S. contain added sugar (Bray & Popkin, 2014). Carbohydrates continue to be the main macronutrient source and account for nearly 50% of total daily energy intake for American adults (National Center for Health Statistics, 2017). Moreover, Americans exceed current added sugar recommendations (<10% total calories) consuming roughly 13% of daily total calories as added sugar which is also associated with an increase in overall calories consumed (Bowman et al., 2017; Fitch & Keim, 2012; Johnson et al., 2017; HHS and USDA, 2015).

Differences between added sugars (i.e., fructose, sucrose, HFCS) also exist with fructose and HFCS most strongly linked to metabolic disease (Johnson et al., 2017; Malik & Hu, 2015; Stanhope, 2016). Sucrose (i.e., table sugar) and HFCS are the most common food and beverage sweeteners in the U.S. (Fitch & Keim, 2012). These sugars are biochemically known as *di*saccharides because they contain two sugar molecules that can be further broken down into two single sugars: fructose and glucose (i.e., *mono*saccharides) (Fitch & Keim, 2012). The fructose component of added sugars is thought to have uniquely detrimental metabolic properties contributing to insulin resistance and risk for prediabetes (Allister & Stanhope, 2016).

Prediabetes is diagnosed when glucose levels are abnormally elevated yet do not meet the diagnostic criteria for T2D. According to the ADA, individuals with IGT, IFG, or a glycosylated hemoglobin A1c (HgbA1c) between 5.7%-6.4% meet diagnostic criteria for prediabetes (ADA, 2019a). Presently, prediabetes rates are almost three times higher (88 versus 34.1 million) than that of T2D. In fact, one in every three adults is considered to have prediabetes (CDC, 2020). Additionally, only 15% of adults with prediabetes are aware of their condition (CDC, 2020). Each year 5% to 10% of adults with prediabetes progress to having T2D. Moreover, 70% of all prediabetic individuals will likely develop T2D in their lifetime (Iranfar & Smith, 2018; Tabak et al., 2012). Estimated total cost of diabetes care is roughly 327 billion U.S. dollars accounting for 20% of total healthcare costs in the U.S. (Zhuo et al., 2014).

Risk Factors and Prediabetes Risk

Advancing age, male gender, family history of T2D, and race/ethnicity (i.e., non-Hispanic Blacks, Hispanic/Latino Americans, American Indians, Pacific Islanders, and some Asian American groups) are predictors of prediabetes. However, the most significant prediabetes risk factor is overweight/obesity status. In fact, 89% of U.S. adults with prediabetes/T2D are considered either overweight (BMI of 25.0-29.9 kg/m^2), obese (BMI 30-39.9 kg/m^2), or morbidly obese (BMI $\geq$ 40 kg/m^2) (ADA, 2019a; CDC, 2020). Overweight/obesity is a consequence of prediabetes; however, it is unclear if greater caloric intake (from added sugars) is primarily responsible for body weight gain and subsequent risk for prediabetes (Hu, 2013; Khan & Sievenpiper, 2016).

Among the two largest minority populations represented in the U.S., total prediabetes and T2D prevalence are significantly higher in non-Hispanic Blacks and Hispanics: 53.3% and 50.1%, respectively in comparison to 45.8% of non-Hispanic Whites (CDC, 2020). Similarly, non-Hispanic Blacks and Hispanic Americans consume greater quantities of added sugar compared to non-Hispanic Whites. For example, 66% of non-Hispanic Black and 58% of Hispanic adults consume >10% of their total daily calories from added sugars as compared to 54% of non-Hispanic White adults (Bowman et al., 2017). Moreover, evidence suggests that among certain racial/ethnic groups (i.e., non-Hispanic Blacks) consumption of a high carbohydrate diet promotes an exaggerated insulin response that is independent of overweight/obesity status (Gower et al., 2020). Yet, it is unclear if added sugars are more detrimental to healthy metabolism in minority groups in comparison to non-Hispanic Whites.

Prediabetes Awareness

Approximately 85% of adults with prediabetes are unaware of their condition (CDC, 2020) placing them at increased risk for developing T2D (ADA, 2019b). Evidence from adults with T2D has indicated awareness of a T2D diagnosis is a significant predictor of dietary risk-reduction behaviors including reduced intake of dietary sugars, carbohydrates (Bardenheier et al., 2014), and fat as compared to unaware individuals (Kristal et al., 1990; Owei et al., 2019). However, among individuals with prediabetes, the results have been mixed. Some studies have found that prediabetes awareness does result in engagement in dietary-risk reduction behaviors, specifically a decrease in calories and total fat intake (Okosun & Lyn, 2015; Owei et al., 2019), whereas others have not observed similar engagements in dietary-risk reduction behaviors (Bardenheier et al., 2014; Strodel et al., 2019). Whether or not participants choosing not to modify dietary intake understood the progressive nature of prediabetes is unknown. Nonetheless, it remains unclear if knowledge of one's prediabetes status is associated with self-reported intake of added sugar.

Mechanisms of Added Sugar Consumption on Prediabetes Risk

Plausible mechanisms by which added sugar promotes incidence of prediabetes have been identified (Allister & Stanhope, 2016). Directly, the fructose component of added sugar causes dysregulation of hepatic fructose metabolism, particularly consumption of amounts ≥15% of total caloric intake. After repeated added sugar exposure, hepatic and whole-body insulin resistance develops and results in an increased risk for prediabetes (Stanhope, 2016). Alternatively, weight gain (the result of excessive

calories from added sugars) is thought to trigger a downstream effect that indirectly promotes insulin resistance. While it has been hypothesized that the correlation between added sugar and prediabetes are strongly linked to dysregulated fructose metabolism (Choo et al., 2018), experimental studies assessing these direct effects are limited since most have not controlled for the effects of body weight and/or fat gain (Choo et al., 2018; Stanhope, 2016). Thus, the potential mechanisms and metabolic effects of added sugar are still being debated by scientists warranting further investigation (Stanhope, 2016).

Percent Intake and Prediabetes Risk

Experimental research has indicated that added sugar at commonly consumed U.S. levels (i.e., ~10-25% total calories) increases metabolic risks attributed to prediabetes (Aeberli et al., 2011; Aeberli et al., 2013; Marriott et al., 2019; Perez-Pozo et al., 2010; Stanhope et al., 2015; Stanhope et al., 2009). Studies have found that added sugar consumed at daily percent intake levels of 10% increases low density lipoprotein (LDL) cholesterol and triglyceride concentrations (Stanhope et al., 2009), at 15% reduces hepatic insulin sensitivity (Aeberli et al., 2013), and at 25% promotes hepatic insulin resistance (Perez-Pozo et al., 2010; Stanhope et al., 2009). While experimental studies have administered various added sugar "doses" to compare and contrast their metabolic health effects, it is unknown if these effects develop in a dose-dependent manner (Stanhope, 2016). Global and U.S. organizations including the AHA, the Institutes of Medicine, the U.S. Dietary Guidelines Advisory Committee, and the World Health Organization recommend various upper limit ranges (from 5-25% daily intake) for added sugar consumption in the general population to encourage the reduction in diet-related

chronic diseases such as CVD, obesity, and T2D (Institutes of Medicine, 2005; Johnson et al., 2009; HHS and USDA, 2015; WHO, 2015). However, there are currently no issued guidelines for the prevention or management of prediabetes (ADA, 2019b). Therefore, studies are needed that assess varying percent intakes of added sugar consumption ranging from lower (<10%), median (10-15%), and upper (>15%) levels to establish what percent intakes may increase the risk for prediabetes; specifically among the general U.S. and in high-risk racial/ethnic minority adult population(s) (i.e., non-Hispanic Blacks and Hispanics).

Summary

Added sugar's precise effects on metabolic health continue to be poorly understood. Whether total or percent intakes (e.g., <10%, > 10-15%, >15% of total calories) of added sugar are associated with prediabetes risk across adult populations, including at-risk minorities groups (e.g., non-Hispanic Blacks and Hispanics) remains unknown. As such, the high incidence of prediabetes in the U.S. and lack of awareness for a majority of those living with the condition indicates a dire need for future studies to examine associations between total added sugar intake and prediabetes. The findings from these studies could be used to inform public health interventions aimed at T2D prevention through the implementation of dietary-risk reduction strategies that limit consumption of added sugar.

Purpose

The purpose of this dissertation was to examine associations between added sugar consumption and prediabetes among U.S. adults ≥20 years. This was achieved through the production of three manuscripts that include a concept analysis review paper (manuscript one) and two cross-sectional, correlational studies that used a nationally representative U.S. adult sample ≥20 years with prediabetes (manuscripts two and three).

Overview of the Three Manuscripts

Manuscript 1: Influences of Added Sugar Consumption in Adults with Type 2 Diabetes Risk: A Principle-Based Concept Analysis

The purpose of manuscript one was to critically appraise the scientific literature regarding added sugar's role on T2D risk (i.e., prediabetes). Penrod and Hupcey's principle-based concept analysis method was used to examine the concept added sugar in the context of T2D risk (Penrod & Hupcey, 2005). The method was chosen because it allows for a scientific investigation and advancement of concepts within nursing and health-related disciplines through the use of four guiding principles (epistemological, pragmatic, linguistic, and logical). Using a systematic search, the principle-based concept analysis method allowed for a thorough appraisal of the current literature to generate knowledge about what is known about added sugar in the context of T2D risk (Penrod & Hupcey, 2005). The findings from this analysis provided justification for this dissertation study and informed the development of research questions for the dissertation.

Manuscript 2: Prediabetes Awareness is not Associated with Lower Consumption of Self-Reported Added Sugar in U.S. Adults: National Health and Nutrition Examination Survey, 2013-2016

The purpose of the study in manuscript two was to examine whether knowledge of one's prediabetes status influenced self-reported consumption of added sugar in U.S. adults ≥20 years, including differences in consumption by age, gender, and/or race ethnicity status. A cross-sectional, correlational study that utilizes population-level data from NHANES 2013-2016 was conducted for this dissertation. Few studies have examined the influence of prediabetes awareness on engagement in dietary-risk reductions behaviors and to our knowledge, none have examined these influences in relation to total dietary intake of added sugar. Also, these influences have not been compared by age, gender, and race/ethnicity status which are important population characteristics used to describe prevalence rates of prediabetes (CDC, 2020). Survey-weighted ordinary least squares regression analysis was used to test whether prediabetes awareness was associated with consumption of added sugar by age, gender, and race/ethnicity after controlling for sociodemographic covariates. The specific aims and hypothesis of the study included:

Aim 1

Examine whether prediabetes awareness is associated with lower self-reported consumption of added sugar in U.S. adults ≥20 years with Hemoglobin A1c defined prediabetes (HgbA1c 5.7% - 6.4%).

Hypothesis 1

Prediabetes awareness is associated with reductions in self-reported consumption of added sugar in U.S. adults ≥20 years with Hemoglobin A1c defined prediabetes (HgbA1c 5.7% - 6.4%).

Aim 2

Examine whether age, gender, and/or race and ethnicity influence self-reported added sugar consumption in U.S. adults ≥20 years with Hemoglobin A1c defined prediabetes (HgbA1c 5.7% - 6.4%).

Hypothesis 1

Differences in self-reported added sugar consumption by prediabetes awareness status will be observed for age, gender, and/or race ethnicity status in U.S. adults ≥20 years with Hemoglobin A1c defined prediabetes (HgbA1c 5.7% - 6.4%).

This study provided new knowledge about prediabetes awareness and engagement in dietary-risk reductions behaviors through the examination of added sugar. Additionally, findings from this study provided details about the mean intake of added sugar for a large, nationally representative population of U.S. adults at high-risk for developing T2D. The data generated from this study has the potential to inform public health strategies aimed at T2D prevention.

Manuscript 3: Total Added Sugar Consumption is not Associated with Risk for Prediabetes among U.S. Adults: National Health and Nutrition Examination Survey, 2013-2018

The purpose of the study in manuscript three was to examine if total added sugar consumption was associated with an increased risk for prediabetes and if the probability of having prediabetes differed by the amount consumed (<10%, 10-15%, >15% added sugar calories/day). The associations were also examined by race/ethnicity status. We also examined if BMI (kg/m^2) mediated the association between added sugar and prediabetes. A plethora of evidence has suggested that added sugars directly (via fructose metabolism) and indirectly (through body weight gain) alter normative energy metabolism (Barrio-Lopez et al., 2013; de Koning et al., 2011; Dhingra et al., 2007; Montonen et al., 2007; Schulze et al., 2004) which promotes hepatic and whole-body insulin resistance (Stanhope, 2016). To our knowledge, no studies have examined if total added sugar consumption (from all dietary sources) increases the risk for having prediabetes or whether risk increases in a dose dependent manner. Studies have also failed to examine these associations by race/ethnicity status. To address this gap within the current literature, a cross-sectional, correlational study of U.S. adults ≥ 20 years that utilized population-level data from NHANES 2013-2018 was conducted for this dissertation. Survey-weighted logistic regression analysis was used to estimate unadjusted and adjusted odds ratios of prediabetes based on usual intake of added sugar (g/day) and included model-estimated risks for prediabetes based on usual percent intakes for added sugar (<10%, 10-15%, and >15% total calories per day). Differences in prediabetes risk by total and percent intakes of added sugar were compared by race and

ethnicity status (i.e., non-Hispanic Black, non-Hispanic White, Hispanic, Other Race). A mediation analysis was used to estimate the direct and indirect 'effects' of added sugar on prediabetes, with BMI (kg/m^2) as a mediator. The specific aims and hypotheses of the study included:

Aim 1

Determine if total added sugar consumption, from all dietary sources, is associated with prediabetes in a nationally representative sample of U.S. adults (≥20 years).

Hypothesis 1

Total added sugar consumption, from all dietary sources, will be positively associated with prediabetes in a nationally representative sample of U.S. adults (≥20 years).

Aim 2

Determine if the probability of having prediabetes is associated with added sugar consumption as a percentage of total caloric intake (defined as <10%, 10-15%, >15% total daily calories).

Hypothesis 1

The probability of having prediabetes will be positively associated with added sugar consumption at intake levels of 10-15% and >15% of total daily calories as compared to <10% of total daily calories.

Aim 3

Determine whether the association between added sugar consumption (total and as a percentage of total caloric intake) and the probability of prediabetes differs by race and ethnicity in a nationally representative sample of U.S. adults (≥20 years).

Hypothesis 1

The association between added sugar consumption (total and as a percentage of caloric intake) and the probability of prediabetes will differ by race and ethnicity in a nationally representative sample of U.S. adults (≥20 years).

Aim 4

Determine if the association between total added sugar consumption and prediabetes prevalence is mediated by overweight or obesity status as measured using body mass index in a nationally representative sample of U.S. adults (≥20 years).

Hypothesis 1

The association between total added sugar consumption and prediabetes prevalence will be partially mediated by overweight and/or obesity status as measured using body mass index in a nationally representative sample of U.S. adults (≥20 years).

New knowledge about the role of added sugar on risk for prediabetes in a general U.S. adult population was generated for this study and differences by race and ethnicity status were evaluated. Findings from this study could help determine whether total added sugar consumption increases an individual's risk for developing prediabetes which could lead to the development of individualized dietary guidance for T2D disease prevention in at-risk adults.

Conceptual Model

The Food and Nutrition System (FNS) conceptual model was adapted for the purposes of this dissertation study. The FNS conceptual model, by Sobal et al. (1998), was developed to provide a framework for the complex systems that make up the food and nutrition environment: agriculture, food, nutrition, health and environmental systems. Sobal and colleagues (1998) define the food and nutrition system as "the set of operations and processes involved in transforming raw materials into foods and transforming nutrients into health outcomes" (p. 853). The model was developed using a systems theory approach in an attempt to integrate existing concepts within the complex food and nutrition system. The FNS model includes three main subsystems; producer, consumer, and nutrition (Sobal et al., 1998). For the purposes of this dissertation the consumer and

nutrition subsystems were included in the adapted theoretical framework presented below (Figure 1).

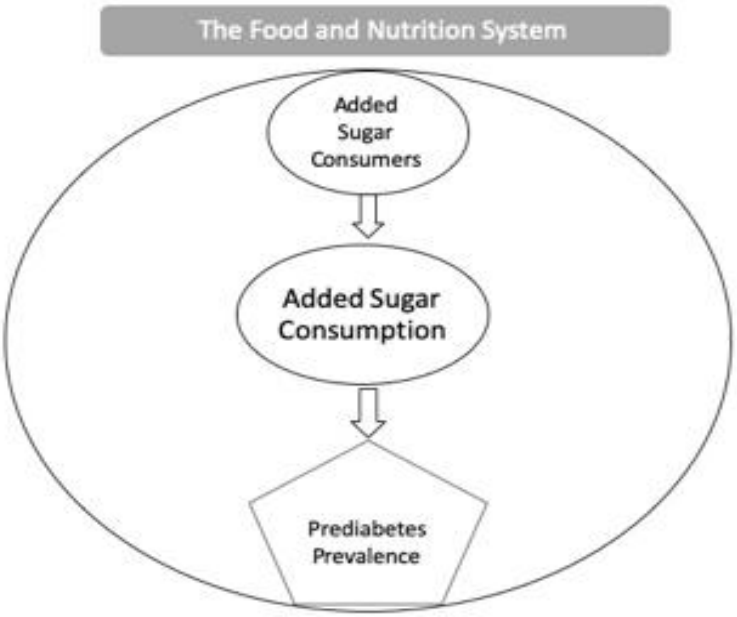


Figure 1. A conceptual model of the food and nutrition system used to guide the generation of research questions for quantitative analyses of this dissertation.

Summary

The overall aim of this dissertation was to examine associations between total added sugar consumption and prediabetes in a nationally representative sample of U.S. adults ≥20 years. This was accomplished through the generation of three manuscripts. Manuscript one used a concept analysis to examine added sugar in the context of T2D risk (i.e., prediabetes). Manuscript two examined how awareness of having prediabetes influenced consumption of total added sugar in U.S. adults. Manuscript three examined if added sugar consumption (total and by percent intakes of <10%, 10-15%, and >15% total energy intake) influenced the risk for prediabetes in U.S. adults. These associations were

also examined by race/ethnicity status and a mediation analysis was used to examine whether the associations between added sugar intake and risk of prediabetes were due, in part, to BMI.

Chapter one has provided a brief overview of the proposed dissertation work by introducing the problem, significance, background, purpose, and an introduction of the three manuscripts proposed for this dissertation. The body of this dissertation will present the three manuscripts of this dissertation individually. Chapter five of this dissertation will include a summary and integration of the findings from the three manuscripts and will include a discussion of the study's advancement of nursing and health research and future research directions.

Key Terms

For the purposes of this proposed dissertation study, key terms were defined as follows:

2015-2020 and 2020-2025 Dietary Guidelines for Americans

The dietary guidelines are a joint publication through the United States (U.S.) Department of Health and Human Services and the Department of Agriculture that serves as a resource for health professional, policy makers, and the general public to improve health and reduce the risk of chronic disease (HHS and USDA, 2015; HHS and USDA, 2020).

Added sugar

Added sugars are defined as sugars added to foods or beverages during processing, preparation, or prior to consumption (HHS and USDA, 2015). The term "added sugar" is also referenced as "nutritive sweeteners", caloric sweeteners", and "sugars" in the literature. Added sugars differ from natural sugars because they are added to foods and beverages to enhance their texture or taste whereas natural sugars are intrinsically present in fruits, vegetables and dairy (Fitch & Keim, 2012). Examples of added sugars include "sucrose, brown sugar, high-fructose corn syrup, corn syrup, agave, dextrose, fructose, raw sugar, honey, invert sugar, maple syrup, concentrated fruit juice, and molasses" (Bailey et al., 2018).

Fructose

Fructose is a single-sugar molecule (monosaccharide) naturally present in foods such as fruit, honey or vegetables. Fructose, when naturally bound with the monosaccharide sugar glucose, makes up the disaccharide sugar "sucrose" (i.e., table sugar). Fructose is used in industrially processed sweeteners like high-fructose corn syrup and is present in an unnatural/unbound form (Allister & Stanhope, 2016; Fitch & Keim, 2012)

Impaired fasting glucose

Impaired fasting glucose is defined by the American Diabetes Association (ADA) as fasting plasma glucose levels between the range of 100 and 125 mg/dL (5.6 and 6.9 mmol/L) (ADA, 2019a).

Impaired glucose tolerance

Impaired glucose tolerance is defined by the ADA as a 2-hour plasma glucose level between 140 and 199 mg/dL (7.8 and 11.0 mmol/L) at the completion of a 75-gram oral glucose tolerance challenge (ADA, 2019a).

Prediabetes

Prediabetes is defined as elevated glucose levels (100 to 125 mg/dL for fasting glucose and 140-199 mg/dL for 2-hour plasma glucose using an oral glucose tolerance test) or hemoglobin A1c (HgbA1c) between 5.7-6.4% (ADA, 2019a). Individuals with a fasting glucose or HgbA1c that exceed these values (i.e., fasting glucose > 126 mg/dL, 2-hour oral glucose tolerance test ≥200 mg/dL, HgbA1c ≥6.5%) meet the criteria for type 2 diabetes (T2D) (ADA, 2019a). T2D risk is a synonymous term used to indicate a prediabetic state (Tabak et al., 2012).

Sugar-sweetened beverages

Sugar-sweetened beverages including sodas, sports drinks, fruit drinks (not consisting of 100% fruit juice), energy drinks, and sweetened water, coffee, or tea beverages that are sweetened with added sugars. They do not include beverages made exclusively with artificial or non-caloric sweeteners (HHS and USDA, 2015).

Type 2 diabetes

Previously termed “non-insulin-dependent diabetes” and “adult-onset diabetes”. T2D is considered a disease where the body does not properly use insulin and may also be characterized by a state of progressive loss of insulin production (ADA, 2019a).

Ultra-processed foods

Industrially manufactured, ready-to-eat or ready-to-heat products which consist of predominately processed foods which bear little resemblance to the whole food from which they were originally derived. They are considered convenience foods containing large quantities of added sugars, salt, and/or saturated fat (Juul et al., 2018).

INFLUENCES OF ADDED SUGAR CONSUMPTION IN ADULTS WITH TYPE 2 DIABETES RISK: A PRINCIPLE-BASED CONCEPT ANALYSIS

by

NADIA MARKIE SNEED, PATRICIA A. PATRICIAN, AND SHANNON A. MORRISON

Nursing Forum, DOI: 10.1111/nuf.12399

MANUSCRIPT 1

INFLUENCES OF ADDED SUGAR CONSUMPTION IN ADULTS WITH TYPE 2 DIABETES RISK: A PRINCIPLE-BASED CONCEPT ANALYSIS

Abstract

Aim: The aim of this study is to describe the concept added sugar in the context of type 2 diabetes (T2D) risk in adults.

Background: Dietary added sugars are associated with a greater risk for T2D; however, it is unclear if added sugars influence T2D risk directly or if their effects are mediated by excess caloric intake and weight gain.

Design: A principle-based concept analysis following the PRISMA guidelines was conducted to clarify the concept of added sugar. A systematic search was conducted using PubMed and Embase. Multi-disciplinary, empirical evidence was appraised using four guiding principles outlined by the principle-based concept analysis method.

Results: Thirty-five publications were included in this concept analysis. The concept, added sugar in the context of T2D risk, was found to be epistemologically immature and lacked conceptual clarity.

Conclusions: Added sugar is an immature concept warranting further refinement for conceptual advancement. To enhance conceptual clarity, the term "added sugar" should be used consistently in the scientific literature when discussing foods or beverages containing added sugars or caloric sweeteners. A clearer delineation of added sugar and

its association with T2D risk in adults is critical to advance this concept within the scientific literature.

Keywords: added sugar, nutrition, prediabetes, principle-based concept analysis, type 2 diabetes risk

Introduction

Experimental and epidemiologic evidence suggests consumption of added sugars (i.e., caloric sugars or sweeteners added to foods and beverages) is associated with chronic disease states like obesity and type 2 diabetes (T2D) and is likely mediated by direct and indirect physiologic mechanisms associated with dysregulated energy metabolism (Allister & Stanhope, 2016; Basu, Yoffe, Hills, & Lustig, 2013). Increased consumption of added sugar contributes to reduced intakes of nutrient-rich foods like fruits and vegetables and higher intakes of nutrient-poor, processed foods like snacks and sweets, grain desserts, and sugar-sweetened beverages (SSBS) (Fitch & Keim; Louie & Tapsell, 2015). Notably, consumption rates of added sugar have paralleled with the rise in T2D, and over the last thirty years T2D rates have continued to climb globally (Basu et al., 2013; Johnson, Sanchez-Lozada, Andrews, & Lanaspa, 2017). According to the World Health Organization (WHO), diabetes rates have nearly doubled in the last 40 years, with 90 percent of diabetes cases attributed to T2D (WHO, 2016, 2018). Additionally, T2D prevalence in the United States (U.S.) is high and approximately 12.2% of Americans are consider to have T2D while an additional 33.9% are at increased risk for developing T2D (i.e., prediabetes) (Basu et al., 2013; Centers for Disease Control and Prevention [CDC], 2017). With the rise in global sugar supplies over the last decade, consumption of added sugar (termed free sugar by the WHO) has been linked with an increased risk for developing non-communicable diseases such as T2D (Basu et al., 2013; WHO, 2015).

Experimental research exploring a causal link between added sugar and T2D risk is inconsistent (Allister & Stanhope, 2016). Likewise, some scientists advocate that added

sugar consumption is not causally linked with T2D but is instead mediated by excessive caloric intake and weight gain (Khan & Sievenpiper, 2016; Lean & Te Morenga, 2016). Lack of a clear conceptual definition of added sugar, as well as inconsistent operationalization of added sugar across the literature, confounds the evidence by limiting generalizability and restricting between-study comparisons. For example, many experimental and observational studies reporting an association between added sugar and T2D risk have used added sugar proxies such as SSBS or food products containing high-fructose corn syrup (HFCS) only in their analyses, thus failing to account for all sources of added sugar consumed (Johnson et al., 2017; J. Ma et al., 2016; Stanhope, 2016; Xu, Park, & Siegel, 2017). Moreover, most experimental studies have been conducted over shorter time periods (e.g., weeks) and methods for quantifying total dietary added sugars in both experimental and observational studies have not been congruent, often including only single added sugar sources (e.g., fructose, glucose, sucrose) (Allister & Stanhope, 2016; Lean & Te Morenga, 2016). Given the significant health burden of T2D, it is imperative that added sugar is clearly defined so scientists may better determine the health consequences of added sugar beyond weight gain and translate the findings into clinical practice. This concept analysis will establish the current "state of the science" surrounding the concept added sugar in adults at risk for T2D (Penrod & Hupcey, 2005).

Background

Both global and U.S. consumption of added sugar across all age groups exceeds current recommendations set forth by the WHO (2015) and the U.S. Departments of Health and Human Services and Agriculture (2015). Both organizations recommend

limiting added sugar consumption to less than 10% of total daily calories (HHS and USDA, 2015; WHO, 2015). Global estimates report that the average person consumes over 280 calories per day from added sugar alone exceeding current recommendations by about 80 calories (Basu et al., 2013; HHS and USDA, 2015; WHO, 2015). Added sugars are typically found in highly refined, processed foods and beverages such as sodas, fruit drinks, sweets, snacks, and grain desserts. Ultra-processed foods and beverages bear little resemblance to the whole foods (i.e., fruits, vegetables, or grains) from which they originated and are generally calorie-dense (i.e., high in calories) (Juul, Martinez-Steele, Parekh, Monteiro, & Chang, 2018; HHS and USDA, 2015). Due to concerns that increased consumption of added sugar contributes to excessive caloric intake and the risk of non-communicable diseases such as T2D, guidelines encouraging reductions in added sugar consumption both globally and in the U.S. are encouraged throughout an individual's life course in order to improve health and prevent disease (HHS and USDA, 2015; WHO, 2015).

Diabetes is a serious public health problem and worldwide, an estimated 380 million adults are living with diabetes. The WHO estimates that diabetes-related costs exceed $827 billion U.S. dollars in annual global spending (WHO, 2016). Additionally, over 1.5 million deaths were attributed to diabetes in 2012, mostly in low- and middle-income countries (WHO, 2016, 2018). Incidence of T2D is most prevalent in North America and affects over 30.3 million Americans (CDC, 2017; International Diabetes Federation [IDF], 2017). T2D is considered the 7th leading cause of death among Americans and contributes to U.S. spending of roughly 245 billion dollars in direct (health care) and indirect (lost wages and productivity) costs (CDC, 2017). Middle and

older aged adults are more likely to have T2D; however, both men and women are similarly affected (CDC, 2017; IDF, 2017). Prediabetes, also referred to as T2D risk, is a progressive state of impaired glucose tolerance and insulin resistance that occurs before the onset of T2D, impacting 352.1 million people worldwide and 84.1 million Americans (American Diabetes Association [ADA], 2018; CDC, 2017; IDF, 2017; Iranfar & Smith, 2018). T2D risk (i.e., prediabetes) is defined by both the WHO and the American Diabetes Association (ADA) as either impaired fasting glucose (fasting plasma glucose between 100-125 mg/dL per the ADA and 110-125 mg/dL per the WHO), impaired glucose tolerance (2-hour plasma glucose from a 75-gram oral glucose tolerance test between 140-199 mg/dL per the ADA and 140-200 mg/dL per the WHO), or an elevated glycosylated hemoglobin A1C level (between 5.7-6.4% per the ADA) (ADA, 2018; WHO, 2016). Many individuals with T2D risk are unaware of their diagnosis due to a common delay observed between onset of dysglycemia and actual prediabetes diagnosis (Tabak, Herder, Rathmann, Brunner, & Kivimaki, 2012 Brunner, & Kivimaki, 2012). Moreover, among individuals with prediabetes, an estimated 5% to 10% will develop T2D annually and roughly 70% are projected to develop T2D in their lifetime (Iranfar & Smith, 2018; Tabak et al., 2012).

The terminology used to define a person's risk for developing T2D is inconsistent within current scientific literature. For example, T2D risk has been defined as prediabetes, intermediate hyperglycemia, and impaired glucose tolerance, (IDF, 2017; Tabak et al., 2012; WHO, 2016). To maintain contextual clarity, the term "T2D risk" will be used throughout the remainder of this paper to describe states of prediabetes or diabetes risk.

Evidence from landmark trials (e.g., Diabetes Prevention Program, the Da Qing China Diabetes Study, and the Finnish Diabetes Prevention Study) suggest that lifestyle and dietary modifications emphasizing caloric restriction, fat reduction, and healthful food choices can reduce the incidence of T2D risk in adults (Knowler et al., 2002; Pan et al., 1997; Tuomilehto et al., 2001). However, recent research indicates that consumption of foods predominately sweetened with added sugars such as sucrose (table sugar) or HFCS likely impose unique metabolic dysregulation contributing to a greater risk for T2D (Johnson et al., 2017; Stanhope, 2016). Added sugars (also termed nutritive or extrinsic sweeteners) consist of caloric sugars and sweeteners "added" to foods and beverages to enhance the quality of foods by altering taste, texture, shape, or consistency. Compared with sugars naturally found in fruits, vegetables, and dairy products, added sugars typically consist of sugar products (e.g., sucrose, cane sugar, honey, HFCS) that are "added" to foods and beverages during processing, preparation, or prior to consumption (Fitch & Keim, 2012). While commonly used sugars like honey and cane sugar (i.e., sucrose) are derived from nature, they are considered "added sugars" because they are used to sweeten food and beverage products (Allister & Stanhope, 2016). Added sugars differ from natural sugars because they are associated with a nutrient-poor diet and increased calorie intake whereas natural sugars are typically derived from healthier, nutrient-rich foods like fruits, vegetables, and dairy products (Kaartinen et al., 2017; Louie & Tapsell, 2015).

Currently, the relationship between added sugar consumption and T2D risk is unclear. Therefore the purpose of this concept analysis is to define added sugar and establish the current state of the science surrounding added sugar consumption in the

context of T2D risk. As such, this analysis permits examination of what is presently known about the concept within the scientific literature, helping establish an approximation of "probable truth" (Penrod & Hupcey, 2005). Penrod and Hupcey's (2005) four philosophical principles (epistemological, pragmatic, linguistic, and logical) will be used for examination of the concept added sugar to critically appraise the current scientific evidence and determine gaps associated with added sugar intake in T2D risk.

Methods

Principle-Based Concept Analysis Method

A principle-based concept analysis was conducted with the purpose of understanding the concept added sugar in the context of T2D risk. Penrod and Hupcey's (2005) principle-based concept analysis was selected because its methods allow for a novel, scientific investigation of concepts. The objective for this paper is to fully comprehend the concept's position within the literature and to advance its understanding in science and nursing. The methods used in this principle-based concept analysis will advance conceptual development and help reveal gaps in the science (Penrod & Hupcey, 2005).

Because this principle-based analysis uses a conceptually driven search method, literature on added sugar consumption in T2D risk was collected and examined based on four guiding principles. These principles include *epistemological*, or a conceptual definition, *pragmatic* which determines applicability, usefulness, and operationalization of the concept within scientific inquiry, *linguistic* used to identify the concepts appropriate use among varying contexts and lastly, *logical* which defines how well a

concept maintains its boundaries amid other concepts (McEwen & Wills, 2014; Penrod & Hupcey, 2005). The concept of added sugar will be described based on its current depiction within the scientific literature and its relationship to T2D risk. Also, conceptual irregularities and knowledge gaps within different scientific disciplines will be identified and explored to highlight requirements for further inquiry. In summary, this paper has the potential to advance the concept of 'added sugar' and in doing so will provide an in-depth analysis of the role of added sugar in T2D risk (Penrod & Hupcey, 2005).

Literature Search Method

A systematic search (Figure 1) was conducted using PubMed and Embase (Moher, Liberati, Tetzlaff, Altman, & The Prisma Group). Electronic searches filtered within the last ten years (2008-2018) were conducted. An initial search including CINHAL, SCOPUS, PubMed, and Embase was conducted; however, CINHAL and SCOPUS did not yield sufficient or relevant material for inclusion in this concept analysis. Therefore, database searches were conducted using PubMed and Embase because they contained a wide variety of interdisciplinary literature relevant to this topic. Both database search terms included the keywords '*added sugar'* OR '*added sugars*' OR '*dietary sugar*' OR '*dietary sugars*' OR '*sucrose*' OR '*sugar consumption*' AND '*prediabetes*' OR '*pre diabetes*' OR '*pre-diabetes*' AND '*diabetes risk*' OR '*type 2 diabetes risk*'. Because Embase uses marginally different key terms based on system suggestions, the following additional terms were searched only in Embase: '*impaired glucose tolerance'* and '*non-insulin dependent diabetes mellitus risk*'. Inclusion criteria incorporated publications from peer-reviewed journals that were written in English and

included human-only, adult subjects. The initial search yielded 287 publications (Figure 1). Next, filters were set to search publications from the years 2008 to 2018 to ensure relevant and up-to-date literature was collected, resulting in 244 articles. After duplicate removal, 222 publications remained for screening. The 222 publication titles and abstracts were reviewed, and publications were excluded if the population included children and adolescents, pregnant women, and animals due to lack of conceptual relevance. Publications with missing full-text and conference abstracts were also discarded. After a thorough screening, forty-eight relevant full-text publications remained for final review. Next, each of the abstracts and full-text publications were examined to determine if added sugar and prediabetes/diabetes risk was discussed. Thirty-one of the remaining forty-eight publications failed to meet the criteria for inclusion, leaving a total of seventeen relevant publications from the original database search.

Due to the *linguistically* immature nature of the concept terms, it was necessary to conduct additional search methods to ensure inclusion of relevant, multi-disciplinary literature. An additional eighteen publications were included that had not previously been cited in the original database search. These publications were sourced by use of secondary search methods (ascendancy approach) and included in the final total due to their conceptual relevance and frequent citation from publications included in the original search. Full-text review of the remaining seventeen publications, plus the additional eighteen secondary search publications resulted in a final count of thirty-five relevant, peer-reviewed publications used in the final concept analysis. Figure 1 highlights the publications retained from the initial search.

Results

Epistemological Principle

Is the Concept Added Sugar Consumption in the Context of Type 2 Diabetes Risk Clearly Defined?

According to Penrod and Hupcey (2005), a concept should be explicit and well-defined within the scientific literature. To truly understand the concept added sugar, it is important for researchers to emphasize in their work what makes dietary sugars "added".

Of the literature reviewed for this analysis, terms describing the concept added sugar were used inconsistently. Researchers tended to focus on specific sugar components such as fructose without specifying whether it had been added or was naturally occurring in the foods or beverages described. Researchers often used multiple terms to describe added sugars. For example, a number of studies only discussed added sugar in the context of SSB consumption (Aeberli et al., 2011; de Koning, Malik, Rimm, Willett, & Hu, 2011; Hu, 2013; Imamura et al., 2016; J. Ma et al., 2016; Ma, He, Yin, Hashem, & MacGregor, 2016; Xu et al., 2017). Among studies exploring added sugar in the context of SSBs, most examined its influence on T2D risk, however, a few studies examined the indirect effects of SSB consumption on T2D risk, particularly effects on glucose metabolism (Aeberli et al., 2011) and insulin resistance (J. Ma et al., 2016).

Other researchers studied added sugar in the form of the sugar disaccharide sucrose (comprised of the two sugar components fructose and glucose), or examined individual added sugar components (i.e., monosaccharides) such as fructose and glucose (Allister & Stanhope, 2016; Basu et al., 2013; Bergman, 2013; Biggelaar et al., 2017; DiNicolantonio, O'Keefe, & Lucan, 2015; Evans, Frese, Romero, Cunningham, & Mills,

2017a, 2017b; Lustig, 2016; Rizkalla, 2010; Sievenpiper, 2017; Tsilas et al., 2017). Of these three forms of sugar evaluated, fructose was most commonly studied, typically as an individual sugar (Biggelaar et al., 2017; Evans et al., 2017a, 2017b; Lustig, 2016; Sievenpiper, 2017; Tsilas et al., 2017) or in combination with foods and beverages specifically containing HFCS (Allister & Stanhope, 2016; Basu et al., 2013; Bergman, 2013; DiNicolantonio et al., 2015; Rizkalla, 2010).

Most studies evaluating individual added sugar components examined the role of either fructose, glucose, or sucrose on T2D risk (Allister & Stanhope, 2016; Basu et al., 2013; Bergman, 2013; DiNicolantonio et al., 2015; Lustig, 2016; Tsilas et al., 2017). However, a few studies explored how added sugar components (i.e., fructose, glucose, and/or sucrose) contribute to changes in insulin resistance or glucose metabolism, indirectly influencing T2D risk (Biggelaar et al., 2017; Evans et al., 2017a, 2017b; Rizkalla, 2010).

Lastly, a number of researchers studied added sugar in the context of dietary added sugar products or high added sugar-containing foods like sweets and desserts. Each study reviewed all sources of added sugars consumed in the diet and did not limit added sugar consumption to individual dietary products (e.g., beverages only). However, certain dietary products like sweets and desserts were often mentioned due to their high added sugar content (Allen et al., 2008; El-Sayed et al., 2017; Hill et al., 2013; Huisman et al., 2018; Koloverou & Panagiotakos, 2016; Vorster, Kruger, Wentzel-Viljoen, Kruger, & Margetts, 2014; Xu et al., 2017). The studies reviewing dietary added sugar sources did so in the context of T2D risk; however, one researcher discussed implications of added sugar on non-communicable disease, including T2D risk (Vorster et al., 2014).

Additionally, El-Sayed et al. (2017) discussed how higher added sugar consumption was more common among individuals with diabetes, though did not specify which form of diabetes (e.g., type 1, type 2, prediabetes).

After review of the literature, it was noted that the role of added sugar in T2D risk remains unclear. Some researchers discuss the lack of direct, experimental evidence to support added sugar's deleterious effects on T2D risk (Allister & Stanhope, 2016; Cefalu, 2014; Khan & Sievenpiper, 2016). Other researchers postulate that added sugar's impact on T2D risk is unlikely a direct influence of added sugar consumption and is more likely the result of calorically dense, unhealthy diets, unhealthy lifestyle choices (e.g., lack of physical activity, cigarette use), and weight gain or excessive body weight; particularly large waist circumference (Bardenheier et al., 2013; Hill et al., 2013; Khan & Sievenpiper, 2016; Lean & Te Morenga, 2016). Similar conclusions were described by studies examining the added sugar proxy, SSB. Specifically, these studies reported that individuals who consume added sugar, mainly from SSBs, increase their total daily caloric intake which can lead to weight gain and thus, increased risk for T2D (Cefalu, 2014; Huisman et al., 2018; Lean & Te Morenga, 2016). Likewise, two studies found no association between consumption of added sugars and adverse health effects contributing to T2D risk (Huisman et al., 2018; Janket, Manson, Sesso, Buring, & Liu, 2003). In a prospective cohort study by Janket et al. (2003), 918 incident cases of T2D developed over a 6-year period from a sample of 39,345 healthy women, ages ≥45 years. However, the authors reported that consumption of added sugar (fructose, glucose, sucrose), measured via semi-structured food-frequency questionnaires (FFQ), was not significantly correlated with the risk of developing T2D (Janket et al., 2003). Additionally, a cross-

sectional study conducted by Huisman et al. (2018) found no association between consumption of a high sugar/fat diet (assessed via FFQs) and T2D in a multi-ethnic population of 4,694 adults ages 18-70 years.

In contrast, multiple studies exploring added sugar, consumed from various dietary sources, did report an association with T2D risk (Allen et al., 2008; Basu et al., 2013; de Koning et al., 2011; El-Sayed et al., 2017). For example, Basu et al. (2013) conducted an econometric analysis of repeated cross-sectional data from 175 countries and found that increases in daily added sugar availability (approximately 150 calories per person) was significantly associated with increased diabetes prevalence (1.1%) after controlling for various factors such as total calories, and overweight and obesity. Two studies examined dietary consumption patterns among ethnically diverse groups (Allen et al., 2008; El-Sayed et al., 2017). Allen et al. (2008) reported that American Indian women, 18-40 years, who participated in a 5-session education lifestyle intervention study had significant reductions in fasting blood glucose levels after 18 months. Additionally, significant reductions in total and added sugars intake (assessed via the Block FFQ) were also noted. El-Sayed et al. (2017) conducted a cross-sectional study in 323 Sudanese adults ≥ 18 years and found that high added sugar intake was associated with diabetes. However, this study did not specify diabetes (e.g., type 1 or type 2) and sugar intake was assessed using a Beverage Intake Questionnaire, therefore excluding added sugars found in non-beverage products (El-Sayed et al., 2017). Lastly, a prospective cohort study by de Koning et al. (2011) found that in a sample of 40,389 healthy men ages 40-75 years, consumption of SSBs (assessed via FFQs) was

significantly correlated with increased risk of T2D. Participants were followed for 20 years and 2,680 incident cases of T2D occurred (de Koning et al., 2011).

As reported in the literature reviewed above, fructose is a commonly studied added sugar component typically found in HFCS (Allister & Stanhope, 2016; Fitch & Keim, 2012; Johnson et al., 2017). HFCS is used to sweeten products like SSBs (e.g., soda, sports drinks, fruit drinks) (Fitch & Keim, 2012). Due to significant, global consumption of SSB products, HFCS's relationship to T2D risk has repeatedly been studied by researchers with some still questioning if HFCS actually increases an individual's risk of developing T2D (Evans et al., 2017b; Johnson et al., 2017; Khan & Sievenpiper, 2016; Sievenpiper, 2017; Tsilas et al., 2017). Results from a systematic review and meta-analysis by Khan and Sievenpiper (2016) did not find evidence to support that fructose contributes to an increase in T2D risk and reported that no controlled trials exist to support the association. Khan and Sievenpiper (2016) postulated that SSB consumption is likely attributed to an unhealthy lifestyle which drives obesity and further increases the risk of T2D. However, evidence from multiple studies looking specifically at the role of SSB consumption on T2D risk did report a positive association between consumption of added sugar and T2D risk (de Koning et al., 2011 2011; El-Sayed et al., 2017; Hu, 2013; Imamura et al., 2016; J. Ma et al., 2016). Additionally, a systematic review and meta-analysis by Imamura et al., (2016) also reported that evidence from observational studies indicate that individuals who regularly consume SSBs have an increased risk of T2D. These mixed findings limit the conceptual clarity of added sugar's role in T2D risk states.

In summary, the concept of added sugar in relation to T2D risk has been defined and operationalized in several different ways, limiting conceptual clarity. The conflicting research findings of added sugar's role in T2D risk are inconclusive. Further investigation is warranted to provide a more concrete understanding of added sugars role in T2D risk.

Pragmatic Principle

Does the Concept Added Sugar Consumption in the Context of Type 2 Diabetes Risk have Usefulness and Applicability?

The pragmatic principle assesses if a concept is applicable and useful within the scope of nursing and interdisciplinary science and how it has been operationalized (Penrod & Hupcey, 2005). Within the literature, added sugar is frequently discussed in an interdisciplinary, health-related context and is not specific to nursing. In fact, no nursing studies were found during the literature search for inclusion in this analysis.

The concept of added sugar and its relationship to the development of T2D risk is of interest and applicable to the field of nursing. Added sugar is reliably operationalized by use of dietary questionnaires like food diaries, food-frequency, beverage intake, and food habit questionnaires, or dietary interviews, daily collection records, or recalls (Aeberli et al., 2011; Allen et al., 2008; Biggelaar et al., 2017; Block et al., 2016; Cano, Hernandez, Leon, & del Valle Laveaga, 2016; de Koning et al., 2011; El-Sayed et al., 2017; Huisman et al., 2018; Janket et al., 2003; Kaartinen et al., 2017; J. Ma et al., 2016; Y. Ma et al., 2016; Raatz, Johnson, & Picklo, 2015; Vorster et al., 2014; Xu et al., 2017) however, the validity of these methods varies by whether dietary intake is self-reported or calculated from controlled feeding trials (Lean & Te Morenga, 2016; Tsilas et al., 2017).

Specifically, dietary self-report is associated with intentional misreporting; typically, under-reporting of dietary intake (Lean & Te Morenga, 2016). Diagnostic methods to determine added sugar's impact on T2D risk were typically measured using blood-serum laboratory tests like glycosylated hemoglobin (HgbA1c), fasting blood glucose, oral glucose tolerance testing, or the homeostatic model assessment for insulin resistance (HOMA-IR) (Cano et al., 2016; Johnson et al., 2017; Koloverou & Panagiotakos, 2016; Lean & Te Morenga, 2016; Lustig, 2016).

In summary, the concept added sugar is applicable and useful in nursing and health-related disciplines and can be appropriately operationalized using a variety of dietary assessment tools and questionnaires. These methods allow researchers, nurses, and other healthcare professionals ways to analyze added sugar quantities and identify typical dietary sources. This can be useful when an assessment of total caloric intake or intake levels of certain foods (e.g., added sugars) is required, specifically when nutrition education may be necessary to improve health outcomes. Additionally, dietary assessments can be combined with physiologic measures (laboratory testing like HgbA1c) to examine associations with T2D risk.

Linguistic Principle

Is the Concept Added Sugar Consumption in the Context of Type 2 Diabetes Risk Consistent and used Appropriately within the Scientific Literature?

The linguistic principle is used to determine if there is consistent and appropriate use of terms to describe a concept (Penrod & Hupcey, 2005). Terms used to describe added sugar often varied in the literature and were not explicitly stated as "added" sugars.

Because added sugar is found in a variety of dietary foods and beverages, terms were often interchanged to describe added sugar or components of added sugar (e.g., glucose and fructose). These examples include words like sugar, sucrose, free sugars, dietary sugars, nutritive sweeteners, sugar-sweetened beverages (SSB), high glycemic carbohydrates, HFCS, fructose, and fructose-containing sugars (Cefalu, 2014; DiNicolantonio et al., 2015; Fitch & Keim, 2012; Johnson et al., 2017; Kaartinen et al., 2017; Khan & Sievenpiper, 2016). Several publications studied SSB consumption which was not always portrayed as an exclusive "added sugar product", but rather as a product containing HFCS (Cefalu, 2014; de Koning et al., 2011 ; El-Sayed et al., 2017; Hu, 2013; Huisman et al., 2018; Khan & Sievenpiper, 2016; Koloverou & Panagiotakos, 2016; Lean & Te Morenga, 2016; Lustig, 2016; J. Ma et al., 2016; Y. Ma et al., 2016; Tsilas et al., 2017; Xu et al., 2017). A few publications described SSBs as caloric sweeteners instead of products containing added sugar (Aeberli et al., 2011; DiNicolantonio et al., 2015).

This analysis found that the primary barrier limiting added sugar's linguistic clarity was due to authors not explicitly mentioning the term "added sugar." Alternate terms depreciate the linguistic value of the concept. The numerous terms used to describe or define added sugars will likely limit advancement of the concept decreasing added sugar's conceptual clarity within the scientific literature.

Logical Principle

Does the Concept Added Sugar Consumption in the Context of Type 2 Diabetes Risk Hold its Boundary when Integrated with Other Related Concepts*?*

Lastly, the logical principle examines how a concept, when incorporated with related concepts, "holds its boundaries" and maintains a clear meaning (Penrod & Hupcey, 2005). This analysis found that several studies used added sugar proxies (e.g., HFCS, SSB, sucrose) as a way to examine added sugar's impact on T2D risk (Aeberli et al., 2011; El-Sayed et al., 2017; Kaartinen et al., 2017; J. Ma et al., 2016; Y. Ma et al., 2016; Raatz et al., 2015; Vorster et al., 2014; Xu et al., 2017). Other studies examining added sugars effect on T2D risk did not distinguish added sugar proxies as actual added sugar-containing products (e.g., sweets, HFCS) and alternatively referred to these products as simply, dietary sugars (Block et al., 2016; Cano et al., 2016; de Koning et al., 2011; Huisman et al., 2018; Janket et al., 2003). Several review articles compared and contrasted sugar sources (e.g., fructose sugars, total sugars, HFCS, sucrose, SSB) in the context of T2D risk, but did not refer to these sugars as "added" sugar sources limiting the conceptual clarity of the concept (Cefalu, 2014; DiNicolantonio et al., 2015; Hu, 2013; Khan & Sievenpiper, 2016; Lean & Te Morenga, 2016; Lustig, 2016; Tsilas et al., 2017).

Researchers studying added sugar linked T2D risk with concepts like energy imbalance from dietary over-consumption and body weight (Khan & Sievenpiper, 2016; Sievenpiper, 2017). Body weight, in connection with T2D risk, was described in several studies which suggested that added sugar consumption might exert a unique influence on

T2D risk even when body weight was controlled (El-Sayed et al., 2017; Hu, 2013; Lean & Te Morenga, 2016; Y. Ma et al., 2016; Rizkalla, 2010).

Another interrelated concept involved consumption of naturally sweetened beverages (e.g., fruit juice) that do not contain added sugars. While fruit juice contains high concentrations of naturally derived fructose (extracted naturally from its fruit form), it is understood that 100% fruit juice sugars are natural and do not contain added sugars (DiNicolantonio et al., 2015; Johnson et al., 2017; Kaartinen et al., 2017). Fruit juice was a topic addressed in the literature, but had potential for misinterpretation when terms such as "fruit drinks" or "juice drinks" were used to describe similarly packaged beverages known to contain added sugar (Allister & Stanhope, 2016; de Koning et al., 2011; DiNicolantonio et al., 2015; Imamura et al., 2016; Johnson et al., 2017; Kaartinen et al., 2017; Khan & Sievenpiper, 2016; Tsilas et al., 2017). An article by Y. Ma et al. (2016) outlined a strategy to reduce free (added) sugars in SSB and clearly reported differences between added sugar beverages and fruit juices, helping clarify conceptual boundaries.

To conclude, the concept of added sugar, when linked to fructose, SSB, and HFCS, holds its boundaries and is well differentiated, though becomes unclear when associated with fruit drinks and fruit juices. Added sugar's relationship in T2D risk was well maintained even when compared with other concepts like energy balance and body weight. Added sugar is not a concept specific to nursing but instead is considered an interdisciplinary concept. However, nurses can benefit from the advancement of this concept by gaining a better understanding of what added sugar is and identifying its impact in adults who are at risk of T2D.

Discussion

This concept analysis allowed for a thorough review of the current state of the science concerning the concept added sugar consumption in the context of T2D risk. Use of Penrod and Hupcey's (2005) principle-based analysis method was advantageous in underlining the various strengths and limitations of this concept. Three important issues were discovered from this analysis. These included a lack of clarity within the literature when defining or measuring added sugar, added sugar's role in T2D risk when consumed via SSBs, and conceptual immaturity of added sugar consumption's relationship in adults with T2D risk.

Lack of Clarity and Linguistic Distinction when Defining Added Sugar

While examining the concept using Penrod and Hupcey's (2005) four principles, added sugar was noted to lack a clear and distinct definition in the scientific literature. Often the term added sugar was not explicitly stated and had numerous descriptors like dietary sugars (DiNicolantonio et al., 2015; Khan & Sievenpiper, 2016; Lean & Te Morenga, 2016), free sugars (El-Sayed et al., 2017; Evans et al., 2017b; Kaartinen et al., 2017; Khan & Sievenpiper, 2016; Lean & Te Morenga, 2016; Y. Ma et al., 2016; Vorster et al., 2014), or nutritive sweeteners (Fitch & Keim, 2012; Raatz et al., 2015). This is due to the variety of added sugar sources found in foods and beverages. Limitations impacting conceptual clarity were due to the methods in which added sugar can be operationalized with biological forms like sucrose, glucose, and fructose. This analysis found that many researchers focused on the sugar component fructose and its link with T2D risk (Biggelaar et al., 2017; DiNicolantonio et al., 2015; Evans et al., 2017a, 2017b;

Raatz et al., 2015; Rizkalla, 2010; Tsilas et al., 2017). While several authors reported fructose as having an adverse effect on T2D risk (Biggelaar et al., 2017; Evans et al., 2017a, 2017b; Raatz et al., 2015), others found no association (Rizkalla, 2010; Tsilas et al., 2017). This analysis raises the issue of how to interpret added sugar's impact on diabetes risk when sugar components are examined in isolation (e.g., fructose) rather than in whole forms from total added sugar products (e.g., table sugar, honey, syrup). This was a persistent literature gap which called into question the exact role of fructose in T2D risk. More research is needed to determine fructose's impact on T2D risk when studied in combination with total dietary added sugars.

Added Sugars Influence in T2D Risk when SSB are the Primary Source of Added Sugar

SSB's role in diabetes risk was frequently discussed due to its high added sugar content (Aeberli et al., 2011; de Koning et al., 2011; El-Sayed et al., 2017; Hill et al., 2013; Hu, 2013; Imamura et al., 2016; J. Ma et al., 2016; Y. Ma et al., 2016; Xu et al., 2017). In the U.S., SSBs are the most consumed source of added sugar, specifically HFCS. Recommendations to limit their consumption and choose alternative, unsweetened beverages or water have been suggested by national organizations to improve health (HHS and USDA, 2015). SSBs have been linked to increased T2D risk, yet because SSB products typically contain HFCS as the primary sweetening agent, much of added sugar's effect on T2D risk is thought to be driven by HFCS (Allister & Stanhope, 2016; Cefalu, 2014; DiNicolantonio et al., 2015; Imamura et al., 2016; Xu et al., 2017). While many researchers contend that SSB intake increases T2D risk (Aeberli et al., 2011; de Koning

et al., 2011; El-Sayed et al., 2017; Hill et al., 2013; Hu, 2013; Imamura et al., 2016; J. Ma et al., 2016; Y. Ma et al., 2016; Xu et al., 2017), some researchers argue that adults who consume SSBs have poor diet and lifestyle habits which influence their T2D risk; not HFCS consumption (Khan & Sievenpiper, 2016; Sievenpiper, 2017; Tsilas et al., 2017). Review of the literature included in this concept analysis found that current evidence lacks unanimous support for SSB consumption as a focal driver in increased T2D risk. More research examining SSBs impact on T2D risk in comparison to other sweetened foods or beverages should be undertaken to strengthen or disprove potential relationships.

Lack of Conceptual Maturity for Added Sugar Consumption and T2D Risk

At present, there is no evidence to support what amount of added sugar intake contributes to an increased risk of type 2 diabetes. While groups like the WHO and the U.S. Departments of Health and Human Services and Agriculture provide specific recommendations to reduce the intake of added sugar, these guidelines are not based on outcomes to prevent diabetes, but instead were developed for the promotion of a healthy diet (DiNicolantonio et al., 2015; HHS and USDA, 2015; WHO, 2015). Also, some research has linked added sugar consumption to a poor-quality diet which was alternatively considered responsible for obesity and thus, risk of T2D development (Bardenheier et al., 2013; Khan & Sievenpiper, 2016). This concept analysis highlights that current research lacks strong, causal links to support the direct relationship between added sugar consumption and T2D risk, though there is evidence to support that added sugar likely contributes to risk for T2D. More research exploring causal links associated with increased risk for T2D is needed.

Limitations

The limitations associated with this review include the use of only two databases (Embase and PubMed), which may have limited the number of relevant publications available for use in this review. However, other databases were previously searched (CINHAL, SCOPUS), but did not yield sufficient or relevant material for inclusion in this concept analysis. Studies were also narrowed to a ten-year period, though the ascendary approach was used and included older publications in the analysis. Publications only written in the English language were selected. This may have limited inclusion of potentially relevant literature. Data analysis and extraction was conducted by the first author which may have resulted in potential bias; however, the first author followed a systematic search strategy to help mitigate this issue.

Conclusion

While this analysis highlights that added sugar lacks conceptual maturity due to limitations in how it is defined linguistically and epistemologically, there is evidence to suggest that added sugar likely increases the risk of T2D, though causal links have not yet been established (Allister & Stanhope, 2016). It is possible this positive association is from a direct relationship (added sugar consumption) or indirect relationship (weight gain triggered by excessive added sugar intake). Because there is considerable evidence to suggest that added sugar consumption from various sources (e.g., SSB and HFCS) may increase the risk of T2D, it is relevant for nurses to be aware of this information. Nurses and other healthcare professionals can use this knowledge to inform patients at risk of

T2D about the potential health hazards associated with consumption of added sugar. As such, the current state of the science portrays that added sugar is likely associated with risk for T2D development in adults. However, more experimental and longitudinal studies are needed to further advance this interdisciplinary concept within the scientific literature.

References

Aeberli, I., Gerber, P. A., Hochuli, M., Kohler, S., Haile, S. R., Gouni-Berthold, I., . . . Berneis, K. (2011). Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: A randomized controlled trial. *American Journal of Clinical Nutrition, 94*(2), 479-485. doi:10.3945/ajcn.111.013540

Allen, P., Thompson, J. L., Herman, C. J., Whyte, A. N., Wolfe, V. K., Qualls, C., & Helitzer, D. L. (2008). Impact of periodic follow-up testing among urban American Indian women with impaired fasting glucose. *Preventing Chronic Disease, 5*(3), A76.

Allister, P. C., & Stanhope, K. L. (2016). Understanding the impact of added sugar consumption on risk for type 2 diabetes. *Journal - California Dental Association, 44*(10), 619-626.

American Diabetes Association. (2018). Classification and diagnosis of diabetes: Standards of medical care in diabetes—2018. *Diabetes Care, 41*(Supplement 1), S13-S27. doi:10.2337/dc18-S002

Bardenheier, B. H., Bullard, K. M., Caspersen, C. J., Cheng, Y. J., Gregg, E. W., & Geiss, L. S. (2013). A novel use of structural equation models to examine factors associated with prediabetes among adults aged 50 years and older: National Health and Nutrition Examination Survey 2001-2006. *Diabetes Care, 36*(9), 2655-2662. doi:10.2337/dc12-2608

Basu, S., Yoffe, P., Hills, N., & Lustig, R. H. (2013). The relationship of sugar to population-level diabetes prevalence: an econometric analysis of repeated cross-sectional data. *PloS One, 8*(2), e57873. doi:10.1371/journal.pone.0057873

Bergman, M. (2013). Inadequacies of current approaches to prediabetes and diabetes prevention. *Endocrine, 44*(3), 623-633. doi:10.1007/s12020-013-0017-9

Biggelaar, L. J., Eussen, S. J., Sep, S. J., Mari, A., Ferrannini, E., Dongen, M. C., . . . Dagnelie, P. C. (2017). Associations of dietary glucose, fructose, and sucrose with beta-cell function, insulin sensitivity, and type 2 diabetes in the Maastricht Study. *Nutrients, 9*(4). doi:10.3390/nu9040380

Block, G., Azar, K. M., Romanelli, R. J., Block, T. J., Palaniappan, L. P., Dolginsky, M., & Block, C. H. (2016). Improving diet, activity and wellness in adults at risk of diabetes: Randomized controlled trial. *Nutrition & Diabetes, 6*(9), e231. doi:10.1038/nutd.2016.42

Cano, J. M. M., Hernandez, J. C., Leon, X. B., & del Valle Laveaga, D. (2016). HOMA-IR anomalies and sugar consumption in young with euglycemia. *Pakistan Journal of Nutrition, 15*(1), 52-57.

Cefalu, W. T. (2014). A "spoonful of sugar" and the realities of diabetes prevention! *Diabetes Care, 37*(4), 906-908. doi:10.2337/dc14-0181

Centers for Disease Control and Prevention. (2017, February 24, 2018). National diabetes statistics report, 2017. Retrieved from https://www.cdc.gov/diabetes/data/statistics/statistics-report.html

de Koning, L., Malik, V. S., Rimm, E. B., Willett, W. C., & Hu, F. B. (2011). Sugar-sweetened and artificially sweetened beverage consumption and risk of type 2

diabetes in men. *American Journal of Clinical Nutrition, 93*(6), 1321-1327. doi:10.3945/ajcn.110.007922

DiNicolantonio, J. J., O'Keefe, J. H., & Lucan, S. C. (2015). Added fructose: A principal driver of type 2 diabetes mellitus and its consequences. *Mayo Clinic Proceedings, 90*(3), 372-381. doi:10.1016/j.mayocp.2014.12.019

El-Sayed, E. F., Awadalla, H., Noor, S. K., Elmadhoun, W. M., Sulaiman, A. A., Almobarak, A. O., & Ahmed, M. H. (2017). Sugar intake in Sudanese individuals was associated with some features of the metabolic syndrome: Population based study. *Diabetes & Metabolic Syndrome*. doi:10.1016/j.dsx.2017.09.001

Evans, R. A., Frese, M., Romero, J., Cunningham, J. H., & Mills, K. E. (2017a). Chronic fructose substitution for glucose or sucrose in food or beverages has little effect on fasting blood glucose, insulin, or triglycerides: A systematic review and meta-analysis. *American Journal of Clinical Nutrition, 106*(2), 519-529. doi:10.3945/ajcn.116145169

Evans, R. A., Frese, M., Romero, J., Cunningham, J. H., & Mills, K. E. (2017b). Fructose replacement of glucose or sucrose in food or beverages lowers postprandial glucose and insulin without raising triglycerides: A systematic review and meta-analysis. *The American Journal of Clinical Nutrition, 106*(2), 506-518. doi:10.3945/ajcn.116.145151

Fitch, C., & Keim, K. S. (2012). Position of the Academy of Nutrition and Dietetics: Use of nutritive and nonnutritive sweeteners. *Journal of the Academy of Nutrition and Dietetics, 112*(5), 739-758. doi:10.1016/j.jand.2012.03.009

Hill, J. O., Galloway, J. M., Goley, A., Marrero, D. G., Minners, R., Montgomery, B., . . . Aroda, V. R. (2013). Scientific statement: socioecological determinants of prediabetes and type 2 diabetes. *Diabetes Care, 36*(8), 2430-2439. doi:10.2337/dc13-1161

Hu, F. B. (2013). Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obesity Reviews, 14*(8), 606-619. doi:10.1111/obr.12040

Huisman, M. J., Soedamah-Muthu, S. S., Vermeulen, E., Muilwijk, M., Snijder, M. B., Nicolaou, M. N., & van Valkengoed, I. G. M. (2018). Does a high sugar high fat dietary pattern explain the unequal burden in prevalence of type 2 diabetes in a multi-ethnic population in the Netherlands? The HELIUS study. *Nutrients, 10*(1). doi:10.3390/nu10010092

Imamura, F., O'Connor, L., Ye, Z., Mursu, J., Hayashino, Y., Bhupathiraju, S. N., & Forouhi, N. G. (2016). Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: Systematic review, meta-analysis, and estimation of population attributable fraction. *British Journal of Sports Medicine, 50*(8), 496-504. doi:10.1136/bjsports-2016-h3576rep

International Diabetes Federation. (2017). IDF diabetes atlas. 8th Edition. Retrieved from http://diabetesatlas.org/resources/2017-atlas.html

Iranfar, N., & Smith, T. C. (2018). When should "pre" carry as much weight in the diabetes comorbidity debate? Insights from a population-based survey. *Preventing Chronic Disease, 15*, E36. doi:10.5888/pcd15.170158

Janket, S.-J., Manson, J. E., Sesso, H., Buring, J. E., & Liu, S. (2003). A Prospective study of sugar intake and risk of type 2 diabetes in women. *Diabetes Care, 26*(4), 1008.

Johnson, R. J., Sanchez-Lozada, L. G., Andrews, P., & Lanaspa, M. A. (2017). Perspective: a historical and scientific perspective of sugar and its relation with obesity and diabetes. *Advances in Nutrition, 8*(3), 412-422. doi:10.3945/an.116.014654

Juul, F., Martinez-Steele, E., Parekh, N., Monteiro, C. A., & Chang, V. W. (2018). Ultra-processed food consumption and excess weight among US adults. *British Journal of Nutrition*, 1-11. doi:10.1017/s0007114518001046

Kaartinen, N. E., Simila, M. E., Kanerva, N., Valsta, L. M., Harald, K., & Mannisto, S. (2017). Naturally occurring and added sugar in relation to macronutrient intake and food consumption: Results from a population-based study in adults. *Journal of Nutrition Science, 6*, e7. doi:10.1017/jns.2017.3

Khan, T. A., & Sievenpiper, J. L. (2016). Controversies about sugars: Results from systematic reviews and meta-analyses on obesity, cardiometabolic disease and diabetes. *European Journal of Nutrition, 55*(Suppl 2), 25-43. doi:10.1007/s00394-016-1345-3

Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., . . . Diabetes Prevention Program Research, G. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine, 346*(6), 393-403. doi:10.1056/NEJMoa012512

Koloverou, E., & Panagiotakos, D. B. (2016). Macronutrient composition and management of non-insulin-dependent diabetes mellitus (NIDDM): A new paradigm for individualized nutritional therapy in diabetes patients. *Review of Diabetic Studies, 13*(1), 6-16. doi:10.1900/RDS.2016.13.6

Lean, M. E., & Te Morenga, L. (2016). Sugar and type 2 diabetes. *British Medical Bulletin, 120*(1), 43-53. doi:10.1093/bmb/ldw037

Louie, J. C., & Tapsell, L. C. (2015). Association between intake of total vs added sugar on diet quality: A systematic review. *Nutrition Reviews, 73*(12), 837-857. doi:10.1093/nutrit/nuv044

Lustig, R. H. (2016). Sickeningly sweet: Does sugar cause type 2 diabetes? Yes. *Canadian Journal of Diabetes, 40*(4), 282-286. doi:https://doi.org/10.1016/j.jcjd.2016.01.004

Ma, J., Jacques, P. F., Meigs, J. B., Fox, C. S., Rogers, G. T., Smith, C. E., . . . McKeown, N. M. (2016). Sugar-sweetened beverage but not diet soda consumption is positively associated with progression of insulin resistance and prediabetes. *Journal of Nutrition, 146*(12), 2544-2550. doi:10.3945/jn.116.234047

Ma, Y., He, F. J., Yin, Y., Hashem, K. M., & MacGregor, G. A. (2016). Gradual reduction of sugar in soft drinks without substitution as a strategy to reduce overweight, obesity, and type 2 diabetes: a modelling study. *Lancet Diabetes Endocrinology, 4*(2), 105-114. doi:10.1016/s2213-8587(15)00477-5

McEwen, M., & Wills, E. M. (2014). *Theoretical basis for nursing* (4th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & The Prisma Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine, 6*(7), e1000097. doi:10.1371/journal.pmed.1000097

Pan, X. R., Li, G. W., Hu, Y. H., Wang, J. X., Yang, W. Y., An, Z. X., . . . Howard, B. V. (1997). Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care, 20*(4), 537-544.

Penrod, J., & Hupcey, J. E. (2005). Enhancing methodological clarity: Principle-based concept analysis. *Journal of Advanced Nursing, 50*(4), 403-409. doi:10.1111/j.1365-2648.2005.03405.x

Raatz, S. K., Johnson, L. K., & Picklo, M. J. (2015). Consumption of honey, sucrose, and high-fructose corn syrup produces similar metabolic effects in glucose-tolerant and -intolerant individuals. *Journal of Nutrition, 145*(10), 2265-2272. doi:10.3945/jn.115.218016

Rizkalla, S. W. (2010). Health implications of fructose consumption: A review of recent data. *Nutrition & Metabolism, 7*, 82. doi:10.1186/1743-7075-7-82

Sievenpiper, J. L. (2017). Fructose: back to the future? *The American Journal of Clinical Nutrition, 106*(2), 439-442. doi:10.3945/ajcn.117.161539

Stanhope, K. L. (2016). Sugar consumption, metabolic disease and obesity: The state of the controversy. *Critical Reviews in Clinical Laboratory Sciences, 53*(1), 52-67. doi:10.3109/10408363.2015.1084990

Tabak, A. G., Herder, C., Rathmann, W., Brunner, E. J., & Kivimaki, M. (2012). Prediabetes: A high-risk state for diabetes development. *Lancet, 379*(9833), 2279-2290. doi:10.1016/s0140-6736(12)60283-9

Tsilas, C. S., de Souza, R. J., Mejia, S. B., Mirrahimi, A., Cozma, A. I., Jayalath, V. H., . . . Sievenpiper, J. L. (2017). Relation of total sugars, fructose and sucrose with incident type 2 diabetes: A systematic review and meta-analysis of prospective cohort studies. *CMAJ: Canadian Medical Association Journal, 189*(20), E711-E720. doi:10.1503/cmaj.160706

Tuomilehto, J., Lindstrom, J., Eriksson, J. G., Valle, T. T., Hamalainen, H., Ilanne-Parikka, P., . . . Finnish Diabetes Prevention Study, G. (2001). Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine, 344*(18), 1343-1350. doi:10.1056/NEJM200105033441801

U.S. Department of Health and Human Services and U.S. Department of Agriculture. (2015). *2015 – 2020 Dietary Guidelines for Americans*. Retrieved from https://health.gov/dietaryguidelines/2015/guidelines/.

Vorster, H. H., Kruger, A., Wentzel-Viljoen, E., Kruger, H. S., & Margetts, B. M. (2014). Added sugar intake in South Africa: Findings from the Adult Prospective Urban and Rural Epidemiology cohort study. *The American Journal of Clinical Nutrition, 99*(6), 1479-1486. doi:10.3945/ajcn.113.069005

World Health Organization. (2015). *Guideline: Sugar intake for adults and children*. Retrieved from

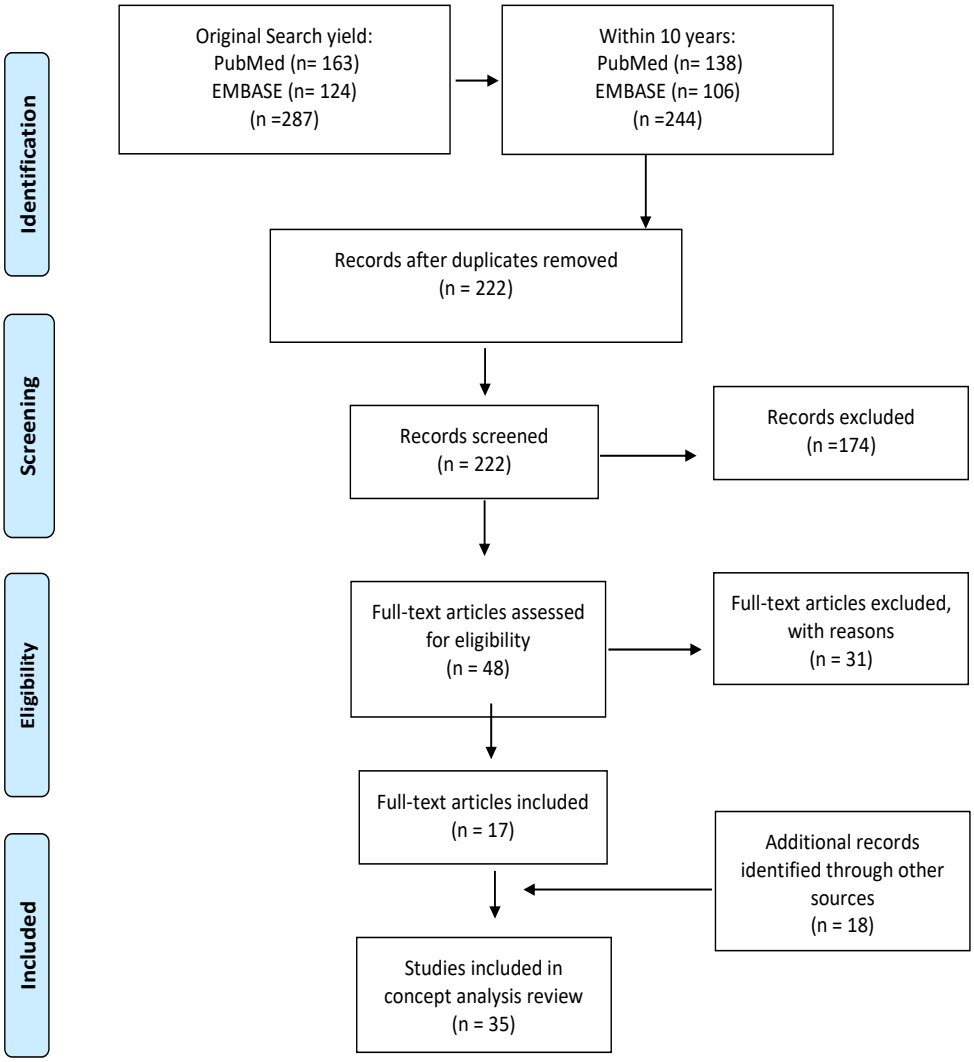
http://apps.who.int/iris/bitstream/handle/10665/149782/9789241549028_eng.pdf;jsessionid=8DB31E3E739C06316556991E93EFC326?sequence=1

World Health Organization. (2016). *Global report on diabetes*: World Health Organization.

World Health Organization. (2018). Diabetes mellitus. Retrieved from http://www.who.int/mediacentre/factsheets/fs138/en/

Xu, F., Park, S., & Siegel, K. R. (2017). Factors associated with frequency of sugar-sweetened beverage consumption among us adults with diabetes or prediabetes. *American Journal of Health Promotion*, 1-9. doi:10.1177/0890117117746187

Figure 1. Literature Flow Diagram



Adapted From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PREDIABETES AWARENESS IS NOT ASSOCIATED WITH LOWER CONSUMPTION OF SELF-REPORTED ADDED SUGAR IN U.S. ADULTS: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2016

by

NADIA MARKIE SNEED AND SHANNON A. MORRISON

Submitted to *Nutrition, Metabolism and Cardiovascular Disease*

Format adapted for dissertation

MANUSCRIPT 2

PREDIABETES AWARENESS IS NOT ASSOCIATED WITH LOWER CONSUMPTION OF SELF-REPORTED ADDED SUGAR IN U.S. ADULTS: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2016

Abstract

Aim: To examine whether prediabetes awareness is associated with lower consumption of added sugar, and whether consumption among those aware of their prediabetes status differs by age, sex, and race/ethnicity.

Methods: Cross-sectional data from 2,432 adults with prediabetes (HgbA1c) were analyzed from 2013-2016 National Health and Nutrition Examination Survey data. Survey-weighted ordinary least squares regression was used to test whether prediabetes awareness was associated with mean consumption of added sugar (g/day) by age, sex, and race/ethnicity after controlling for sociodemographic covariates.

Results: Prediabetes awareness was not associated with lower consumption of added sugar (b=-3.85, p=.49), though differences in consumption were observed by age, sex, and race/ethnicity. Younger age was associated with greater consumption (b=-17.63, p<.01), males consumed more than females (b=20.73, p<.01), and non-Hispanic Whites (b=20.6, p <.01) and Blacks (b=18.8, p <.01) consumed more than the lowest consumer group Other.

Conclusions: Study findings suggest individuals aware of their prediabetes status do not lower their consumption of added sugar and being younger, male, and non-Hispanic

White and Black was attributed to greater consumption. Specific limits for added sugar in adults with prediabetes are needed to promote dietary risk-reduction behaviors for type 2 diabetes mellitus prevention.

Keywords: prediabetes, prediabetes awareness, added sugar, NHANES, dietary risk-reduction

Introduction

Prediabetes is characterized by glucose intolerance and insulin resistance (American Diabetes Association [ADA], 2020; Stanhope, 2016) and is a precursor to type 2 diabetes mellitus (T2D) (Tabak et al., 2012). Approximately 88 million United States (U.S.) adults have prediabetes, yet only 15% are aware of their condition (Centers for Disease Control and Prevention [CDC], 2020b). Moreover, non-Hispanic Black and Hispanic groups are disproportionally impacted by prediabetes and are at increased risk for developing T2D (CDC, 2020b) in comparison to non-Hispanic Whites, contributing to chronic disease disparities (Kulick et al., 2016) and all-cause mortality (Huang et al., 2016). Prediabetes was previously a condition observed during mid- to late- adulthood affecting an estimated 42% of middle (i.e., 45-64 years) and 47% of older-aged (i.e., ≥ 65 years) adults (CDC, 2020b). However, prediabetes rates have increased in all age groups over the past decade, including young adults (i.e.,19-34 years), who now make up nearly 25% of the total U.S. cases. Even more concerning is that only about 15% of individuals with prediabetes are aware of their condition (CDC, 2020b) and among individuals 19-44 years, only 9% are aware of their prediabetes status (Andes et al., 2019; CDC, 2020b). Such estimates are alarming, particularly since 5-10% of individuals with prediabetes are projected to develop T2D annually and 70% projected to develop T2D within their lifetime (Tabak et al., 2012).

Individuals with T2D are at higher risk of death and have greater cardiovascular disease (Huang et al., 2016) and poorer overall health outcomes compared to the general population (CDC, 2020b). Thus, interventions to prevent T2D are critical. Landmark clinical trials have shown that progression from prediabetes to T2D can be delayed or

prevented with lifestyle modifications including dietary changes emphasizing reduced calorie (Knowler et al., 2002; Pan et al., 1997; Tuomilehto et al., 2001), total sugar (Pan et al., 1997), and saturated fat intake (Knowler et al., 2002; Tuomilehto et al., 2001) as well as greater fruit and vegetable consumption (Pan et al., 1997; Tuomilehto et al., 2001). Evidence suggests adults who are aware of their T2D diagnosis typically engage in dietary changes such as reduced dietary sugar, carbohydrate (Bardenheier et al., 2014), and fat intake (Kristal et al., 1990; Owei et al., 2019). However, it is less clear if individuals aware of their prediabetes status understand the importance of engaging in dietary risk-reduction behaviors to prevent a future diagnosis of T2D. Two studies have reported that prediabetes aware individuals engage in dietary risk-reduction behaviors (i.e., decreased calorie and/or fat intake) (Okosun & Lyn, 2015; Owei et al., 2019) either after receiving lifestyle recommendations from a health care provider (Okosun & Lyn, 2015) or being told of their condition (Owei et al., 2019). Conversely, two studies have found prediabetes awareness is not associated with dietary risk-reduction behaviors in individuals made aware of their condition by a health care provider. Neither study addressed the influence of health care provider counseling on engagement in dietary risk-reduction behaviors (Bardenheier et al., 2014; Strodel et al., 2019).

Dietary modifications are a cornerstone of T2D prevention and the American Diabetes Association (ADA) recommends individuals with diabetes (including prediabetes) receive dietetic counseling to achieve optimal body weight, glycemic, blood pressure, and lipid goals to prevent or delay diabetes-related complications (e.g., microvascular complications) (ADA, 2020). Counseling should emphasize an individualized eating pattern consisting of nutrient-dense, high fiber, complex

carbohydrates from vegetables, fruit, dairy, and whole grain sources with limited intake of refined carbohydrates like added sugars (i.e., fructose-containing caloric sweeteners added to foods and beverages during processing, preparation, or before consumption) (ADA, 2019; Fitch & Keim, 2012). Yet, studies of dietary interventions among individuals aware of their prediabetes status have focused on reduced calorie and fat intake (Geiss et al., 2010; Okosun & Lyn, 2015; Owei et al., 2019) likely due to seminal diabetes prevention studies showing these changes can prevent T2D (Knowler et al., 2002; Tuomilehto et al., 2001).

Emerging research suggests consumption of added sugars is linked to conditions such as obesity, cardiovascular disease, T2D, and prediabetes (de Koning et al., 2011; Montonen et al., 2007; Rodriguez et al., 2016; Yang et al., 2014). Moreover, the fructose-component of added sugar is thought to directly impair lipid metabolism and glucose tolerance resulting in hypertriglyceridemia and insulin resistance (Stanhope et al., 2009). Added sugar is highly prevalent in the U.S. diet and found in 75% of all food and beverage products (Bray & Popkin, 2014; Fitch & Keim, 2012). Americans consume an average of 270 calories per day from added sugars (S. A. Bowman et al., 2017); well above the recommend 2015 – 2020 U.S. Dietary Guidelines intake level of less than 200 calories per day based on a 2,000 calorie diet (U.S. Department of Health and Human Services and U.S. Department of Agriculture [HHS and USDA], 2015). Limited evidence related to the influence of prediabetes awareness on dietary behaviors exists and to our knowledge, no study has examined whether knowledge of one's prediabetes status influences self-reported consumption of added sugar or whether age, sex, and/or race and ethnicity uniquely influences self-reported added sugar consumption in adults with

prediabetes. To address this gap, the hypothesis "prediabetes awareness is associated with lower consumption of added sugar" was tested. Quantities of added sugar were compared by prediabetes awareness status (i.e., yes/no) for U.S. adults ages ≥20 using nationally representative, cross-sectional data from the 2013-2016 National Health and Nutrition Examination Surveys (NHANES). Additionally, given that prediabetes disproportionately affects non-Hispanic black and Hispanic adults, middle to older-aged adults, and males (CDC, 2020b), analyses were conducted to assess whether self-reported added sugar consumption differs by race/ethnicity, age, and sex.

Subjects, Materials and Methods

Survey Design, Population, and Protocols

A cross-sectional, descriptive study was conducted using NHANES data collected between 2013-2014 and 2015-2016. NHANES is a continuous, annual survey conducted by the National Center for Health Statistics and the Centers for Disease Control and Prevention (Johnson et al., 2014). The survey collects health and nutrition information using a complex, multistage, probability sampling design to recruit a representative sample of approximately 5,000 noninstitutionalized U.S. civilians (age 0 years and older) annually (Johnson et al., 2014; Zipf et al., 2013). Data from NHANES is released in two-year cycles and for the purposes of this study, data collected between 2013-2016 were included in the analysis. NHANES response rates for 2013-2014 and 2015-2016 were 68.5% and 58.7% respectively (CDC, 2020c). Recruited participants undergo an in-home interview and eligible participants are invited to the mobile examination unit for additional interviews, a physical examination, and laboratory as well as body

assessments/tests. Some laboratory and body assessments/tests are conducted on a randomly selected subsample of participants (Zipf et al., 2013). Interviews and examinations are conducted by highly trained staff with prior training in research and data collection techniques (Zipf et al., 2013). During interviews, demographic, health, and nutrition information is collected while medical, dental, and physical measurement information is collected during physical and laboratory examinations (Johnson et al., 2014).

The analysis was limited to non-pregnant adults ≥20 years of age (n =10,927). Those identified as having T2D based on HgbA1c ≥ 6.5% (n = 1,292) or having normal HgbA1c levels <5.7% (n = 6,224) were excluded from the analysis. A sample of 2,956 individuals with HgbA1c defined prediabetes were included in the final analysis.

The NHANES study protocol is approved by the National Center for Health Statistics Research Ethnics Review Board (National Center for Health Statistics, 2017) and is compliant with the Health and Human Services Policy for Protection of Human Research Subjects (45 CFR part 46) (Office for Human Research Protections, 2018; Zipf et al., 2013). The Office of the Institutional Review Board at the University of Alabama at Birmingham considers NHANES an existing dataset not constituted as human subjects research and approval was not required to conduct this secondary analysis (University of Alabama at Birmingham: Institutional Review Board (IRB), n.d.).

Definition and Assessment of Prediabetes

For the purposes of this study, prediabetes was defined as a HgbA1c level between 5.7% to 6.4% (inclusive) based on the American Diabetes Association (ADA)

"Standards of Medical Care in Diabetes" classification (ADA, 2020). To determine whether an individual was aware of their prediabetes status, participants were asked if they had "ever been told by a doctor or other health professional" of their prediabetes status. Participants were considered "aware" of their prediabetes status if they answered yes to being told they had the following condition(s): "prediabetes, impaired fasting glucose, impaired glucose tolerance, borderline diabetes, and/or a blood sugar higher than normal but not high enough to be considered diabetes or sugar diabetes". Individuals who responded "no" to the above question but whose lab values indicated otherwise were classified as unaware of their prediabetes status. Among those in the final sample with HgbA1c defined prediabetes, 342 were defined as aware while 2,090 were defined as unaware of their prediabetes status.

Definition and Assessment of Added Sugar

As part of the NHANES dietary collection process, 24-hour dietary recalls are collected from participants using the United States Department of Agriculture's Automated Multiple-Pass Method (AMPM) (Zipf et al., 2013). The AMPM is a computer-assisted, five-step, multiple-pass method conducted by a trained interviewer that includes standardized probes and follow-up questions to estimate dietary intake within a 24-hour period (Raper et al., 2004). Interviewers also use food models to assist with portion size estimates (Ahluwalia et al., 2016). Validity and reliability assessments of the AMPM support the accuracy of its recall intake information (Moshfegh et al., 2008). Participants are invited to complete a pre-announced, in-person 24-hour dietary recall during the mobile examination center visit on either weekdays or weekend days

(Zipf et al., 2013). For the purposes of this analysis, added sugar was the main outcome of interest and was obtained from the Food Patterns Equivalents Database (FPED) which converts foods and beverages collected from NHANES dietary recalls into food pattern components used to estimate total added sugar consumption (S. Bowman et al., 2017). The FPED defines added sugar as "sugars that are added to foods as an ingredient during preparation, processing, or at the table […] and do not include naturally occurring sugars such as lactose present in milk and fructose present in whole or cut fruit and 100% fruit juice" which are reported in teaspoon equivalents consumed per person per day (S. Bowman et al., 2017). Added sugar on nutrition facts labels is reported in grams, therefore added sugar was converted from teaspoon equivalents to grams (4.2 grams per 1 teaspoon equivalent) (United States Food and Drug Administration, 2020). Prior to conducting the final analyses, 2013-2016 FPED and NHANES diet recall datasets were merged to include total energy intake (kcals/day) and added sugar (grams/day). The "mean method" was used to estimate the mean intake of added sugar for the sample collected from a single dietary recall day (day 1) (Tooze, 2020). The final sample included 2,215 individuals with self-reported prediabetes awareness status (yes/no) and self-reported dietary recall information.

Predictors

Regression analyses include the following predictors of added sugar consumption: age, sex, race or ethnicity, education level, annual household income, marital status, and body mass index (BMI). In regression analyses and analyses comparing differences in added sugar consumption and prediabetes awareness by age group, a categorical variable

was created (20-44 years, 45-64 years, ≥ 65 years). Sex was defined as either male or female. Race and ethnicity were defined as either non-Hispanic White, non-Hispanic Black, Hispanic (including Mexican Americans), or "Other Race" which included Asian Americans and other persons not included in the above categories. BMI was calculated for each participant using height and weight measures (kg/m^2) collected during the medical examination and categorized using the CDC classification for underweight (<18.5 kg/m^2), normal weight (18.5 – 24.9 kg/m^2), overweight (25 – 29.9 kg/m^2), obese (30 – 39.9 kg/m^2), and severely obese (≥ 40 $kg/m^{2)}$ (CDC, 2020a). In regression analyses, BMI was analyzed as a continuous variable and for all other analyses reported as a categorical variable as previously described.

Statistical Analysis

All analyses were performed using SAS Studio version 3.8, Enterprise Edition (SAS Institute Inc., Cary, NC, USA). Survey data from 2013-2014 and 2015-2016 were combined, and appropriate sampling weights were used in all analyses. Added sugar consumption was modeled as a continuous variable collected from day one of participant 24-hour dietary recalls. A dichotomous indicator of prediabetes awareness was constructed based on respondents' reports of having been told by a health care provider that they have prediabetes. Survey weighted ordinary least squares (OLS) regression was used to test whether awareness of prediabetes was associated with added sugar intake after controlling for covariates (Table 3). Survey weighted Rao-Scott chi-square tests were used to test for significant differences in the sociodemographic characteristics of respondents who were aware and unaware of their prediabetes status and were stratified

by sex for age category, race/ethnicity, BMI, educational level, annual household income category, and marital status (Table 1). Lastly, survey weighted OLS regression was used to examine demographic differences in awareness of prediabetes by sex for hemoglobin A1c (Table 1) and for mean total energy and total added sugar intake for the population sample, and added sugar intake by age and race/ethnicity (Table 2). *P* values < .05 were considered statistically significant.

Results

Sample Characteristics

In a nationally representative sample of non-pregnant adults (≥ 20 years), 2,432 individuals were identified as aware of their prediabetes status. Table 1 reports weighted descriptive statistics of individuals by prediabetes awareness status. The majority of individuals were unaware of their prediabetes status (86% among males and 83.7% among females) with males reporting lower rates of awareness compared to females (14% vs 16.3%). Among males who reported being aware of their prediabetes status, a majority were middle aged (50.8% aged 45-64), non-Hispanic White (67.4%), married (66.7%), had a college degree and some graduate education (39.2%), had an annual household income between $20,000 to $99,999 (53.1%), were obese (42.4%), and had a mean hemoglobin A1c of 5.98%. Among males who reported being unaware of their prediabetes status, a majority were middle aged (44.7% aged 45-64), non-Hispanic White (55.6%), married (65.1%), had a high school diploma or GED (26.5%), had an annual household income between $20,000 to $99,999 (62.5%), were overweight (38.9%), and had a mean hemoglobin A1c of 5.87%. Among females who reported being aware of

their prediabetes status, a majority were middle aged (41.8% aged 45-64), non-Hispanic White (63.6%), married (52%), had some college education (37.1%), had an annual household income between $20,000 to $99,999 (64.2%), were obese (44.3%), and had a mean hemoglobin A1c of 5.91%. Among females who reported being unaware of their prediabetes status, a majority were middle aged (42.7% aged 45-64), non-Hispanic White (59.7%), married (50.7%), had some college education (30.2%), had an average annual household income between $20,000 to $99,999 (54.8%), were obese (37.7%), and had a mean hemoglobin A1c of 5.87%. Statistically significant differences in the distribution of individuals across age (p = .005), race/ethnicity (p = .003), and education categories (p = .007) by prediabetes awareness status were found among males but not females. Only statistically significant differences for both sexes were observed by hemoglobin A1c values [males (p = <.001) and females (p = .04)] (Table 1).

Added Sugar Intake by Prediabetes Awareness Status for Sex, Age and Race/Ethnicity

Table 2 reports weighted mean intakes for total energy, added sugar, and added sugar by race/ethnicity and age category. Among aware males, the mean intake of added sugar was 80 g/day and among aware females was 56.4 g/day. Alternatively, consumption was higher in unaware males who consumed 84.2 g/day and unaware females who consumed 62.9 g/day. Overall, females consumed less added sugar than males for all categories (total sample, age category, race/ethnicity) and consumed less total energy in calories. Additionally, more females were aware of their prediabetes status

(19%) as compared to males (15%). No statistically significant differences in added sugar consumption were found by prediabetes awareness status for males or females (Table 2).

When comparing the mean intake of added sugar by prediabetes awareness status and age, consumption was highest in the 20-44 years age category (aware: 91.5 g/day male and 73 g/day female; unaware: 96.8 g/day male and 70.8 g/day female) and lowest in the ≥ 65 years age category (aware: 61.1 g/day male and 47.1 g/day female; unaware: 65.7g/day male and 49.6 g/day female). Overall, as age increased, consumption of added sugar by awareness status and sex decreased. Prediabetes awareness status was associated with less added sugar consumption for each age category; however aware individuals 45-64 years who were male consumed more added sugar than unaware males (90.2 g/day vs 87.2 g/day) and aware individuals 20-44 years who were female consumed more added sugar than unaware females (73 g/day vs. 70.8 g/day). No significant differences in added sugar consumption were found by prediabetes awareness status and sex regardless of age (Table 2).

When comparing the mean intake of added sugar by prediabetes awareness status and race/ethnicity, consumption was highest in non-Hispanic Blacks (aware: 91.5 g/day male and 67.3 g/day female; unaware: 89.7 g/day male and 74.6 g/day female) and lowest in the Other Race category (aware: 56.2 g/day male and 50 g/day female; unaware: 53.3 g/day male and 53.6 g/day female). Being aware of one's prediabetes status was generally associated with less added sugar consumption compared to being unaware; however aware non-Hispanic Black males consumed more added sugar than unaware non-Hispanic Black males (91.5 g/day vs 89.7 g/day) and aware Hispanic females consumed more added sugar than unaware Hispanic females (56.2 g/day vs 55.2 g/day).

Significant differences in added sugar consumption were found by prediabetes awareness status in Hispanic males only (aware: 69.1 g/day and unaware: 100.6 g/day; $p = .03$) (Table 2).

Overall, multivariable analysis indicated that prediabetes awareness was not significantly associated with the mean intake of added sugar ($b = -3.85$, $p = .49$); however, significant differences in added sugar consumption were observed by age, sex, and race/ethnicity. Younger age was associated with higher consumption of added sugar ($b = -17.6$, $p < .01$), males consumed more added sugar than females ($b = 20.73$, $p < .01$), and non-Hispanic Whites and non-Hispanic blacks consumed more than the lowest consumer group Other Race (non-Hispanic Whites: $b = 20.6$, $p < .01$; non-Hispanic Blacks: $b = 18.3$, $p < .01$) (Table 3).

Discussion

Findings from this nationally representative study indicate that, contrary to the study hypothesis, individuals aware of their prediabetes status do not report consuming less added sugar than individuals unaware of their prediabetes status. These findings are consistent with similar studies using NHANES data (Bardenheier et al., 2014; Siegel et al., 2018). For example, in a cross-sectional study of adults ≥20 years, dietary intake was assessed by diabetes awareness (pre- and type 2) and no significant differences in macronutrient intakes, including total sugars, by prediabetes awareness status were found. The authors did not differentiate between total and added sugar in their study, limiting comparative interpretation (Bardenheier et al., 2014). However, the lack of significant differences in total sugar intake between adults aware and unaware of their

prediabetes status suggests prediabetes awareness does not influence related dietary sugar intake.

In a similar cross-sectional study of non-diabetic adults ≥20 years the proportion of American adults who engage in T2D risk reduction behaviors, including a healthy diet (i.e., MyPlate recommendations) was examined (Siegel et al., 2018). Approximately half of the sample met diagnostic criteria for prediabetes (no self-reported diabetes diagnosis and a HgbA1c of 5.7% to 6.4% or a fasting plasma glucose of ≥ 100 mg/dL to <126 mg/dL); however, prediabetes awareness status was not reported. Data collected from two consecutive 24-hour dietary recall days and self-reported leisure-time/ physical activity were used to assess T2D risk reduction behavior goals (i.e., four or more MyPlate recommendations of either fruit, vegetable, dairy, grain, meat, beans, and egg consumption, the maximum allowances for added sugar, total or saturated fat, cholesterol and alcohol consumption, and a physical activity goal of ≥ 150 min/week). Fewer than 30% of American adults met T2D dietary risk reduction goals (MyPlate recommendations) and only 3.1% met a majority of T2D prevention goals (Siegel et al., 2018).

The results of this study differ from other studies that did report dietary behavior changes after prediabetes awareness (Okosun & Lyn, 2015; Owei et al., 2019; Zhuang et al., 2015); however, diet questionnaires were used in these studies to obtain dietary intake estimates (Okosun & Lyn, 2015; Owei et al., 2019). In one 18-month longitudinal study of adults 18-65 years (Owei et al., 2019), an 18-item "Food Habits Questionnaire" (focused on dietary fat intake/reduction) was used to assess dietary change (Kristal et al., 1990). A second cross-sectional NHANES study of adults ≥18 years, used a single survey

question to assess dietary risk reduction behaviors: “to lower your risk for certain diseases, are you now […] reducing the amount of fat or calories in your diet?” (Okosun & Lyn, 2015). In contrast, the NHANES dietary data used for this study was collected with the validated, 5-step, 24-hour dietary recall method, AMPM (Ahluwalia et al., 2016). Diet questionnaires, in comparison to 24-hour dietary recall methods such as the AMPM, provide less reliable estimates for energy intake due to participant underreporting (Burrows et al., 2019). It is possible greater measurement error in dietary intake estimates may have accounted for the differences in study findings.

While studies assessing dietary behavior change in adults with prediabetes are sparse, dietary-risk reduction behaviors have been observed in individuals with T2D (Bardenheier et al., 2014; Vaccaro & Huffman, 2017; Zhang et al., 2017). For example, studies have reported significant differences in dietary intake by T2D awareness status; specifically lower carbohydrate and total calorie intake (Zhang et al., 2017). A NHANES study from 2014 reported lower total sugar consumption in adults aware of having a T2D diagnosis but not in individuals with prediabetes regardless of awareness status (Bardenheier et al., 2014). Perception of risk may be greater in aware individuals with T2D compared to those aware of their prediabetes status. T2D is a clinical diagnosis, whereas prediabetes is considered a T2D risk factor (ADA, 2020). This distinction likely undermines the clinical importance of prediabetes; a condition which is attributed to the early onset of microvascular (e.g., nephropathy, retinopathy) and macrovascular complications (e.g., heart disease, stroke), and increased mortality risk (Cefalu, 2016). Furthermore, one third of the U.S. population is at risk for developing T2D since prediabetes is the single most significant T2D risk-factor (CDC, 2020b). These

differences suggest adults aware of their prediabetes status may lack an understanding of the health implications of T2D risk making them less likely to engage in dietary modifications that prevent T2D.

Evidence suggests when health care providers recommend lifestyle modifications, patients generally comply and modify their health behaviors (Vaccaro & Huffman, 2017). National survey data has found only 33.4% of individuals with prediabetes actually receive dietary risk-reduction counseling by physicians during health care visits (Karve & Hayward, 2010), with physicians generally emphasizing reductions in calorie and fat intake (Vaccaro & Huffman, 2017). In addition, the ADA recommends all individuals with prediabetes be referred for nutrition counseling by a certified dietitian nutritionist (ADA, 2019); a service reimbursed through most health insurance plans (ADA, 2019). However, only about 36% of patients with prediabetes are referred to diabetes lifestyle programs such as the ADA diabetes education program or the Diabetes Prevention Program (Tseng et al., 2019). It is possible that a lack of health care provider counseling and nutrition counseling referrals in patients with prediabetes contributed to the null findings of this study.

Whether or not prediabetes awareness motivates dietary behavior change such as added sugar consumption in the general population is unclear. This study did, however, observe differences in awareness status and added sugar consumption by sex, age, and race/ethnicity. Overall, men consumed significantly more added sugar than women after controlling for prediabetes awareness, age, and race (Table 3). Evidence suggests women consume healthier diets (Tseng et al., 2019), lower in added sugar in comparison to men (Partnership for Health in Aging Workgroup on Interdisciplinary Team Training in

Geriatrics, 2014). Also, women with prediabetes are more likely to report engaging in risk-reduction behaviors such as weight loss or fat/calorie reduction compared to men (Geiss et al., 2010). This sex difference may explain why less added sugar consumption was observed in females compared to males in this study.

This study found that younger adults consumed significantly more added sugar than middle to older-aged adults (Table 3). Studies suggest older adults are more likely to be under the care of a health care provider, have multiple chronic conditions (Partnership for Health in Aging Workgroup on Interdisciplinary Team Training in Geriatrics, 2014), and receive risk-reduction counseling for various medical condition (e.g., hypertension, obesity) (Karve & Hayward, 2010). It is possible that older individuals in this study had previously received dietary risk-reduction counseling from a health care provider for another health conditions which may have contributed to the significantly lower intakes of added sugar for this group. Additionally, the daily caloric needs of older adults are lower compared to young adults (400-600 calories less), which may have attributed to the differences observed (Johnson et al., 2014).

Lastly, non-Hispanic Whites and non-Hispanic Blacks consumed significantly more added sugar than the Other Race category (Table 3). Nationally representative survey data indicates both non-Hispanic Whites and non-Hispanic Blacks do not meet current U.S. dietary recommendations to limit added sugar to <10% of total daily calories (S. A. Bowman et al., 2017). Moreover, non-Hispanic Blacks consume the highest quantities of added sugar (> 25% daily total energy) compared to other racial/ethnic groups (Marriott et al., 2010). The results from this study showed that among individuals with prediabetes, non-Hispanic Whites consume marginally more added sugar than non-

Hispanic Blacks (~21 grams compared to ~19 grams) (Table 3). Research suggests non-Hispanic Blacks with T2D are more likely to be told by a physician to engage in dietary behaviors such as reducing total calories and fat and when told, are more likely to follow a physician's recommendations compared to non-Hispanic Whites (Vaccaro & Huffman, 2017). It is possible non-Hispanic Whites with prediabetes are less likely to receive medical advice about engaging in dietary risk-reduction behavior which may have contributed to the higher overall intake of added sugar observed in this study. More research is needed comparing differences in dietary advice provided to patients by race/ethnicity status.

Compared to non-Hispanic Whites and non-Hispanic Blacks, the Other Race category consumed the lowest quantities of added sugar (Table 3). In this study, Asian American adults were included in the Other Race category. Compared to other racial/ethnic groups, Asian Americans consume the lowest quantities of added sugar (64% consume <10% of their total daily calories from added sugar) (S. A. Bowman et al., 2017). The inclusion of Asian Americans in the "Other" category likely contributed to their lower consumption rates overall.

The major strengths of this study are the use of a large national data set representative of the U.S. population and the use of standardized, laboratory collected hemoglobin A1c measures to identify prediabetes in the sample. However, this study also has some limitations. First, the cross-sectional nature of this study allows for examination of associations only and causality or temporal associations cannot be determined. Second, prediabetes awareness status was based on self-reported data and may be subject to recall bias. Third, added sugar was estimated using self-reported dietary intake data which is

also subject to recall bias. While the validated AMPM used in this study has been shown to reduce recall bias and provide fairly accurate estimates for total energy intake in normal weight individuals, being overweight or obese is associated with underreporting of total energy intake (Moshfegh et al., 2008). Similarly, individuals with diagnosed T2D have also been shown to underreport their energy intake (Salle et al., 2006). Since the sample included individuals with prediabetes and a mean BMI of >30 kg/m2, underreporting of added sugar was possible. However, a majority of the sample was unaware of their prediabetes status, therefore the issue of underreporting due to a diabetes diagnosis is less likely.

Conclusions

Findings from this study indicate individuals aware of their prediabetes status do not reduce their added sugar intake. Whether these findings indicate a lack of general awareness about the metabolic consequences of added sugar consumption on prediabetes or an overall lack of health care provider lifestyle counseling or referrals remains unclear and requires further investigation. While there is strong evidence to suggest that added sugar promotes metabolic dysregulation of lipid and glucose promoting a state of insulin resistance (Stanhope, 2016) no guidelines exist that specify added sugar limits for adults with prediabetes. Furthermore a lack of patient referral to diabetes education for nutrition counseling is likely exacerbating the issue (Tseng et al., 2019).

Due to the alarming number of individuals with prediabetes unaware of their condition (CDC, 2020b) as well as U.S. overconsumption of added sugar (HHS and USDA, 2015), guidelines specifying limits on added sugar consumption specific to those

with prediabetes are needed to curb consumption and prevent T2D. Such guidelines would also be valuable to health care providers offering dietary advice to patients with prediabetes. Lastly, continued efforts are needed to not only increase prediabetes screening and improve awareness, but to ensure patients are referred for diabetes-specific nutrition counseling and that health care providers are made aware of the importance of limiting added sugar to reduce the incidence of T2D.

References

Ahluwalia, N., Dwyer, J., Terry, A., Moshfegh, A., & Johnson, C. (2016). Update on NHANES dietary data: Focus on collection, release, analytical considerations, and uses to inform public policy. *Advances in Nutrition, 7*(1), 121-134. https://doi.org/10.3945/an.115.009258

American Diabetes Association. (2019). Lifestyle management: Standards of Medical Care in diabetes—2019. *Diabetes Care, 42*(Supplement 1), S46. https://doi.org/10.2337/dc19-S005

American Diabetes Association. (2020). 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes-2020. *Diabetes Care, 43*(Suppl 1), S14.

Andes, L. J., Cheng, Y. J., Rolka, D. B., Gregg, E. W., & Imperatore, G. (2019). Prevalence of prediabetes among adolescents and young adults in the United States, 2005-2016. *JAMA Pediatrics*, e194498-e194498. https://doi.org/10.1001/jamapediatrics.2019.4498

Bardenheier, B. H., Cogswell, M. E., Gregg, E. W., Williams, D. E., Zhang, Z., & Geiss, L. S. (2014). Does knowing one's elevated glycemic status make a difference in macronutrient intake? *Diabetes Care, 37*(12), 3143-3149. https://doi.org/10.2337/dc14-1342

Bowman, S., Clemens, J., Friday, J., Lynch, K., & Moshfegh, A. (2017). *Food Patterns Equivalents Database 2013-14: Methodology and user guide*. U.S. Department of

Agriculture. Retrieved March 28, 2020 from http://www.ars.usda.gov/nea/bhnrc/fsrg

Bowman, S. A., Clemens, J. C., Martin, C. L., Anand, J., Steinfeldt, L. C., & Moshfegh, A. J. (2017). *Added sugars intake of Americans: What We Eat in America, NHANES 2013-2014.* Food Surveys Research Group. Retrieved April 18, 2020 from https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/DBrief/18_Added_Sugars_Intake_of_Americans_2013-2014.pdf

Bray, G. A., & Popkin, B. M. (2014). Dietary sugar and body weight: Have we reached a crisis in the epidemic of obesity and diabetes?: Health be damned! Pour on the sugar. *Diabetes Care, 37*(4), 950-956. https://doi.org/10.2337/dc13-2085

Burrows, T. L., Ho, Y. Y., Rollo, M. E., & Collins, C. E. (2019). Validity of dietary assessment methods when compared to the method of doubly labeled water: A systematic review in adults. *Frontiers in Endocrinology, 10*(850). https://doi.org/10.3389/fendo.2019.00850

Cefalu, W. T. (2016). "Prediabetes": Are there problems with this label? No, we need heightened awareness of this condition! *Diabetes Care, 39*(8), 1472-1477. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4955936/pdf/dc161143.pdf

Centers for Disease Control and Prevention. (2020a). *About adult BMI*. U.S. Department of Health and Human Services. Retrieved August 27, 2020 from https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html

Centers for Disease Control and Prevention. (2020). National Diabetes Statistics Report, 2020. Atlanta, GA: Centers for Disease Control and Prevention, US Department

of Health and Human Services. Retrieved August 27, 2020 from https://www.cdc.gov/diabetes/data/statistics-report/index.html

Centers for Disease Control and Prevention. (2020c). *NHANES response rates and population totals*. CDC and National Center for Health Statistics. Retrieved August 19, 2020 from https://wwwn.cdc.gov/nchs/nhanes/ResponseRates.aspx

de Koning, L., Malik, V. S., Rimm, E. B., Willett, W. C., & Hu, F. B. (2011). Sugar-sweetened and artificially sweetened beverage consumption and risk of type 2 diabetes in men. *American Journal of Clinical Nutrition, 93*(6), 1321-1327. https://doi.org/10.3945/ajcn.110.007922

Fitch, C., & Keim, K. S. (2012). Position of the Academy of Nutrition and Dietetics: Use of nutritive and nonnutritive sweeteners. *Journal of the Academy of Nutrition and Dietetics, 112*(5), 739-758. https://doi.org/10.1016/j.jand.2012.03.009

Geiss, L. S., James, C., Gregg, E. W., Albright, A., Williamson, D. F., & Cowie, C. C. (2010). Diabetes risk reduction behaviors among U.S. Adults with prediabetes. *American Journal of Preventive Medicine, 38*(4), 403-409. https://doi.org/https://doi.org/10.1016/j.amepre.2009.12.029

Huang, Y., Cai, X., Mai, W., Li, M., & Hu, Y. (2016). Association between prediabetes and risk of cardiovascular disease and all cause mortality: Systematic review and meta-analysis. *BMJ, 355*, i5953.

Johnson, C. L., Dohrmann, S. M., Burt, V. L., & Mohadjer, L. K. (2014). National Health and Nutrition Examination Survey: Sample design, 2011-2014. *Vital and Health Statistics. Series 2: Data Evaluation and Methods Research*(162), 1-33. https://www.ncbi.nlm.nih.gov/pubmed/25569458

Karve, A., & Hayward, R. A. (2010). Prevalence, diagnosis, and treatment of impaired fasting glucose and impaired glucose tolerance in nondiabetic U.S. adults. *Diabetes Care, 33*(11), 2355-2359. https://doi.org/10.2337/dc09-1957

Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., Nathan, D. M., & Diabetes Prevention Program Research, G. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine, 346*(6), 393-403. https://doi.org/10.1056/NEJMoa012512

Kristal, A. R., Shattuck, A. L., & Henry, H. J. (1990). Patterns of dietary behavior associated with selecting diets low in fat: Reliability and validity of a behavioral approach to dietary assessment. *Journal of the American Dietetic Association, 90*(2), 214-220.

Kulick, E. R., Moon, Y. P., Cheung, K., Willey, J. Z., Sacco, R. L., & Elkind, M. S. (2016). Racial-ethnic disparities in the association between risk factors and diabetes: The Northern Manhattan Study. *Preventive Medicine, 83*, 31-36. https://doi.org/10.1016/j.ypmed.2015.11.023

Marriott, B. P., Olsho, L., Hadden, L., & Connor, P. (2010). Intake of added sugars and selected nutrients in the United States, National Health and Nutrition Examination Survey (NHANES) 2003-2006. *Critical Reviews in Food Science and Nutrition, 50*(3), 228-258. https://doi.org/10.1080/10408391003626223

Montonen, J., Järvinen, R., Knekt, P., Heliövaara, M., & Reunanen, A. (2007). Consumption of sweetened beverages and intakes of fructose and glucose predict type 2 diabetes occurrence. *Journal of Nutrition, 137*(6), 1447-1454.

http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L46855484

Moshfegh, A. J., Rhodes, D. G., Baer, D. J., Murayi, T., Clemens, J. C., Rumpler, W. V., Paul, D. R., Sebastian, R. S., Kuczynski, K. J., & Ingwersen, L. A. (2008). The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *The American Journal of Clinical Nutrition, 88*(2), 324-332. https://doi.org/ 10.1093/ajcn/88.2.324

National Center for Health Statistics. (2017). *NCHS Research Ethics Review Board (ERB) Approval*. Centers for Disease Control and Prevention and National Center for Health Statistics. Retrieved April 17, 2020 from https://www.cdc.gov/nchs/nhanes/irba98.htm

Office for Human Research Protections. (2018). *Revised common rule regulatory text*. Office for Human Research Protections. Retrieved April 17, 2020 from https://www.hhs.gov/ohrp/regulations-and-policy/regulations/revised-common-rule-regulatory-text/index.html

Okosun, I. S., & Lyn, R. (2015). Prediabetes awareness, healthcare provider's advice, and lifestyle changes in American adults. *International Journal of Diabetes Mellitus, 3*(1), 11-18. https://doi.org/https://doi.org/10.1016/j.ijdm.2010.12.001

Owei, I., Umekwe, N., Ceesay, F., & Dagogo-Jack, S. (2019). Awareness of prediabetes status and subsequent health behavior, body weight, and blood glucose levels. *Journal of the American Board of Family Medicine, 32*(1), 20-27. https://doi.org/10.3122/jabfm.2019.01.180242

Pan, X. R., Li, G. W., Hu, Y. H., Wang, J. X., Yang, W. Y., An, Z. X., Hu, Z. X., Lin, J., Xiao, J. Z., Cao, H. B., Liu, P. A., Jiang, X. G., Jiang, Y. Y., Wang, J. P., Zheng, H., Zhang, H., Bennett, P. H., & Howard, B. V. (1997). Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care, 20*(4), 537-544. https://www.ncbi.nlm.nih.gov/pubmed/9096977

Partnership for Health in Aging Workgroup on Interdisciplinary Team Training in Geriatrics. (2014). Position statement on interdisciplinary team training in geriatrics: An essential component of quality health care for older adults. *Journal of the American Geriatrics Society, 62*(5), 961-965. https://doi.org/10.1111/jgs.12822

Raper, N., Perloff, B., Ingwersen, L., Steinfeldt, L., & Anand, J. (2004). An overview of USDA's dietary intake data system. *Journal of Food Composition Analysis, 17*(3-4), 545-555.

Rodriguez, L. A., Madsen, K. A., Cotterman, C., & Lustig, R. H. (2016). Added sugar intake and metabolic syndrome in US adolescents: Cross-sectional analysis of the National Health and Nutrition Examination Survey 2005-2012. *Public Health Nutrition, 19*(13), 2424-2434. https://doi.org/10.1017/s1368980016000057

Salle, A., Ryan, M., & Ritz, P. (2006). Underreporting of food intake in obese diabetic and nondiabetic patients. *Diabetes Care, 29*(12), 2726-2727. https://care.diabetesjournals.org/content/diacare/29/12/2726.full.pdf

Siegel, K. R., Bullard, K. M., Imperatore, G., Ali, M. K., Albright, A., Mercado, C. I., Li, R., & Gregg, E. W. (2018). Prevalence of major behavioral risk factors for type 2 diabetes. *Diabetes Care*. https://doi.org/10.2337/dc17-1775

Stanhope, K. L. (2016). Sugar consumption, metabolic disease and obesity: The state of the controversy. *Critical Reviews in Clinical Laboratory Sciences, 53*(1), 52-67. https://doi.org/10.3109/10408363.2015.1084990

Stanhope, K. L., Schwarz, J. M., Keim, N. L., Griffen, S. C., Bremer, A. A., Graham, J. L., Hatcher, B., Cox, C. L., Dyachenko, A., Zhang, W., McGahan, J. P., Seibert, A., Krauss, R. M., Chiu, S., Schaefer, E. J., Ai, M., Otokozawa, S., Nakajima, K., Nakano, T., Beysen, C., Hellerstein, M. K., Berglund, L., & Havel, P. J. (2009). Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *Journal of Clinical Investigation, 119*(5), 1322-1334. https://doi.org/10.1172/JCI37385

Strodel, R. J., Chang, C. H., Khurana, S. G., Camp, A. W., Magenheimer, E. A., & Hawley, N. L. (2019). Increased awareness, unchanged behavior: Prediabetes diagnosis in a low-income, minority population. *Diabetes Educator, 45*(2), 203-213. https://doi.org/10.1177/0145721719826578

Tabak, A. G., Herder, C., Rathmann, W., Brunner, E. J., & Kivimaki, M. (2012). Prediabetes: A high-risk state for diabetes development. *Lancet, 379*(9833), 2279-2290. https://doi.org/10.1016/s0140-6736(12)60283-9

Tooze, J. A. (2020). Estimating usual intakes from dietary surveys: Methodologic challenges, analysis approaches, and recommendations for low-and middle-

income countries. Retrieved June 1, 2020 from https://www.intake.org/resource/estimating-usual-intakes-dietary-surveys-methodologic-challenges-analysis-approaches-and

Tseng, E., Greer, R. C., O'Rourke, P., Yeh, H.-C., McGuire, M. M., Albright, A. L., Marsteller, J. A., Clark, J. M., & Maruthur, N. M. (2019). National survey of primary care physicians' knowledge, practices, and perceptions of prediabetes. *Journal of General Internal Medicine, 34*(11), 2475-2481.

Tuomilehto, J., Lindstrom, J., Eriksson, J. G., Valle, T. T., Hamalainen, H., Ilanne-Parikka, P., Keinanen-Kiukaanniemi, S., Laakso, M., Louheranta, A., Rastas, M., Salminen, V., Uusitupa, M., & Finnish Diabetes Prevention Study, G. (2001). Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine, 344*(18), 1343-1350. https://doi.org/10.1056/NEJM200105033441801

U.S. Department of Health and Human Services and U.S. Department of Agriculture. (2015). *2015 - 2020 Dietary Guidelines for Americans* (8th ed.). Retrieved April 20, 2021 from https://health.gov/our-work/food-nutrition/previous-dietary-guidelines/2015.

United States Food and Drug Administration. (2020). *Added sugars on the new nutrition facts label*. U.S. Food and Drug Administration. Retrieved November 3, 2020 from https://www.fda.gov/food/new-nutrition-facts-label/added-sugars-new-nutrition-facts-label

University of Alabama at Birmingham: Institutional Review Board (IRB). (n.d.). *Is IRB review required for use of public datasets?* Retrieved October 30, 2020 from

https://www.uab.edu/research/administration/offices/IRB/FAQs/Pages/PublicDatasets.aspx

Vaccaro, J. A., & Huffman, F. G. (2017). Sex and race/ethnicity differences in following dietary and exercise recommendations for US representative sample of adults with type 2 diabetes. *American journal of men's health*, *11*(2), 380-391. https://journals.sagepub.com/doi/pdf/10.1177/1557988316681126

Yang, Q., Zhang, Z., Gregg, E. W., Flanders, W. D., Merritt, R., & Hu, F. B. (2014). Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Intern Med*, *174*(4), 516-524. https://doi.org/10.1001/jamainternmed.2013.13563

Zhang, N., Yang, X., Zhu, X., Zhao, B., Huang, T., & Ji, Q. (2017). Type 2 diabetes mellitus unawareness, prevalence, trends and risk factors: National Health and Nutrition Examination Survey (NHANES) 1999-2010. *Journal of International Medical Research*, *45*(2), 594-609. https://doi.org/10.1177/0300060517693178

Zhuang, Q., Wu, L., Lu, Y., Du, J., & Guo, G. (2015). Awareness and intervention status of prediabetes among Chinese adults: Implications from a community-based investigation. *International Journal of Clinical and Experimental Medicine, 8*(3), 4480-4486.

Zipf, G., Chiappa, M., Porter, K. S., Ostchega, Y., Lewis, B. G., & Dostal, J. (2013). National Health and Nutrition Examination Survey Plan and Operations, 1999-2010. *Vital and Health Statistics, 1*(56). https://www.cdc.gov/nchs/data/series/sr_01/sr01_056.pdf

Table 1. Sociodemographic and descriptive statistics for non-pregnant adults ≥20 years compared by sex who are aware or unaware of their prediabetes status by a healthcare provider, the National Health and Nutrition Examination Survey 2013-2016

	Male			Female		
	Prediabetes Aware	**Prediabetes Unaware**	***p* value**	**Prediabetes Aware**	**Prediabetes Unaware**	***p* value**
Participants (n=2432)	N=143 (14%)	N=1001 (86%)		N=199 (16.3%)	N=1089 (83.7%)	
Age (years) (n=2432)	N=143 (14%)	N=1001 (86%)	**.005**	N=199 (16.3%)	N=1089 (83.7%)	.76
Younger aged: 20-44 yrs	12.3	28.7		18.7	21.2	
Middle aged: 45-64 yrs	50.8	44.7		41.8	42.7	
Older aged: ≥65 yrs	36.8	26.6		39.5	36.1	
Race/Ethnicity (n=2432)	N=143 (14%)	N=1001 (86%)	**.003**	N=199 (16.3%)	N=1089 (83.7%)	.60
Non-Hispanic White	67.4	55.6		63.6	59.7	
Non-Hispanic Black	13.4	17.2		12.9	16.1	
Hispanic	9.2	18.8		13.5	14.7	
Other Race	10.0	8.4		10.0	9.5	
Education (n=2431)	N=143 (14%)	N=1001 (86%)	**.007**	N=199 (16.3%)	N=1088 (83.7%)	.19
< High School	8.7	22.5		12	18.7	
High School or GED	22.4	26.5		18.3	24.4	
Some College	29.7	25.9		37.1	30.2	
≥ College Graduate	39.2	25		32.6	26.7	
Annual household income (n=2272)	N=137 (14.5%)	N=933 (85.5%)	.72	N=183 (16.3%)	N=1019 (83.7%)	.43
≤$20,000	9.9	11.9		13.9	19.5	
$20,000-$99,999	53.1	62.5		64.2	54.8	
≥$100,000	33.4	21.5		17.8	19.9	

Other income	3.5	4.1		4.1	5.7	
Marital Status (n=2431)	N=143 (14%)	N=1001 (86%)	.12	N=199 (16.3%)	N=1088 (83.7%)	.43
Married	66.7	65.1		52	50.7	
Widowed	4.5	3.9		15.8	15.7	
Divorced	14.5	8.5		16.9	14	
Separated	4.6	2.5		1.7	3.4	
Partner	3.5	12.6		12	10.7	
Never married	6.2	7.3		1.6	5.4	
BMI kg/m^2 (n= 2410)	N=142 (14.1%)	N=991 (85.9%)	[a]	N=198 (16.4%)	N=1079 (83.6%)	[a]
≤ 18.49 (underweight)	.6	.7		0	1.2	
18.5-24.99 (normal)	16.1	17.2		7.8	21.0	
25-29.99 (overweight)	36.7	38.9		28.3	28.3	
30-39.99 (obese)	42.4	37		44.3	37.7	
≥40 (severely obese)	4.3	6.2		19.6	11.7	
Hemoglobin A1c (%) (n=2437)	N=143 (14%)	N=1001 (86%)	**<.001** [b]	N=199 (16.3%)	N=1089 (83.7%)	**.04**[b]
	5.98 ± .023	5.87 ± .008		5.91 ± .02	5.87 ± .007	

All percentages rounded to the nearest tenth of a percent. Rao-Scott chi-square tests were used to examine the characteristics of awareness versus unawareness by sex among individuals for variables age, race/ethnicity, BMI (body mass index), education, household income, and marital status. Survey-weighted ordinary least squares regression was used to examine demographic differences in awareness of prediabetes by sex and hemoglobin A1c and means and standard errors (±) were reported to the nearest thousandth of a percentage.

[a] indicates Rao-Scott chi square tests could not be calculated due to one cell (underweight females aware of having prediabetes) having 0 observations.

[b]indicates significant differences in mean for hemoglobin A1c by awareness status estimated using survey weighted regression analyses. Estimated difference is -.11 for hemoglobin A1c between aware and unaware males and -.04 between aware and unaware females.

P-values <.05 are considered statistically significant.

Table 2. Survey weighted mean intakes for total energy, added sugar, and added sugar by age category and race/ethnicity for non-pregnant adults ≥20 years compared by sex who are aware or unaware of their prediabetes status by a healthcare provider, the National Health and Nutrition Examination Survey 2013-2016

	Male				Female			
	Prediabetes Aware	**Prediabetes Unaware**	**Estimated Difference**	***p* value**	**Prediabetes Aware**	**Prediabetes Unaware**	**Estimated Difference**	***p* value**
Participants (n=2215)	N=135 (15%)	N=908 (85%)			N=190 (19%)	N=982 (81%)		
Total Energy (kcals)	2508 ± 73	2362 ± 40	-145.3	.08	1876 ± 52	1803 ± 27	-73.5	.26
Added Sugar (g): Total sample	80 ± 14	84.2 ± 4.1	4.3	.77	56.4 ± 4.5	62.9 ± 2.7	6.5	.29
Added Sugar (g): Age category								
20-44 (n=535)	91.5 ± 17.5	96.8 ± 6.7	5.2	.79	73.0 ± 8.6	70.8 ± 4.3	-4.7	.67
45-64 (n=946)	90.2 ± 29.2	87.2 ± 7.9	-3.0	.92	56.6 ± 7	70.1 ± 4.5	13.5	.13
≥65 (n=734)	61.1 ± 9.3	65.7 ± 3.7	4.6	.62	47.1 ± 5.9	49.6 ± 2.6	2.4	.72
Added Sugar (g): Race / Ethnicity								
Non-Hispanic White (n=730)	81.7 ± 20	82.4 ± 5.7	.77	.97	54.7 ± 6.6	63 ± 3.5	8.4	.32
Non-Hispanic Black (n=582)	91.5 ± 12.5	89.7 ± 5.9	-1.8	.90	67.3 ± 9.8	74.6 ± 5	7.7	.52
Hispanic (n=616)	69.1 ± 8.6	100.6 ± 8.6	31.5	**.03**	56.2 ± 6.9	55.2 ± 3.7	-.97	.89
Other Race (n=287)	56.2 ± 11.8	53.3 ± 6.5	-2.9	.81	50 ± 8	53.6 ± 4.7	.23	.98

Survey-weighted ordinary least squares regression was used to estimate differences in awareness of prediabetes by sex for Day 1 of NHANES dietary data and included total energy (kilocalories), total added sugar (grams) for the population sample, and total added sugar (grams) by race/ ethnicity and age category.

Means and standard errors (±) were reported to the nearest tenth of a percentage.

Estimated difference represents mean intake of added sugar in grams per day for Day 1 of NHANES dietary data.

P-values <.05 are considered statistically significant.

Table 3. Associations between the mean intake of added sugar in grams per day and prediabetes awareness status by age, sex, and race/ethnicity among non-pregnant US adults ≥20 years (*n*=2068), the National Health and Nutrition Examination Survey 2013-2016

	Estimated Difference	Standard Error	95% Confidence Intervals	P-value
(Intercept)	90.8	18.48	[53.06, 128.54]	**< .01**
Prediabetes Aware	-3.85	5.47	[-15.03, 7.33]	.49
Age	-17.63	3.02	[-23.81, -11.45]	**< .01**
Male	20.73	5.58	[9.33, 32.13]	**< .01**
Female (ref)	-	-	-	-
Non-Hispanic White	20.59	4.18	[12.06, 27.23]	**<.01**
Non-Hispanic Black	18.82	4.91	[8.79, 28.86]	**<.01**
Hispanic	12.13	7.39	[-22.67, 5.74]	.11
Other Race (ref)	-	-	-	-

Estimated difference represents the mean intake of added sugar in grams per day for Day 1 of NHANES dietary data.
Ordinary least squares regression model included adjustments for age, sex, race, education level, income level, marital status, and body mass index.
Age variable represented as category of ≤19 years, ≥20 to ≤44 years, ≥45 to ≤64 years, ≥65 years.
(Ref) indicates reference category not reported in model estimates.
P-values <.05 are considered statistically significant.

TOTAL ADDED SUGAR CONSUMPTION IS NOT ASSOCIATED WITH RISK FOR PREDIABETES AMONG U.S. ADULTS: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2018

by

NADIA MARKIE SNEED, GREG PAVELA, ANDRES AZUERO, JACQUELINE MOSS, AMY M. GOSS, AND SHANNON A. MORRISON

In preparation for *Journal of the Academy of Nutrition and Dietetics*

Format adapted for dissertation

MANUSCRIPT 3

TOTAL ADDED SUGAR CONSUMPTION IS NOT ASSOCIATED WITH RISK FOR PREDIABETES AMONG U.S. ADULTS: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY, 2013-2018

Abstract

Background: Added sugars are linked to risk for prediabetes, a condition of insulin resistance affecting 34.1% of U.S. adults. Added sugar proxies (e.g., sugar-sweetened beverages) have primarily been used to examine added sugar's association with prediabetes. Yet, whether total added sugar consumption, from all dietary sources, increases the risk for prediabetes remains unclear.

Objective: Examine whether added sugar, total (g/day) and percent caloric intakes of <10%, 10-15%, or >15%, are associated with an increased odds for prediabetes in U.S. adults.

Design: A secondary analysis of 2013-2018 NHANES data. Prediabetes was defined as a HgbA1c of 5.7%-6.4%. Added sugar (g/day and percentage of total calories) was collected from two 24-hour diet recalls and usual mean intakes were estimated using the National Cancer Institute Method.

Participants/setting: Nationally representative US sample of 13,406 adults ≥ 20 years with normoglycemia (n = 8,905) and prediabetes (n = 4,501).

Main outcome measures: Prediabetes (% HgbA1c).

Statistical analysis: Survey-weighted logistic regression analysis was used to estimate unadjusted and adjusted odds ratios of prediabetes based on usual intake of added sugar and usual percent intakes (<10%, 10-15%, and >15%). Differences in prediabetes risk and usual intake of added sugar were compared by race/ethnicity. A mediation analysis estimated the direct and indirect 'effects' of added sugar on prediabetes, with body mass index (BMI) as a mediator.

Results: Total added sugar (g/day) and percent intakes of added sugar (g/day) were not significantly associated with having an increased odds of prediabetes (Total intake: adjusted- OR: 1.001, 95% CI: .99 - 1.006, p = .58 and percent intakes: adjusted [<10%: (ref); 10-15%: OR: 1.026, 95% CI: .827 - 1.273, p = .812; >15%: OR: 1.061, 95% CI: .835 - 1.347, p = .623]). Similar non-significant associations were observed by race/ethnicity status. The mediation analysis indicated that direct and indirect 'effects' of total usual intake of added sugar (g/day) on HgbA1c were not statistically significant.

Conclusions: Findings suggest total added sugar consumption, including greater percent intakes, does not increase the odds of having prediabetes in U.S. adults. However, future prospective cohort and experimental studies are needed to further examine this relationship to confirm these results.

Key words: added sugar, prediabetes, HgbA1c, national health and nutrition examination survey, prediabetes risk

Introduction

Prediabetes is a relatively asymptomatic, but serious medical condition characterized by insulin resistance and intermittent hyperglycemia (American Diabetes Association [ADA], 2020) that affects approximately 88 million U.S. adults (Centers for Disease Control and Prevention [CDC], 2020b). Prediabetes is a precursor to type 2 diabetes (T2D) (ADA, 2020) and is associated with chronic kidney disease (Plantinga et al., 2010) and cardiovascular disease risks (i.e., hypertension, dyslipidemia) (Ali et al., 2018), independent of T2D progression. Significant disparities in the prevalence of prediabetes are observed among minority populations, particularly non-Hispanic Blacks and Hispanics, in comparison to non-Hispanic Whites (32%, 35.3%, 31%, respectively) (Zhu et al., 2019). Due to the slow but progressive nature of prediabetes pathology, roughly 85% of adults are unaware of their condition (ADA, 2020; World Health Organization, 2016) and many times remain unaware of their metabolic dysfunction until after the condition has progressed to T2D (Tabak et al., 2012). Currently about 5-10% of adults with prediabetes progress to T2D annually and 70% of adults with prediabetes develop T2D within their lifetime (Tabak et al., 2012; Teng et al., 2019). Whether factors such as diet, genetics, advancing age, other lifestyle choices (e.g., physical activity) or a combination of these factors increase the risk for prediabetes is not fully known. However, longitudinal, observational studies examining the role of nutrition on metabolic conditions suggest diet is a primary predictor of a plethora of cardiac and metabolic health conditions, including prediabetes (Basiak et al., 2019; Bauer et al., 2013; Chen et al., 2018; Esposito et al., 2010; Glechner et al., 2018).

Skyrocketing cardiovascular disease of the 1950s and 1960s were hypothesized to be a consequence of excessive fat consumption and subsequently hyperlipidemia. Thus, a change in the recommended consumption of dietary fats and carbohydrates (i.e., dietary guidelines) was published in the late 1970s. In short, the new dietary guidelines suggested reducing changes in daily macronutrient consumption. Specifically, the recommended percent of total daily energy intake from dietary fat decreased from 40% to 30% (Kritchevsky, 1998). In contrast, recommended percent of total daily energy intake from dietary carbohydrate consumption increased from 39% to approximately 55% - 60% (Hite et al., 2010; Kritchevsky, 1998). Unfortunately, the shift in dietary intake observed after publication of new dietary guidelines paralleled a drastic rise in obesity and metabolic disease across the 1980s and 1990s and has had little influence on cardiovascular disease prevalence (CDC, 2020c; Hales et al., 2020).

Concurrent with the shift in diet trends, food manufacturers increased production of carbohydrate rich, low fat foods. In short, food manufacturers substituted carbohydrates in lieu of fats, primarily in the form of added sugars across a multitude of foods and beverages (Fitch & Keim, 2012) and these ultra-processed, sugary foods became a mainstay in the U.S. diet (Johnson et al.). The most common added sugars are sucrose, used predominately in solid foods, and high-fructose corn (HFCS), used predominately in sugar-sweetened beverages (SSBs) (Malik & Hu, 2015). Evidence linking obesity and metabolic disease to added sugar prompted an additional modification to the U.S. Dietary Guidelines (U.S. Department of Health and Human Services and U.S. Department of Agriculture [HHS and USDA], 2015). In 2015, total dietary intake of added sugar was recommended to not exceed 10% of an individual's daily caloric intake,

a recommendation that persists today. Nonetheless, most American consume approximately 13% of their daily calories exclusively from added sugars, exacerbating the issue of overconsumption (HHS and USDA, 2015; HHS and USDA, 2020).

Compared to natural sugars found in fruits and vegetables, added sugars contain high concentrations of fructose (~50% to 55%). Fructose imparts unique negative metabolic consequences by promoting an increase in hepatic lipid synthesis (i.e., de novo lipogenesis) and reduced hepatic fatty acid oxidation resulting in fatty liver and subsequent hepatic insulin resistance (DiNicolantonio et al., 2015; Malik & Hu, 2015). Evidence suggests this metabolic effect is exacerbated with chronic consumption of a diet high in added sugar (i.e., ~15-25% total energy intake) and occurs independent of total energy intake or body mass index (BMI) (Aeberli et al., 2011; Aeberli et al., 2013; Maersk et al., 2011; Stanhope et al., 2015). However, the link between added sugar and risk for prediabetes has primarily been observed from studies examining added sugar proxies such as SSBs, HFCS, and fructose-sweetened beverages (Aeberli et al., 2013; Barrio-Lopez et al., 2013; Dhingra et al., 2007; Faeh et al., 2005; Green et al., 2014; Lana et al., 2014; Lê et al., 2009; Lecoultre et al., 2013; Ma et al., 2016; Stanhope et al., 2009; Teshima et al., 2015).

Lastly, minority populations demonstrate significant health disparities in obesity and T2D in comparison to non-Hispanic Whites (Ward et al., 2019; Zhu et al., 2019). Moreover, there is evidence to suggest that consumption of a high carbohydrate diet in minority populations (i.e., non-Hispanic Blacks) promotes an exaggerated insulin response that occurs independent of overweight/obesity status (Gower et al., 2020). Hispanics and non-Hispanic Blacks consume greater quantities of added sugar compared

to non-Hispanic whites (i.e., 17.5%, 15.8%, and 14.6% total daily calories, respectively) (S. A. Bowman et al., 2017) raising the question as to whether differences in dietary intake (e.g., added sugar) are primarily responsible for these health disparities.

To our knowledge, no study has examined if total added sugar consumption increases the risk for prediabetes or if consumption of greater quantities of total added sugar (e.g., >15% total caloric intake) is attributed to greater risk for prediabetes. Moreover, it is unclear whether total and/or greater percent intakes of added sugar uniquely influence the risk for prediabetes by race/ethnicity, particularly in vulnerable minority groups (i.e., non-Hispanic Black, Hispanic).

The main objective of this study was to examine whether total added sugar consumption is associated with prediabetes in a large nationally representative sample of U.S. adults. Secondly, we examined if greater total added sugar consumption, as a percentage of total energy consumption (<10%, 10-15%, >15% added sugar calories/day), is associated with an increased probability (i.e., risk) for prediabetes. Lastly, we explored whether the associations between total and percent intakes of added sugar and prediabetes risk differ by race/ethnicity, and whether the association between added sugar intake and risk of prediabetes are due, in part, to BMI.

Materials and Methods

Study Sample

A secondary analysis was conducted using 2013-2018 NHANES data which is supported by the National Center for Health Statistics (NCHS) and the Centers for Disease Control and Prevention (CDC, 2017). Study protocols are approved by the

NCHS Research Ethnics Review Board (National Center for Health Statistics, 2017) and are compliant with the Health and Human Services Policy for Protection of Human Research Subjects (45 CFR part 46) (Office for Human Research Protections, 2018; Zipf et al., 2013). Only unidentified, publicly-available data were included in this study, therefore the study was designated as 'Not Human Subjects Research' by the University of Alabama at Birmingham (University of Alabama at Birmingham: Institutional Review Board (IRB), n.d.).

NHANES is a repeated cross-sectional survey that employs a complex, multistage, probability sampling design to collect health and nutrition information from ~5,000 noninstitutionalized U.S. civilians (age 0 years and older) annually (Johnson et al., 2014; Zipf et al., 2013). Specific details about the design and operations of NHANES, including sampling and data collection procedures, have has been previously described elsewhere (CDC, 2018; Zipf et al., 2013).

For this analysis, 13,406 adults ≥20 years of age with normoglycemia (n=8,905) or HgbA1c defined prediabetes (n=4,501) were identified. Individuals were classified by race/ethnicity as Hispanic (including Mexican American and other Latino populations), non-Hispanic Black, non-Hispanic White, and Other Race which included Asian Americans and persons not self-identifying with any of the prior categories. Pregnant women (n=190) and those with HgbA1c ≥ 6.5% defined T2D (*n* = 2,037) were excluded from all analyses. The final sample included 10,671 non-pregnant adults with dietary recall information.

Prediabetes Assessment

The outcome variable for this study was prediabetes which was defined as a HgbA1c from 5.7% to 6.4% (39-47 mmol/mol) based on the American Diabetes Association "Standards of Medical Care in Diabetes - 2020" classification (ADA, 2020). NHANES collects a variety of biospecimens from participants including whole blood specimens of glycohemoglobin (i.e., HgbA1c) (CDC, n.d.). Samples are collected from participants ages ≥12 years during medical examination center visits (Zipf et al., 2013) using a Tosoh G8 Automated Glycohemoglobin Analyzer. NHANES follows laboratory procedures outlined by the National Glycohemoglobin Standardization Program (CDC, n.d.).

Estimating Usual Intake of Added Sugar

Dietary intake data, including added sugars and total calories, were collected for the dietary assessment component of NHANES which uses the 24-hour dietary recall method (Ahluwalia et al., 2016). Diet recalls are pre-announced and performed by trained interviewers using the validated U.S. Department of Agriculture's Automated Multiple-Pass Method (AMPM) previously described elsewhere (Ahluwalia et al., 2016; Zipf et al., 2013). The first diet recall is administered in-person during the mobile examination center visit (on either weekdays or weekends) and the second is administered over the phone 3-10 days later (Zipf et al., 2013).

Added sugars are defined as sugars, syrups, fruit juice concentrates, or caloric sweeteners added during processing, preparation, or prior to food and beverage consumption that exclude natural sugars present in dairy and fruit (including whole fruit

and 100% fruit juice) (Bowman, 2017). Estimates for added sugar were obtained from the Food Patterns Equivalents Database (FPED) of the Food and Nutrient Database for Dietary Studies. The FPED uses the sugar content of foods and beverages collected during NHANES dietary recalls to estimate added sugars, reported in teaspoon equivalents. Total calories from day 1 and day 2 dietary recalls were obtained from the NHANES nutrient intake files and were reported in kilocalories (kcals). The FPED files were merged with NHANES total nutrient intake files to combine estimates for added sugar and total calories. In order to reflect updates to nutrition facts labeling (United States Food and Drug Administration, 2020), added sugar was converted from teaspoon equivalents to grams (1 teaspoon equivalent = 4.2 grams) and from grams to calories (1 gram = 4 kilocalories) for day 1 and day 2 dietary recalls before the final dataset merge (S. Bowman et al., 2017; United States Food and Drug Administration, 2020). Once all 2013-2018 data files were merged, ratios for percent intakes of added sugar (<10%, 10-15%, and >15%) were calculated by dividing grams of added sugar by total calories.

The usual intake distributions for added sugar and total calories were estimated for the study population. Similar to the National Cancer Institute (NCI) method, we used a curvilinear transformation of the raw intake data and linear mixed effects modeling to estimate usual intake for added sugar and total calories. The NCI method requires two or more dietary recalls on a random subset of the population to account for between- and within-person variation in intake. This method can be used to estimate the distribution of usual nutrient intakes or dietary components for a population that are consumed daily or episodically (National Cancer Institute, 2020; Tooze et al., 2010). The method consists of a two-part model where Part I estimates the probability of consuming a food on a

particular day and Part II specifies the amount consumed on the consumption day. The purpose of this study was to estimate daily nutrient intake quantities of added sugar, a frequently consumed dietary component for which the probability of daily consumption is assumed to be "1"; therefore only steps from Part II of the NCI model were followed (National Cancer Institute, 2020; Tooze et al., 2010). Covariates were not included in any of the usual intake models. The following steps were used to estimate usual nutrient intake for added sugar and total calories: 1) transformation of the raw data to remove skewness, 2) a mixed-effects model was fitted to estimate random effects for each individual, and 3) the random effects for each individual were added to the overall mean and then back-transformed to the original scale to estimate individual usual nutrient intake (National Cancer Institute, 2020).

Covariates

Regression models included the following covariates: age, gender, race/ethnicity, BMI (kg/m^2), usual intake for total calories (kcals), physical activity status, smoking status, educational attainment, and annual household income.

Race and ethnicity were categorized into non-Hispanic White, non-Hispanic Black, Hispanic (including Mexican Americans and Latinos), and Other Race (including Asian Americans and persons not identifying with the previously reported categories). BMI was categorized using the following CDC classifications for adults: underweight (18.5 kg/m^2), normal (18.5-24.9 kg/m2), overweight (25-29.9 kg/m^2), or obese ($\geq$ 30 kg/m^2) (CDC, 2020a). Health behaviors and sociodemographic factors, including physical activity status, smoking status, education level, and household income were

based on self-reported questionnaire data. Physical activity status was classified as either sedentary (<10 minutes of moderate or vigorous recreational activity) or non-sedentary (≥10 minutes of moderate or vigorous recreational activity). Smoking status was defined as either current smoker (tobacco use within the last 5 days) or non-smoker (no reported use within last 5 days). Education level was defined as having either less than a high school degree, having a high school degree or GED, or having more than a high school degree. Annual household income was categorized using the following income ranges: < $20,000, $20,000-$99,000, or ≥ $100,000.

Statistical Analysis

All analyses were performed using SAS Studio version 3.8, Enterprise Edition (SAS Institute Inc., Cary, NC, USA) with procedures appropriate for complex survey designs. Survey data from 2013-2014, 2015-2016, and 2017-2018 were combined and appropriate sampling weights were created for the combined dataset and applied to all models prior to analyses. Data on characteristics were reported using means and standard errors for continuous variables and percentages and standard errors for categorical variables. Characteristics were reported for the overall sample and by normoglycemia or prediabetes status. Rao Scott chi square tests were used to examine differences in sample characteristics for categorical variables by normoglycemia and prediabetes status. Ordinary least squares (OLS) regression was used to examine differences in sample characteristics for continuous variables by normoglycemia and prediabetes status.

Usual intake of added sugar was modeled as a continuous variable (g/day) and non-linear associations for added sugar as a percentage of total caloric intake were tested

(<10%, 10-15%, >15% g/day). A dichotomous indicator for prediabetes was constructed from HgbA1c values, with prediabetes indicated by HgbA1c values between 5.7%-6.4%. Survey weighted logistic regression was used to test whether usual intake of added sugar (either total and percent usual intake) was associated with an increased odds of prediabetes relative to normoglycemia. To aid in interpretation, model-estimated risks for prediabetes by usual intake of total added sugar (g/day) were estimated and reported for mean and quartile intakes. Additionally, model-estimated risks for prediabetes by usual percent intakes of added sugar represented as percent intakes in g/day were estimated and reported as <10%, 10-15%, and >15%. Adjusted models included the following covariates: age in years, gender, race/ethnicity, BMI, total energy intake (kcal/day), physical activity status, smoking status, education, and income. Interaction terms between usual intake of added sugar (g/day) and race/ethnicity were used to examine differences in the relationship between prediabetes risk and usual intake of added sugar by race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and Other Race). Lastly, a mediation analysis was conducted to estimate direct and indirect 'effects' (with body weight as mediator) of usual intake of added sugar on prediabetes. For this analysis, OLS regressions were used to examine associations between total added sugar consumption (g/day), prediabetes (represented as continuous HgbA1c variable), and BMI (represented as continuous variable); and the delta-method was used to estimate the standard error of the indirect effect (Baron & Kenny, 1986). All tests were two-sided and a p value < .05 was considered statistically significant.

Results

Sample Characteristics

A total of 13,406 adults with normoglycemia and prediabetes were included in the sample and reported consuming 10.2% of their total calories from added sugar. Consumption was similar for adults with prediabetes (33%) who reported consuming 10.4% of their total calories from added sugar. Table 1 shows the overall characteristics of adults ≥20 years and by normoglycemia and prediabetes status.

There were no significant differences in gender or smoking status by normoglycemia compared to prediabetes status; however, significant differences were noted by race/ethnicity, BMI status, physical activity status, education, and income. Compared to participants with normoglycemic, those with prediabetes were more likely to be older and non-Hispanic Black, Hispanic, or Other race. Additionally, adults with prediabetes were more likely to be obese, sedentary, and were more likely to report having less than high school degree and an annual household income between $20,000 to $99,000. Overall, mean usual intake of added sugar for the total sample was 49.5 g/day. Differences in added sugar consumption by normoglycemia versus prediabetes status were not statistically different; however, participants with prediabetes consumed slightly more added sugar compared to participants with normoglycemia (49.8 g/day, 196.1 kcal/day, 10.4% calories from added sugar vs 49.3 g/day, 194.6 kcal/day, 10.2% calories from added sugar respectively). Alternatively, those with normoglycemia consumed significantly more total calories than individuals with prediabetes (1866.4 kcal/day vs 1837.4 kcal/day respectively; $p = .0058$). Percent intakes of added sugar varied

marginally between groups, though were not statistically different. Compared to participants with normoglycemia, those with prediabetes consumed greater quantities (i.e., 10-15% and >15% total daily calories) of added sugar (28.6% and 18.3% vs 30.6% and 18.5% respectively).

Added Sugar Intake and Prediabetes Risk

Usual Intake of Total Added Sugar

Findings from both unadjusted and adjusted models (Table 2) indicated that usual mean consumption of total added sugar (g/day) was not significantly associated with having an increased odds of prediabetes (unadjusted: OR: 1.001, 95% CI: .99 - 1.003, p = .62; adjusted: OR: 1.001, 95% CI: .99 - 1.006, p = .58). However, significant differences in the odds for prediabetes were noted for some covariates in the adjusted model. For example, being older, being non-Hispanic Black, Hispanic, or Other race, and being obese were associated with a greater odds of having prediabetes, whereas being a non-smoker or having an education beyond a high school degree (relative to no high school degree) was associated with a lower odds of having prediabetes (Table 2). Table 3 reports the estimated probability (i.e., risk) for prediabetes at mean (49.4 g/day) and quartile (27.44 g/day, 43.86 g/day, 64.85 g/day) intakes for total added sugar as estimated from unadjusted and adjusted models. In the unadjusted model, the estimated risk for prediabetes at mean consumption of total added sugar was 27.2% and ranged from 26.9% to 27.3% between the lowest and highest quartiles. In the adjusted model, the estimated risk for prediabetes at mean consumption for total added sugar was 27.9% and ranged from 27.3% to 28.2% between the lowest and highest quartiles. Overall, model estimates

indicated that as total added sugar consumption increased, the risk for prediabetes also increased. However, the model-estimated increases in risk were of a very small magnitude and not significantly different from one another.

Results of the mediation analysis indicated that both direct and indirect effects of total usual intake of added sugar (g/day) on HgbA1c were of small magnitude and not statistically significant. The standardized direct effect was estimated at .007 (p = .59) and the indirect effect through BMI was estimated at .008 (p = .06). However, BMI was significantly, positively associated with HgbA1c (standardized b = .241; p < .001) (Figure 1).

Usual Percent Intakes of Added Sugar

Findings from both unadjusted and adjusted models (Table 4) indicated that usual mean consumption for percent intakes of added sugar (g/day) were not significantly associated with having an increased odds of prediabetes (unadjusted [<10%: (ref); 10-15%: OR: 1.119, 95% CI: .938 - 1.334, p = .206; >15%: OR: 1.057, 95% CI: .886 - 1.262, p = .531] and adjusted [<10%: (ref); 10 - 15%: OR: 1.026, 95% CI: .827 -1.273, p = .812; >15%: OR: 1.061, 95% CI: .835 - 1.347, p = .623]). In the adjusted model, significant differences in the odds for prediabetes were noted for some covariates including age, race/ethnicity, BMI, smoking status, and education (Table 4). Findings were similar to what was previously reported for the total added sugar adjusted model in Table 2. The estimated risk of prediabetes by percent intakes of added sugar (<10%, 10-15%, >15% added sugar calories in grams) were reported in unadjusted and adjusted models (Table 5). In the unadjusted model, the estimated risk for prediabetes was 26.3%

for the <10% usual intake group and 28.6% for 10-15% usual intake group. In the adjusted model, the estimated risk for prediabetes was 27.5% risk for the <10% usual intake group and 29% for the >15% usual intake group (Table 5). Similar to the findings from the total added sugar consumption models (Table 3), the differences in model-estimated risks were of a very small magnitude and not significantly different from one another (Table 5).

Total and Percent Intake of Added Sugar by Race and Ethnicity

Results from these sensitivity analyses (Table 6 and 7) indicated that the association between added sugar consumption and risk for prediabetes did not differ by race/ethnicity (Type 3 tests for interaction of race/ethnicity by total added sugar: unadjusted model [$p = .65$]; adjusted model [$p = .51$] and percent intake of added sugar: unadjusted model [$p = .12$]; adjusted model [$p = .24$]). However, overall model-estimated risks for prediabetes did differ between race/ethnicity groups. For total added sugar, the adjusted model-estimated risk for prediabetes was highest among non-Hispanic Blacks and lowest among non-Hispanic Whites (39% vs 16% mean intake, respectively). Similarly, for percent intakes of added sugar, the adjusted model-estimated risk for prediabetes was greatest for non-Hispanic blacks and lowest for non-Hispanic Whites (Table 7). Among non-Hispanic Whites, greater consumption correlated with a greater risk for prediabetes (16% risk for <10% added sugar and 19% risk for >15% added sugar) not observed for non-Hispanic Blacks who had the greatest risk for prediabetes (43%) at consumption levels of <10%. Similar to findings from the main analysis, there were no significant differences in the model-estimated risk of prediabetes at mean and quartiles

ranges for total added sugar and by percent intakes of added sugar. In all models, the estimated differences in risk by added sugar intake within each race/ethnicity groups were of a very small magnitude and not significantly different from one another.

Discussion

To our knowledge, this is the first study to examine the association between total added sugar consumption and prediabetes risk in a large nationally representative U.S. adult sample. In our sample of 13,406 adults, added sugars accounted for 10.1% of total calories for adults with normoglycemia, whereas adults with prediabetes consumed approximately 10.4%. Overall, the study findings suggest that after controlling for total energy intake, BMI, and pertinent health behaviors and sociodemographic factors, consumption of total added sugar does not increase the odds of having prediabetes in U.S. adults ≥20 years.

The findings from this study differ from our hypothesis that total added sugar consumption would increase the risk of prediabetes. Both observational and experimental findings on this topic are mixed with some studies supporting that added sugars increase the risk for prediabetes (Faeh et al., 2005; Green et al., 2014; Lana et al., 2014; Lê et al., 2009; Lecoultre et al., 2013; Ma et al., 2016; Teshima et al., 2015; Weber et al., 2018) and others reporting no relationship (Biggelaar et al., 2017; Black et al., 2006; Brynes et al.; Lewis et al., 2013; Lowndes et al., 2015; Matikainen et al.; Raben et al.). Differences between study designs (observational, experimental), characterization of prediabetes risk, length of intervention(s), inclusion of representative minority groups, and dietary intake estimates, including the use of proxies such as SSB or fructose-only beverages, in lieu of

total added sugar from all sources as in our study has likely contributed to the inconsistent findings. For example, metabolic indicators of prediabetes risk (i.e., insulin resistance and reduced insulin sensitivity) have been highly variable between experimental and observational studies. In experimental studies, insulin resistance has been measured using either the hyperinsulinemic clamp (Aeberli et al., 2013; Black et al., 2006; DeFronzo et al., 1979; Faeh et al., 2005; Lewis et al., 2013) or the homeostatic model assessment of insulin resistance (HOMA-IR) (Brynes et al., 2003; Lowndes et al., 2015; Matthews et al., 1985; Raben et al., 2001) whereas insulin sensitivity has been measure with the hyperinsulinmeic-euglycemic clamp (Aeberli et al., 2013; Lê et al., 2009; Lecoultre et al., 2013; Stanhope et al., 2009), the hepatic insulin sensitivity index (Lecoultre et al., 2013), or a 75 g oral-glucose tolerance test (OGTT) (Stanhope et al., 2009). The majority of studies have used a cross-over design with ≥ 4-week washout periods (Black et al., 2006; Brynes et al., 2003; Faeh et al., 2005; Lê et al., 2009; Lecoultre et al., 2013; Lewis et al., 2013). In observational studies, HOMA-IR has commonly been used to assess insulin resistance (Green et al., 2014; Lana et al., 2014; Ma et al., 2016; Teshima et al., 2015). Interestingly, only a single, prospective cohort study has reported a significant association between added sugar and incident prediabetes measured via fasting plasma glucose or OGTT (Ma et al., 2016). In our study, prediabetes risk was identified with HgbA1c which is a unique distinction from other studies. The American Diabetes Associations considers HgbA1c a highly reliable individual estimate for prediabetes in adults (ADA, 2020). This fact, paired with NHANES collecting HgbA1c in over half of participants ≥ 12 years of age allowed us to include a large

sample with prediabetes in our study (National Health and Nutrition Examination Survey, 2020).

Sample characteristics have also widely varied between studies with experimental studies predominately using a homogenous sample of either male-only (Aeberli et al., 2013; Black et al., 2006; Brynes et al., 2003; Faeh et al., 2005; Lê et al., 2009; Lecoultre et al., 2013) or female-only participants (Raben et al., 2001) whereas observational studies have mainly included heterogeneous samples (Green et al., 2014; Lana et al., 2014; Ma et al., 2016; Teshima et al., 2015). Overall, these studies did not include diverse populations consisting of different racial and ethnic groups and thus lack generalizability. Thus, a strength of our study was the inclusion of a diverse and heterogeneous population that explicitly tested whether the associations between added sugar consumption and prediabetes differed by race/ethnicity. Given the significant disparities in prediabetes and T2D rates in minority groups such as non-Hispanic Blacks and Hispanics, in comparison to non-Hispanic Whites, as well as their greater consumption of added sugar, replication of our findings is warranted. In addition, our lack of significant associations by race/ethnicity status indicates a need for future studies that directly compare total added sugar's effects on prediabetes risk factors (e.g., insulin resistance measures) by race/ethnicity. Future studies that assess whether consumption of specific types of added sugars (i.e., fructose, sucrose, HFCS) promote diverging metabolic consequences in minority populations is also warranted. These studies could provide clarity about added sugar's role on risk for prediabetes in minority populations.

BMI is also an important prediabetes and T2D risk factor since overweight and obesity are causally linked to these conditions (CDC, 2020c). In our study, adjusted

models controlled for BMI (kg/m^2). However, in experimental studies, added sugar's direct effects on prediabetes risk factors (e.g., insulin resistance) have been examined in normal weight-only (BMI 18.5 – 24.9 kg/m^2) and overweight and/or obese-only adults (BMI > 25 kg/m^2) without the use of weight-maintaining diets (Aeberli et al., 2013; Brynes et al., 2003; Lê et al., 2009; Lecoultre et al., 2013; Matikainen et al., 2017; Stanhope et al., 2009). As such, the weight-independent effects of added sugar on risk for prediabetes from these studies cannot be determined.

Operationalization of added sugar has varied widely between studies, likely confounding the effects of added sugar on metabolic outcomes. For example, a plethora of observational studies have primarily relied on added sugar proxies, such as SSB sweetened with HFCS, to approximate total added sugar consumption (Barrio-Lopez et al., 2013; Dhingra et al., 2007; Green et al., 2014; Lana et al., 2014; Ma et al., 2016; Teshima et al., 2015) which are strongly correlated to risk for prediabetes and T2D. In addition, experimental studies have reported significant effects between added sugar and indicators of prediabetes risk with exaggerated concentrations of fructose (>15% total caloric intake) (Aeberli et al., 2013; Faeh et al., 2005; Lê et al., 2009; Lecoultre et al., 2013; Stanhope et al., 2009) not commonly consumed by most Americans (average is 9.1% of total energy from fructose) (Marriott et al., 2009). Greater fructose consumption (15% to ≥ 25% of total energy) has been shown to impair insulin resistance (Faeh et al., 2005; Lê et al., 2009; Lecoultre et al., 2013), increase fasting plasma glucose concentrations (Stanhope et al., 2009), and decrease insulin sensitivity (Lê et al., 2009; Lecoultre et al., 2013; Stanhope et al., 2009). For our study, we assessed total added sugar from all sources (i.e., food and beverages) regardless of the type of added sugar.

Thus, lack of standardization for total added sugar estimates and differences in the level of measurement of total added sugar (i.e., ordinal versus continuous) confounds between study finding comparisons. Also for our study, we categorized total added sugar into three groups (<10%, 10-15%, and >15% for total energy intake) to represent dietary guideline recommendations, average U.S. consumption levels, and above average intake levels (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2020). Other studies, however, have used different amounts to represent below average, average, or above average intake (e.g., 10%, 18%, 25%) (Black et al., 2006; Lowndes et al., 2015; Stanhope et al., 2009).

Interestingly, our study observed that total added sugar consumption was relatively lower in our sample (i.e., 10.2% total caloric intake) compared to prior (2015) and recent (2020) population estimates reported at 13% (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2020). These differences in consumption are likely due to a few reasons. First, our study only included adults ≥20 years with normoglycemia and prediabetes. This differs from national estimates which calculate intakes for the entire U.S. population, including children (ages 9-13) and adolescents who consume the most added sugar compared to any other age group. Secondly, added sugar in our study was based on two days of dietary recall data that allowed us to estimate the "usual" mean intake for our population which is in contrast to population estimates for added sugar that use a single day of dietary recall data to estimate average "mean" intake (Tooze et al., 2010; U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2020). Nonetheless, findings from our study suggest that adults with normoglycemia and prediabetes appear to closely follow

the U.S. dietary guideline recommendation for added sugar as evidence of their consumption rates of 10.1% and 10.4% respectively (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2020). Whether this has been a conscious effort by these groups to follow the guidelines or is the result of public health initiatives that have restricted added sugar intake in the U.S. (e.g., soda taxes) is unclear. Future studies comparing differences in mean and usual intakes of added sugar by age groups (with/without prediabetes) are needed to establish trends over time.

To our knowledge, no studies have examined if *total* consumption of added sugar, from all dietary sources, is associated with an increased risk for prediabetes in adults. It is possible that grouping total added sugars from all sources in a single category, in lieu of examination of added sugar by type (fructose, glucose, sucrose) and/or source (solid foods versus beverages) in our study contributed to the lack of significant associations observed. Yet, our study findings are not in complete contrast to what has previously been reported about consumption of added sugar at amounts <15% total caloric intake (Lowndes et al., 2015; Matikainen et al., 2017; Weber et al., 2018), and it is possible that lower total consumption (~10%) may protect against developing prediabetes. However, this should be confirmed in prospective cohort and experimental studies. Additionally, few studies have examined if the effect of total added sugar consumption from liquid versus solid foods influences metabolic risk factors (including insulin resistance) in adults (O'Connor et al., 2018) and therefore, should be examined in future studies.

Strengths and Limitations

This study has some major strengths. To our knowledge, this is the first study to assess the associations between total and percent intakes of added sugar and risk for prediabetes in a nationally representative sample of U.S. adults. We also assessed differences by race and ethnicity status to improve the generalizability of our results. Additionally, we used steps outlined by the NCI method to estimate usual mean and percent intakes for added sugar which allowed us to account for between- and within-person variation in intake (National Cancer Institute; Tooze et al., 2010).

This study also has limitations. First, the cross-sectional nature of this study did not allow for the assessment of causal or temporal inferences between added sugar and risk for prediabetes. Second, we used self-reported 24-hour dietary recalls to estimate usual intake of added sugars and total calories which may be subject to under- or overreporting. However, use of the AMNP method, which has been found to accurately estimate usual nutrient intake, may have reduced this concern (Moshfegh et al., 2008; Rhodes et al., 2013). We also estimated usual mean intake of added sugar using steps outlined by the NCI method. However, we did not use the SAS macro provided by NCI which may have resulted in slightly different estimates for usual added sugar and total calorie intake compared to similar studies using NHANES data between 2013-2018 (National Cancer Institute, 2020). Usual intake estimates for added sugar in our study were similar to previous population-based estimates from NHANES data (S. A. Bowman et al., 2017) implicating the soundness of our dietary assessment method. Third, using HgbA1c as the primary estimate for prediabetes may have resulted in our lack of significant findings since some studies have reported no associations between added

sugar consumption and HgbA1c while concurrently observing significant associations with measures of insulin resistance (HOMA-IR) (Lana et al., 2014; O'Connor et al., 2018).

Conclusions

Results from our cross-sectional analysis revealed that consumption of total added sugar, which in our study averaged ~10% of total energy intake, was not statistically, significantly associated with prediabetes in U.S. adults. Due to the limitations inherent in a cross-sectional observational study, including self-reported dietary intake, prospective cohort and experimental studies are needed to further assess whether the consumption of added sugar is associated with prediabetes in adults.

References

Aeberli, I., Gerber, P. A., Hochuli, M., Kohler, S., Haile, S. R., Gouni-Berthold, I., Berthold, H. K., Spinas, G. A., & Berneis, K. (2011). Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: A randomized controlled trial. *American Journal of Clinical Nutrition, 94*(2), 479-485. https://doi.org/10.3945/ajcn.111.013540

Aeberli, I., Hochuli, M., Gerber, P. A., Sze, L., Murer, S. B., Tappy, L., Spinas, G. A., & Berneis, K. (2013). Moderate amounts of fructose consumption impair insulin sensitivity in healthy young men: A randomized controlled trial. *Diabetes Care, 36*(1), 150-156. https://doi.org/10.2337/dc12-0540

Ahluwalia, N., Dwyer, J., Terry, A., Moshfegh, A., & Johnson, C. (2016). Update on NHANES dietary data: Focus on collection, release, analytical considerations, and uses to inform public policy. *Advances in Nutrition, 7*(1), 121-134. https://doi.org/10.3945/an.115.009258

Ali, M. K., Bullard, K. M., Saydah, S., Imperatore, G., & Gregg, E. W. (2018). Cardiovascular and renal burdens of prediabetes in the USA: Analysis of data from serial cross-sectional surveys, 1988-2014. *The Lancet. Diabetes & endocrinology, 6*(5), 392-403. https://doi.org/10.1016/S2213-8587(18)30027-5

Allister, P. C., & Stanhope, K. L. (2016). Understanding the impact of added sugar consumption on risk for type 2 diabetes. *Journal - California Dental Association, 44*(10), 619-626.

American Diabetes Association. (2020). 2. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2020. *Diabetes Care, 43*(Suppl 1), S14.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*(6), 1173-1182. https://doi.org/10.1037//0022-3514.51.6.1173

Barrio-Lopez, M. T., Martinez-Gonzalez, M. A., Fernandez-Montero, A., Beunza, J. J., Zazpe, I., & Bes-Rastrollo, M. (2013). Prospective study of changes in sugar-sweetened beverage consumption and the incidence of the metabolic syndrome and its components: The SUN cohort. *British Journal of Nutrition, 110*(9), 1722-1731. https://doi.org/10.1017/S0007114513000822

Basiak, A., Różańska, D., Połtyn–Zaradna, K., Wołyniec, M., Szuba, A., & Zatońska, K. (2019). Comparison of intake of food groups between participants with normoglycemia, impaired fasting glucose, and type 2 diabetes in PURE Poland population. *International Journal of Diabetes in Developing Countries, 39*(2), 315-324. https://doi.org/10.1007/s13410-018-0675-5

Bauer, F., Beulens, J. W. J., Van Der, A. D. L., Wijmenga, C., Grobbee, D. E., Spijkerman, A. M. W., Van Der Schouw, Y. T., & Onland-Moret, N. C. (2013). Dietary patterns and the risk of type 2 diabetes in overweight and obese

individuals. *European Journal of Nutrition*, *52*(3), 1127-1134. https://doi.org/10.1007/s00394-012-0423-4

Biggelaar, L. J., Eussen, S. J., Sep, S. J., Mari, A., Ferrannini, E., Dongen, M. C., Denissen, K. F., Wijckmans, N. E., Schram, M. T., Kallen, C. J., Koster, A., Schaper, N., Henry, R. M., Stehouwer, C. D., & Dagnelie, P. C. (2017, Apr 13). Associations of dietary glucose, fructose, and sucrose with beta-cell function, insulin sensitivity, and type 2 diabetes in the maastricht study. *Nutrients*, *9*(4). https://doi.org/10.3390/nu9040380

Black, R. N., Spence, M., McMahon, R. O., Cuskelly, G. J., Ennis, C. N., McCance, D. R., Young, I. S., Bell, P. M., & Hunter, S. J. (2006). Effect of eucaloric high- and low-sucrose diets with identical macronutrient profile on insulin resistance and vascular risk: a randomized controlled trial. *Diabetes*, *55*(12), 3566-3572. https://doi.org/10.2337/db06-0220

Bowman, S. (2017). Added sugars: Definition and estimation in the USDA Food Patterns Equivalents Databases. *2019*(March 28). https://doi.org/10.1016/j.jfca.2017.07.013

Bowman, S., Clemens, J., Friday, J., Lynch, K., & Moshfegh, A. (2017). *Food Patterns Equivalents Database 2013-14: Methodology and user guide*. U.S. Department of Agriculture. Retrieved March 28, 2020 from http://www.ars.usda.gov/nea/bhnrc/fsrg

Bowman, S. A., Clemens, J. C., Martin, C. L., Anand, J., Steinfeldt, L. C., & Moshfegh, A. J. (2017). *Added sugars intake of Americans: What We Eat in America, NHANES 2013-2014.* Food Surveys Research Group. Retrieved April 18, 2020

from https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/DBrief/18_Added_Sugars_Intake_of_Americans_2013-2014.pdf

Brynes, A. E., Mark Edwards, C., Ghatei, M. A., Dornhorst, A., Morgan, L. M., Bloom, S. R., & Frost, G. S. (2003). A randomised four-intervention crossover study investigating the effect of carbohydrates on daytime profiles of insulin, glucose, non-esterified fatty acids and triacylglycerols in middle-aged men. *British Journal of Nutrition, 89*(2), 207-218. https://doi.org/10.1079/bjn2002769

Centers for Disease Control and Prevention. (2017). *About the National Health and Nutrition Examination Survey*. Centers for Disease Control and Prevention and National Center for Health Statistics. Retrieved December 9, 2020 from https://www.cdc.gov/nchs/nhanes/about_nhanes.htm

Centers for Disease Control and Prevention. (2018). *National Health and Nutrition Examination Survey (NHANES): Analytic guidelines, 2011-2014 and 2015-2016*. Centers for Disease Control and Prevention. Retrieved February 22, 2021 from https://wwwn.cdc.gov/nchs/data/nhanes/2011-2012/analyticguidelines/analytic_guidelines_11_16.pdf

Centers for Disease Control and Prevention. (2020a). *About adult BMI*. U.S. Department of Health and Human Services. Retrieved August 27, 2020 from https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html

Centers for Disease Control and Prevention. (2020b). National diabetes statistics report, 2020. *Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services*, 12-15.

Centers for Disease Control and Prevention. (n.d.). *NHANES 2013-2014 Laboratory methods- laboratory procedure manual: Glycohemoglobin*. Retrieved March 28, 2020 from https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/labmethods/GHB_H_MET_GLYCOHEMOGLOBIN.pdf

Chen, G. C., Koh, W. P., Neelakantan, N., Yuan, J. M., Qin, L. Q., & van Dam, R. M. (2018). Diet quality indices and risk of type 2 diabetes mellitus: The Singapore Chinese Health Study. *American Journal of Epidemiology, 187*(12), 2651-2661. https://doi.org/10.1093/aje/kwy183

DeFronzo, R. A., Tobin, J. D., & Andres, R. (1979). Glucose clamp technique: a method for quantifying insulin secretion and resistance. *American Journal of Physiology-Endocrinology And Metabolism, 237*(3), E214.

Dhingra, R., Sullivan, L., Jacques, P. F., Wang, T. J., Fox, C. S., Meigs, J. B., D'Agostino, R. B., Gaziano, J. M., Vasan, R. S., Dhingra, R., Sullivan, L., Jacques, P. F., Wang, T. J., Fox, C. S., Meigs, J. B., D'Agostino, R. B., Gaziano, J. M., & Vasan, R. S. (2007). Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. *Circulation, 116*(5), 480-488. http://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=105995076&site=ehost-live

DiNicolantonio, J. J., O'Keefe, J. H., & Lucan, S. C. (2015). Added fructose: A principal driver of type 2 diabetes mellitus and its consequences. *Mayo Clinic Proceedings, 90*(3), 372-381. https://doi.org/10.1016/j.mayocp.2014.12.019

Esposito, K., Kastorini, C.-M., Panagiotakos, D. B., & Giugliano, D. (2010). Prevention of type 2 diabetes by dietary patterns: A systematic review of prospective studies and meta-analysis. *Metabolic syndrome and related disorders, 8*(6), 471-476. https://www.liebertpub.com/doi/10.1089/met.2010.0009?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

Faeh, D., Minehira, K., Schwarz, J. M., Periasamy, R., Park, S., & Tappy, L. (2005). Effect of fructose overfeeding and fish oil administration on hepatic de novo lipogenesis and insulin sensitivity in healthy men. *Diabetes, 54*(7), 1907-1913. https://doi.org/10.2337/diabetes.54.7.1907

Fitch, C., & Keim, K. S. (2012). Position of the Academy of Nutrition and Dietetics: Use of nutritive and nonnutritive sweeteners. *Journal of the Academy of Nutrition and Dietetics, 112*(5), 739-758. https://doi.org/10.1016/j.jand.2012.03.009

Glechner, A., Keuchel, L., Affengruber, L., Titscher, V., Sommer, I., Matyas, N., Wagner, G., Kien, C., Klerings, I., & Gartlehner, G. (2018). Effects of lifestyle changes on adults with prediabetes: A systematic review and meta-analysis. *Primary Care Diabetes*, *12*(5), 393-408. https://www.primary-care-diabetes.com/article/S1751-9918(18)30196-7/pdf

Gower, B. A., & Fowler, L. A. (2020). Obesity in African-Americans: The role of physiology. *Journal of Internal Medicine, 288*(3), 295-304. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/joim.13090?download=true

Green, A. K., Jacques, P. F., Rogers, G., Fox, C. S., Meigs, J. B., & McKeown, N. M. (2014). Sugar-sweetened beverages and prevalence of the metabolically abnormal

phenotype in the Framingham Heart Study. *Obesity, 22*(5), E157-E163. https://doi.org/10.1002/oby.20724

Hales, C. M., Carroll, M. D., Fryar, C. D., & Ogden, C. L. (2020). Prevalence of obesity and severe obesity among adults: United States, 2017–2018. Hyattsville, MD: National Center for Health Statistis. NCHS Data Brief, no 360.

Hite, A. H., Feinman, R. D., Guzman, G. E., Satin, M., Schoenfeld, P. A., & Wood, R. J. (2010). In the face of contradictory evidence: Report of the Dietary Guidelines for Americans Committee. *Nutrition, 26*(10), 915-924.

Johnson, C. L., Dohrmann, S. M., Burt, V., & Mohadjer, L. K. (2014). National Health and Nutrition Examination Survey: Sample design, 2011–2014. *Vital and Health Statistics. Series 2, Data Evaluation and Methods Research*, (162), 1–33.

Johnson, R. J., Sanchez-Lozada, L. G., Andrews, P., & Lanaspa, M. A. (2017). Perspective: A Historical and scientific perspective of sugar and its relation with obesity and diabetes. *Advances in Nutrition, 8*(3), 412-422. https://doi.org/10.3945/an.116.014654

Kritchevsky, D. (1998). History of recommendations to the public about dietary fat. *The Journal of Nutrition, 128*(2), 449S-452S. https://doi.org/10.1093/jn/128.2.449S

Lana, A., Rodríguez-Artalejo, F., & Lopez-Garcia, E. (2014). Consumption of sugar-sweetened beverages is positively related to insulin resistance and higher plasma leptin concentrations in men and nonoverweight women. *Journal of Nutrition, 144*(7), 1099-1105. https://doi.org/10.3945/jn.114.195230

Lê, K. A., Ith, M., Kreis, R., Faeh, D., Bortolotti, M., Tran, C., Boesch, C., & Tappy, L. (2009). Fructose overconsumption causes dyslipidemia and ectopic lipid

deposition in healthy subjects with and without a family history of type 2 diabetes. *American Journal of Clinical Nutrition, 89*(6), 1760-1765. https://doi.org/10.3945/ajcn.2008.27336

Lecoultre, V., Egli, L., Carrel, G., Theytaz, F., Kreis, R., Schneiter, P., Boss, A., Zwygart, K., Le, K. A., Bortolotti, M., Boesch, C., & Tappy, L. (2013). Effects of fructose and glucose overfeeding on hepatic insulin sensitivity and intrahepatic lipids in healthy humans. *Obesity (Silver Spring), 21*(4), 782-785. https://doi.org/10.1002/oby.20377

Lewis, A. S., McCourt, H. J., Ennis, C. N., Bell, P. M., Courtney, C. H., McKinley, M. C., Young, I. S., & Hunter, S. J. (2013). Comparison of 5% versus 15% sucrose intakes as part of a eucaloric diet in overweight and obese subjects: Effects on insulin sensitivity, glucose metabolism, vascular compliance, body composition and lipid profile. A randomised controlled trial. *Metabolism: Clinical and Experimental, 62*(5), 694-702. https://doi.org/10.1016/j.metabol.2012.11.008

Lowndes, J., Sinnett, S. S., & Rippe, J. M. (2015). No Effect of Added Sugar Consumed at Median American Intake Level on Glucose Tolerance or Insulin Resistance. *Nutrients, 7*(10), 8830-8845. https://doi.org/10.3390/nu7105430

Ma, J., Jacques, P. F., Meigs, J. B., Fox, C. S., Rogers, G. T., Smith, C. E., Hruby, A., Saltzman, E., & McKeown, N. M. (2016). Sugar-Sweetened beverage but not diet soda consumption is positively associated with progression of insulin resistance and prediabetes. *Journal of Nutrition, 146*(12), 2544-2550. https://doi.org/10.3945/jn.116.234047

Maersk, M., Belza, A., Stødkilde-Jørgensen, H., Ringgaard, S., Chabanova, E., Thomsen, H., Pedersen, S. B., Astrup, A., & Richelsen, B. (2011). Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study. *The American Journal of Clinical Nutrition, 95*(2), 283-289. https://doi.org/10.3945/ajcn.111.022533

Malik, V. S., & Hu, F. B. (2015). Fructose and cardiometabolic health: What the evidence from sugar-sweetened beverages tells us. *Journal of the American College of Cardiology*, *66*(14), 1615-1624. https://doi.org/10.1016/j.jacc.2015.08.025

Marriott, B. P., Cole, N., & Lee, E. (2009). National estimates of dietary fructose intake increased from 1977 to 2004 in the United States. *Journal of Nutrition, 139*(6), 1228s-1235s. https://doi.org/10.3945/jn.108.098277

Matikainen, N., Söderlund, S., Björnson, E., Bogl, L. H., Pietiläinen, K. H., Hakkarainen, A., Lundbom, N., Eliasson, B., Räsänen, S. M., Rivellese, A., Patti, L., Prinster, A., Riccardi, G., Després, J. P., Alméras, N., Holst, J. J., Deacon, C. F., Borén, J., & Taskinen, M. R. (2017). Fructose intervention for 12 weeks does not impair glycemic control or incretin hormone responses during oral glucose or mixed meal tests in obese men. *Nutrition, Metabolism & Cardiovascular Diseases, 27*(6), 534-542. https://doi.org/10.1016/j.numecd.2017.03.003

Matthews, D. R., Hosker, J. P., Rudenski, A. S., Naylor, B. A., Treacher, D. F., & Turner, R. C. (1985). Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia, 28*(7), 412-419. https://doi.org/10.1007/bf00280883

Moshfegh, A. J., Rhodes, D. G., Baer, D. J., Murayi, T., Clemens, J. C., Rumpler, W. V., Paul, D. R., Sebastian, R. S., Kuczynski, K. J., & Ingwersen, L. A. (2008). The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *The American Journal of Clinical Nutrition, 88*(2), 324-332. https://doi.org/ 10.1093/ajcn/88.2.324

National Cancer Institute. (2020). *Usual dietary intakes: The NCI method*. Retrieved February 22, 2021 from https://epi.grants.cancer.gov/diet/usualintakes/method.html

National Center for Health Statistics. (2017). *NCHS Research Ethics Review Board (ERB) approval*. Centers for Disease Control and Prevention and National Center for Health Statistics. Retrieved April 17, 2020 from https://www.cdc.gov/nchs/nhanes/irba98.htm

National Health and Nutrition Examination Survey. (2020). *Glycohemoglobin (GHB-J)*. Centers for Disease Control and Prevention and National Center for Health Statistics. https://wwwn.cdc.gov/Nchs/Nhanes/2017-2018/GHB_J.htm#LBXGH

O'Connor, L., Imamura, F., Brage, S., Griffin, S. J., Wareham, N. J., & Forouhi, N. G. (2018). Intakes and sources of dietary sugars and their association with metabolic and inflammatory markers. *Clinical Nutrition, 37*(4), 1313-1322. https://doi.org/10.1016/j.clnu.2017.05.030

Office for Human Research Protections. (2018). *Revised Common Rule regulatory text*. Office for Human Research Protections. Retrieved April 17, 2020 from https://www.hhs.gov/ohrp/regulations-and-policy/regulations/revised-common-rule-regulatory-text/index.html

Plantinga, L. C., Crews, D. C., Coresh, J., Miller, E. R., Saran, R., Yee, J., Hedgeman, E., Pavkov, M., Eberhardt, M. S., & Williams, D. E. (2010). Prevalence of chronic kidney disease in US adults with undiagnosed diabetes or prediabetes. *Clinical Journal of the American Society of Nephrology, 5*(4), 673-682.

Raben, A., Holst, J. J., Madsen, J., & Astrup, A. (2001). Diurnal metabolic profiles after 14 d of an ad libitum high-starch, high-sucrose, or high-fat diet in normal-weight never-obese and postobese women. *American Journal of Clinical Nutrition, 73*(2), 177-189. http://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=107020468&site=ehost-live

Rhodes, D. G., Murayi, T., Sebastian, R. S., Clemens, J. C., Baer, D. J., & Moshfegh, A. J. (2013). The USDA Automated Multiple-Pass Method accurately assesses population sodium intakes. *The American Journal of Clinical Nutrition, 97*(5), 958-964. https://doi.org/10.3945/ajcn.112.044982

Stanhope, K. L., Medici, V., Bremer, A. A., Lee, V., Lam, H. D., Nunez, M. V., Chen, G. X., Keim, N. L., & Havel, P. J. (2015). A dose-response study of consuming high-fructose corn syrup-sweetened beverages on lipid/lipoprotein risk factors for cardiovascular disease in young adults. *American Journal of Clinical Nutrition, 101*(6), 1144-1154. https://doi.org/10.3945/ajcn.114.100461

Stanhope, K. L., Schwarz, J. M., Keim, N. L., Griffen, S. C., Bremer, A. A., Graham, J. L., Hatcher, B., Cox, C. L., Dyachenko, A., Zhang, W., McGahan, J. P., Seibert, A., Krauss, R. M., Chiu, S., Schaefer, E. J., Ai, M., Otokozawa, S., Nakajima, K., Nakano, T., Beysen, C., Hellerstein, M. K., Berglund, L., & Havel, P. J. (2009).

Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *Journal of Clinical Investigation, 119*(5), 1322-1334. https://doi.org/10.1172/JCI37385

Tabak, A. G., Herder, C., Rathmann, W., Brunner, E. J., & Kivimaki, M. (2012). Prediabetes: a high-risk state for diabetes development. *Lancet, 379*(9833), 2279-2290. https://doi.org/10.1016/s0140-6736(12)60283-9

Teng, A., Blakely, T., Scott, N., Jansen, R., Masters-Awatere, B., Krebs, J., & Oetzel, J. (2019). What protects against pre-diabetes progressing to diabetes? Observational study of integrated health and social data. *Diabetes Research and Clinical Practice, 148*, 119-129. https://doi.org/10.1016/j.diabres.2018.12.003

Teshima, N., Shimo, M., Miyazawa, K., Konegawa, S., Matsumoto, A., Onishi, Y., Sasaki, R., Suzuki, T., Yano, Y., Matsumoto, K., Yamada, T., Gabazza, E. C., Takei, Y., & Sumida, Y. (2015). Effects of sugar-sweetened beverage intake on the development of type 2 diabetes mellitus in subjects with impaired glucose tolerance: The Mihama diabetes prevention study [Article]. *Journal of Nutritional Science and Vitaminology, 61*(1), 14-19. https://doi.org/10.3177/jnsv.61.14

Tooze, J. A., Kipnis, V., Buckman, D. W., Carroll, R. J., Freedman, L. S., Guenther, P. M., Krebs-Smith, S. M., Subar, A. F., & Dodd, K. W. (2010). A mixed-effects model approach for estimating the distribution of usual intake of nutrients: The NCI method. *Statistics in Medicine, 29*(27), 2857-2868. https://doi.org/10.1002/sim.4063

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (2020). *Dietary Guidelines for Americans, 2020-2025*. Retrieved January 28, 2021 from DietaryGuidelines.gov

U.S. Department of Health and Human Services and U.S. Department of Agriculture. (2015). *2015 - 2020 Dietary Guidelines for Americans* (8th ed.) https://health.gov/our-work/food-nutrition/previous-dietary-guidelines/2015.

United States Food and Drug Administration. (2020). *Added sugars on the new nutrition facts label*. U.S. Food and Drug Administration Retrieved November 3, 2020 from https://www.fda.gov/food/new-nutrition-facts-label/added-sugars-new-nutrition-facts-label

University of Alabama at Birmingham: Institutional Review Board (IRB). (n.d.). *Is IRB review required for use of public datasets?* Retrieved October 30, 2020 from https://www.uab.edu/research/administration/offices/IRB/FAQs/Pages/PublicDatasets.aspx

Ward, Z. J., Bleich, S. N., Cradock, A. L., Barrett, J. L., Giles, C. M., Flax, C., Long, M. W., & Gortmaker, S. L. (2019). Projected U.S. state-level prevalence of adult obesity and severe obesity. *New England Journal of Medicine, 381*(25), 2440-2450. https://doi.org/10.1056/NEJMsa1909301

Weber, K. S., Simon, M.-C., Markgraf, D. F., Szendroedi, J., Müssig, K., Roden, M., Strassburger, K., & Buyken, A. E. (2018). Habitual fructose intake relates to insulin sensitivity and fatty liver index in recent-onset type 2 diabetes patients and individuals without diabetes. *Nutrients, 10*(6), 774. https://doi.org/10.3390/nu10060774

World Health Organization. (2016). *Global report on diabetes*. World Health Organization. https://books.google.com/books?id=tNsEkAEACAAJ

Zhu, Y., Sidell, M. A., Arterburn, D., Daley, M. F., Desai, J., Fitzpatrick, S. L., Horberg, M. A., Koebnick, C., McCormick, E., Oshiro, C., Young, D. R., & Ferrara, A. (2019). Racial/ethnic disparities in the prevalence of diabetes and prediabetes by BMI: Patient Outcomes Research To Advance Learning (PORTAL) multisite cohort of adults in the U.S. *Diabetes Care, 42*(12), 2211. https://doi.org/10.2337/dc19-0532

Zipf, G., Chiappa, M., Porter, K. S., Ostchega, Y., Lewis, B. G., & Dostal, J. (2013). National Health and Nutrition Examination Survey plan and operations, 1999-2010. *Vital and Health Statistics, 1*(56). https://www.cdc.gov/nchs/data/series/sr_01/sr01_056.pdf

Table 1. Overall characteristics of adults ≥20 years and by normoglycemia and prediabetes status, the NHANES 2013- 2018

Characteristics	Overall, % (SE)	Normoglycemia, % (SE)	Prediabetes % (SE)	*p* value
Age (years)		N = 8,905	N = 4,501	<.0001
	47.1 (.30)	43.5 (.34)	56.8 (.38)	
Gender		N = 8,905	N = 4,501	.13
Female	52 (.47)	51.6 (.84)	46.9 (.84)	
Male	48 (.47)	48.4 (.53)	53.1 (.53)	
Race/ethnicity		N = 8,905	N = 4,501	<.0001
Non-Hispanic White	65.3 (1.85)	67.6 (1.82)	59.2 (2.12)	
Non-Hispanic Black	10.5 (.98)	8.6 (.81)	15.6 (.1.47)	
Hispanic	15.1 (1.32)	15 (1.32)	15.3 (.1.44)	
Other Race	9.1 (.64)	8.8 (.63)	9.9(.85)	
BMI status[a]		N = 8,809	N = 4,449	<.0001
Underweight ≤ 18.49 kg/m^2	1.6 (.13)	1.8 (.14)	.9 (.29)	
Normal 18.5-24.99 kg/m^2	27.9 (.72)	32.2 (.82)	16.4 (.75)	
Overweight 25-29.99 kg/m^2	32.8(.56)	33 (.70)	32.3 (1.11)	
Obese ≥30 kg/m^2	37.7(.85)	33 (1.00)	50.4 (1.13)	
Physical activity status[b]		N = 8,904	N = 4,500	<.0001
Sedentary	44.1 (1.03)	40.7 (1.15)	53.1 (1.21)	
Physically active	55.9 (1.03)	59.3 (1.15)	46.8 (1.21)	
Smoking status[c]		N = 8,184	N = 4,179	.38
Smoker	21.9 (.74)	22.2 (.88)	21.1 (1.09)	
Non-smoker	78.1 (.74)	77.7 (.88)	78.9 (1.09)	
Education[d]		N = 8,900	N = 4,492	<.0001
< High school degree	12.9 (.80)	11.3 (.77)	17.2 (1.19)	
High school degree	23.1 (.82)	22.2 (.89)	25.4 (.1.04)	
> High school degree	64 (1.30)	66.5 (.1.36)	57.4 (1.55)	
Annual household income		N = 7,936	N = 3,936	<.0001
< $20,000	12.5 (.76)	11.4 (.84)	15.4 (1.13)	
$20,000-99,000	58 (1.17)	56.9 (1.31)	61.1 (.1.45)	

≥ 100,000	29.5 (1.51)	31.7 (1.63)	23.4 (1.6)	
HgbA1c (%)[e]		N = 8,905	N = 4,501	<.0001
	5.43% (.006)	5.24% (.004)	5.91% (.004)	
Percent intakes of total added sugar[f]		N = 7,072	N = 3,559	.37
% of participants with <10% calories from added sugars	52.5 (1.07)	53.1 (1.27)	50.9 (1.52)	
% of participants with 10-15% calories from added sugars	29.1 (.73)	28.6 (1.01)	30.6 (1.15)	
% of participants with >15% calories from added sugars	18.4 (.89)	18.3 (.95)	18.5 (1.25)	
Usual mean intakes for total calories and total added sugar		N = 7,072	N = 3,599	
Total calories (kcal/day)	1858.5 (7.9)	1866.4 (9.25)	1837.4 (10.32)	.0058
Added sugars (g/day)	49.4 (.66)	49.3 (.72)	49.8 (.97)	.677
Added sugars (kcal/day)	194.6 (2.6)	194.1 (2.92)	196.1 (3.90)	.6829
Added sugar calories (%)	10.2 (.12)	10.1 (.13)	10.4 (.19)	.4587

BMI (body mass index); HgbA1c (hemoglobin a1c); g (grams); kcal (kilocalories); NHANES (National Health and Nutrition Examination Survey); SE (standard error).

Sample sizes are weighted using appropriate NHANES weights. Pregnant women and individuals with type 2 diabetes were excluded.

All percentages rounded to the nearest tenth of a percent. Means and standard errors (±) were reported to the nearest thousandth of a percentage.

Rao-Scott chi-square tests were used to examine the characteristics of normoglycemia versus prediabetes for gender, race/ethnicity, BMI, physical activity, smoking, education, household income. Survey-weighted ordinary least squares regression was used to examine demographic differences in normoglycemia versus prediabetes for age, HgbA1c, and added sugar/ total calorie consumption (percent intakes and usual mean intakes).

P-values <0.05 are considered statistically significant.

[a] BMI was based on standard weight status categories using CDC criteria for underweight, normal weight, overweight, obese.

[b] Physical activity status based on self-reported data about participation/non-participation in either moderate- and/or vigorous-intensity sports, fitness, or recreational activity for ≥10 minutes continuously (yes/no). Sedentary was defined as not engaging in ≥ 10 minutes of activity. Physically active was defined as engaging in ≥ 10 minutes of activity.

[c] Smoking status was based on self-reported data about the use of tobacco products within the last 5 days (yes/no). Smoker was defined as using products within the last 5 days. Non-smoker was defined as no use of tobacco products within the last 5 days.

[d] Education was based on self-reported data asking participants their highest grade or level of school completed/received. < High school includes less than high school degree or no high school diploma. High school includes being a graduate or having a GED or equivalent. > High school includes some college/ associate degree or greater.

[e] HgbA1c was laboratory collected during NHANES medical examination center visits and based on the American Diabetes Association classification guidelines for prediabetes defined as HgbA1c of 5.7% - 6.4%.

[f] Percent intakes of added sugar were based on a ratio estimate of usual mean intakes for added sugar (g) and usual intake of total calories (kcals).

Table 2. Unadjusted and adjusted odds of prediabetes for usual intake of total added sugar (g) in U.S. adults ≥20 years with normoglycemia and prediabetes, the NHANES 2013-2018

		Estimate[c]	SE	*p* value	OR	95% CI
Unadjusted (n=10,671)[a]	Intercept	-1.01	.06	.0001	-	-
	Usual intake total added sugar (g)	.0005	.0011	.62	1.001	.99-1.003
Adjusted (n=9,189)[a,b]	Intercept	-5	.49	<.01	-	-
	Usual intake total added sugar (g)	.0012	.002	.58	1.001	.997-1.006
Age (years)		.06	.0026	<.01	1.063	1.057-1.068
Gender	Female (Ref.)	-	-	-	-	-
	Male	.039	.002	.68	1.04	.861-1.255
Race and ethnicity	Non-Hispanic White (Ref.)	-	-	-	-	-
	Non-Hispanic Black	1.201	.098	<.01	3.325	2.728-4.051
	Hispanic	.682	.121	<.01	1.978	1.549-2.525
	Other Race	.974	.109	<.01	2.65	2.127-3.300
BMI	Underweight ≤ 18.49 kg/m2 (Ref.)	-	-	-	-	-
	Normal 18.5-24.99 kg/m2	.082	.489	.87	1.086	.405-2.908
	Overweight 25-29.99	.644	.486	.19	1.903	.716-5.061
	Obese ≥30 kg/m2	1.273	.476	.01	3.57	1.369-9.309
Total calorie intake (kcal/day)		.0001	.0001	.3	1	1.00-1.00
Physical activity status	Sedentary (Ref.)	-	-	-	-	-
	Physically active	-.101	.08	.21	.769	.769-1.063
Smoking status	Smoker (Ref.)	-	-	-	-	-
	Non-smoker	-.238	.105	.03	.789	.638-.974
Education	< High school degree (Ref.)	-	-	-	-	-
	High school degree	-.27	.163	.105	.763	.549-1.061
	> High school degree	-.359	.133	.009	.699	.534-.913
Income	<$20,000 (Ref.)	-	-	-	-	-
	$20,000-99,000	.09	.128	.48	1.094	.846-1.415
	≥100,000	-.086	.139	.54	.917	.693-1.215

BMI (body mass index); CI (confidence interval); HgbA1c (hemoglobin a1c); g (grams); kcal (kilocalories); NHANES (National Health and Nutrition Examination Survey); OR (odds ratio); Ref (reference category); SE (standard error)

Sample sizes are weighted using appropriate NHANES weights. Pregnant women and individuals with type 2 diabetes and those with missing dietary data, laboratory data (HgbA1c), or missing covariate data were excluded during analyses. Dietary weights for Day 2 were used for all analyses.

P-values <0.05 are considered statistically significant.

[a] Model fit- C statistic: .487 unadjusted and .765 adjusted

[b] Covariates included in the adjusted models are represented below.

[c] Estimate (β Coefficient) for usual intake of added sugar (g) represents a change in the odds of having prediabetes for every 1-gram increase in added sugar.

Table 3. Model-estimated risk of prediabetes at mean and quartiles of usual intake of total added sugar (g) in adults ≥20 years, the NHANES 2013-2018

	Total Added Sugar	Estimate[b]	SE
Unadjusted[†]	Mean (49.40 g)	.272	.007
	1st Q (27.44 g)	.269	.007
	Median Q (43.86 g)	.271	.007
	3rd Q (64.85 g)	.273	.008
Adjusted[†,a]	Mean (49.40 g)	.279	.02
	1st Q (27.44 g)	.273	.02
	Median Q (43.86 g)	.277	.02
	3rd Q (64.85 g)	.282	.02

g (grams); NHANES (National Health and Nutrition Examination Survey); Q (quartiles); SE (standard error)

[†]P-values for Unadjusted model (p=.62) and adjusted model (p=.58); Model fit- C statistic: .487 unadjusted and .765 adjusted

[a] Adjusted for age, gender, race/ethnicity, BMI, total calorie intake (kcal/day), physical activity status, smoking status, education, income.

[b] Estimate represents the risk probability for prediabetes based on mean and quartile intakes of added sugar in grams per day.

Table 4. Unadjusted and adjusted odds of prediabetes for percent intakes of total added sugar (g) in U.S. adults ≥20 years with normoglycemia and prediabetes, the NHANES 2013-2018

		Estimate[c]	SE	*p* value	OR	95% CI
Unadjusted (n=10,671)[a]	Intercept	-1.03	.05	<.001	-	-
	Usual intake: <10% g (Ref.)	-	-	-	-	-
	Usual intake: 10-15% g	.112	.087	.206	1.119	.938 - 1.334
	Usual intake: >15% g	.055	.088	.531	1.057	.886-1.262
Adjusted (n=9,189)[a,b]	Intercept	-5.017	.475	<.01	-	-
	Usual intake: <10% g (Ref.)	-	-	-	-	-
	Usual intake: 10-15% g	.026	.107	.812	1.026	.827-1.273
	Usual intake: >15% g	.059	.119	.623	1.061	.835-1.347
Age (yr)		.061	.003	<.01	1.063	1.057-1.068
Gender	Female (Ref.)	-	-	-	-	-
	Male	.037	.092	.692	1.037	.861-1.250
Race/ethnicity	Non-Hispanic White (Ref.)	-	-	-	-	-
	Non-Hispanic Black	1.201	.098	<.01	3.323	2.726-4.050
	Hispanic	.679	.121	<.01	1.973	1.546-2.518
	Other Race	.971	.107	<.01	2.639	2.126-3.277
BMI	Underweight ≤ 18.49 kg/m2 (Ref.)	-	-	-	-	-
	Normal 18.5-24.99 kg/m2	.078	.493	.876	1.081	.4-2.921
	Overweight 25-29.99	.638	.491	.2	1.893	.704-5.087
	Obese ≥30 kg/m2	1.268	.481	.01	3.553	1.350-9.354
Total energy intake (kcal/day)		.0001	.00009	.06	1	1.00-1.00
Physical Activity Status	Sedentary (Ref.)	-	-	-	-	-
	Physically Active	-.103	.082	.213	.902	.765-1.063
Smoking status	Smoker (Ref.)	-	-	-	-	-
	Non-smoker	-.239	.105	.027	.787	.637-.972
Education	<High school degree (Ref.)	-	-	-	-	-

	High School Degree	-.271	.163	.105	.763	.549-1.061
	>High School Degree	-.36	.132	.009	.698	.534-.912
Income	<$20,000 (Ref.)	-	-	-	-	-
	$20,000-99,000	.087	.128	.5	1.091	.842-1.415
	≥100,000	-.091	.14	.52	.913	.689-1.211

BMI (body mass index); CI (confidence interval); HgbA1c (hemoglobin a1c); g (grams); kcal (kilocalories); NHANES (National Health and Nutrition Examination Survey); OR (odds ratio); Ref (reference category); SE (standard error)

Sample sizes are weighted using appropriate NHANES weights. Pregnant women and individuals with type 2 diabetes and those with missing dietary data, laboratory data for prediabetes, or missing covariate data were excluded during analyses. Dietary weights for Day 2 were used for all analyses.

P-values <0.05 are considered statistically significant.

[a] Model fit- C statistic: .505 unadjusted and .765 adjusted

[b] Covariates included in the adjusted models are represented below.

[c] Estimate (β Coefficient) for percent usual intake of added sugar (g) represents a change in the odds of having prediabetes for every 1-gram increase in added sugar.

Table 5. Model-estimated risk of prediabetes by percent of usual intake of total added sugar (g) consumed for U.S. adults ≥20 years, the NHANES 2013-2018

	Percent Intakes for Total Added Sugar	**Estimate**[b]	**SE**
Unadjusted[†]	Usual intake: <10%	.263	.009
Prediabetes (n=3599)	Usual intake: 10-15%	.286	.013
	Usual intake: >15%	.274	.017
Adjusted[†,a]	Usual intake: <10%	.275	.02
Prediabetes (n=3083)	Usual intake: 10-15%	.28	.03
	Usual intake: >15%	.29	.04

g (grams); NHANES (National Health and Nutrition Examination Survey); SE (standard error)

[†]P-values for Unadjusted model (p=.45) and adjusted model (p=.89); Model fit- C statistic: .505 unadjusted and .765 adjusted

[a] Adjusted for age, gender, race/ethnicity, BMI, total calorie intake (kcal/day), physical activity status, smoking status, education, income.

[b] Estimate represents the risk probability for prediabetes based on percent intakes of added sugar in grams per day.

Table 6. Model-estimated risk of prediabetes at mean and quartiles of usual intake of total added sugar (g) by race/ethnicity status for U.S. adults ≥20 years, the NHANES 2013-2018

		Unadjusted[†]		Adjusted[†,a]	
	Total Usual intake	**Estimate**[b]	**SE**	**Estimate**[b]	**SE**
Non-Hispanic White[^]	Mean (49.40 g)	-	-	.16	.016
	1st Q (27.44 g)	-	-	.15	.015
	Median Q (43.86 g)	-	-	.16	.016
	3rd Q (64.85 g)	-	-	.16	.019
Non-Hispanic Black	Mean (49.40 g)	.41	.012	.39	.027
	1st Q (27.44 g)	.41	.013	.39	.031
	Median Q (43.86 g)	.41	.012	.39	.028
	3rd Q (64.85 g)	.4	.015	.39	.029
Hispanic	Mean (49.40 g)	.28	.013	.27	.032
	1st Q (27.44 g)	.28	.014	.28	.03
	Median Q (43.86 g)	.28	.014	.27	.031
	3rd Q (64.85 g)	.28	.013	.27	.035
Other Race	Mean (49.40 g)	.29	.02	.33	.038
	1st Q (27.44 g)	.29	.02	.34	.03
	Median Q (43.86 g)	.29	.02	.33	.034
	3rd Q (64.85 g)	.28	.03	.32	.049

g (grams); NHANES (National Health and Nutrition Examination Survey); Q (quartiles); SE (standard error)

[†]P-values for Unadjusted model (p=.65) and adjusted model (p=.51); Model fit- C statistic: .576 unadjusted and .766 adjusted

[^]Model estimates not calculated by model.

[a] Adjusted for age, gender, race/ethnicity, BMI, total calorie intake (kcal/day), physical activity status, smoking status, education, income.

[b] Estimate represents the risk probability for prediabetes based on mean and quartile intakes of added sugar in grams per day.

Table 7. Model-estimated risk of prediabetes by percent of usual intake of total added sugar (g) consumed by race/ethnicity status for U.S. adults ≥20 years, the NHANES 2013-2018

		Unadjusted[†]		Adjusted[†,a]	
	Total Usual intake	**Estimate[b]**	**SE**	**Estimate[b]**	**SE**
Non-Hispanic White	<10%	.23	.012	.16	.014
	10-15%	.28	.018	.18	.026
	>15%	.24	.021	.19	.032
Non-Hispanic Black	<10%	.41	.017	.43	.037
	10-15%	.4	.022	.4	.038
	>15%	.4	.028	.39	.036
Hispanic	<10%	.29	.017	.3	.033
	10-15%	.26	.022	.28	.043
	>15%	.28	.025	.28	.047
Other Race	<10%	.31	.022	.39	.038
	10-15%	.22	.027	.26	.047
	>15%	.31	.054	.35	.087

g (grams); NHANES (National Health and Nutrition Examination Survey); SE (standard error)

[†]P-values for Unadjusted model (p=.12) and adjusted model (p=.24); Model fit- C statistic: .573 unadjusted and .765 adjusted

[a] Adjusted for age, gender, race/ethnicity, BMI, total calorie intake (kcal/day), physical activity status, smoking status, education, income.

[b] Estimate represents the risk probability for prediabetes based on percent intakes of added sugar in grams per day.

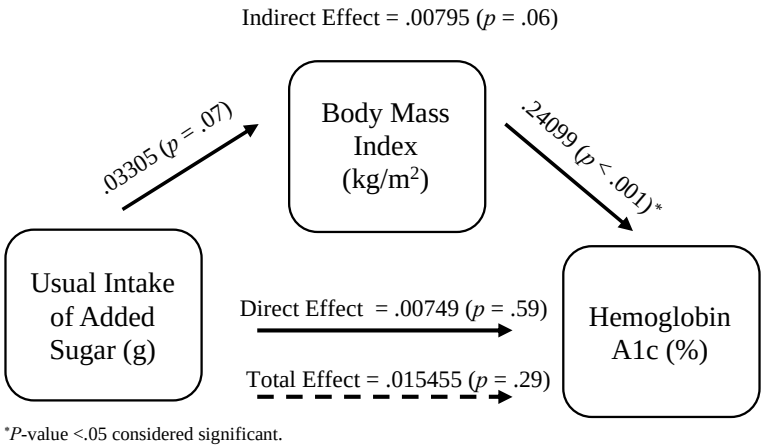


Figure 1: Direct and indirect 'effects' of usual intake of total added sugar (g) on prediabetes (HgbA1c) with BMI as a mediator in adults ≥20 years, the NHANES 2013-2018

CHAPTER 5

CONCLUSIONS

The purpose of this dissertation was to examine associations between added sugar consumption and prediabetes among U.S. adults ≥20 years. This goal was accomplished through the production of a concept analysis review and two cross-sectional, correlational studies which resulted in the production of three manuscripts. Manuscript one provided a conceptual understanding of the concept added sugar in the context of T2D risk (i.e., prediabetes). Manuscript two and three used nationally representative data from the National Health and Nutrition Examination Survey (NHANES) from 2013-2016 and 2013-2018 (respectively) to examine cross-sectional associations between total added sugar consumption and prediabetes awareness (manuscript two) and prediabetes risk (manuscript three) in U.S. adults ≥20 years. The purpose of this chapter five is to: 1) briefly summarize and integrate the findings of each manuscript, 2) discuss pertinent strengths and limitations of the dissertation study, 3) describe how findings from this dissertation will advanced nursing and health science, and 4) discuss implications for future research.

Summary of the Three Manuscripts

Manuscript 1: Influences of Added Sugar Consumption in Adults with Type 2 Diabetes Risk: A Principle-Based Concept Analysis

Manuscript one served as a review paper for this dissertation and followed Penrod and Hupcey's "principle-based concept analysis method" which allowed for a novel, scientific investigation of the concept added sugar in the context of T2D risk in adults (Penrod & Hupcey, 2005). A systematic search resulted in 35 articles, collected between 2008-2018, for inclusion in the review. Findings were categorized and described using Penrod and Hupcey's (2005) four guiding principles: epistemological, pragmatic, linguistic, and logical.

Analysis using the epistemological principle (i.e., conceptual definition) revealed that differences in added sugar's definitions (e.g., nutritive sweeteners, fructose, sucrose), including methods used to operationalize added sugar (e.g., food-frequency questionnaires, diet recalls, beverage intake questionnaires), varied which limited conceptual clarity of the concept. However, findings from analysis of the pragmatic principle (i.e., operationalization of concept and conceptual applicability within science) revealed that added sugar in the context of T2D risk was applicable in nursing and other health-related disciplines and was reliably operationalized using various dietary assessment methods (e.g., self-reported and controlled feeding methods). The linguistic principle (i.e., consistent and appropriate use of a concept) indicated that a lack of consistent use of the term "added sugar" in the literature prevents clarity of the concept, particularly since terms like "fructose, sucrose, and HFCS" have frequently been used to describe added sugars. Finally, the logical principle (i.e., integration of the concept with

similar concepts) revealed that when added sugar was discussed in the context of added sugar proxies (e.g., fructose, SSBs, HFCS), their meaning was clear; however, when discussed with interrelated concepts such as fruit drinks, the conceptual boundaries were less clear since fruit drinks can be misinterpreted as fruit juice (which often contains no added sugars). Overall findings revealed that the concept added sugar has applicability in nursing and other health-related disciplines; however, a clearer delineation of added sugar in the context of T2D risk in adult populations is required to advance the concept within science.

Manuscript 2: Prediabetes Awareness is not Associated with Lower Consumption of Self-Reported Added Sugar in U.S. Adults: National Health and Nutrition Examination Survey, 2013-2016

Manuscript two examined the associations between prediabetes awareness and self-reported added sugar consumption in U.S. adults. A secondary, cross-sectional analysis was conducted using NHANES data collected between 2013-2016 which included 2,432 adults (≥20 years) with prediabetes (HgbA1c defined: 5.7%-6.4%) who were dichotomized by awareness status (yes/no) by a healthcare provider. The primary aim of the study was to assess if prediabetes awareness was associated with lower consumption of added sugar (g/day) and if consumption among those aware of having prediabetes differed by age, gender, and race/ethnicity status. Survey-weighted ordinary least squares regression indicated that prediabetes awareness was not associated with a reduced mean intake of added sugar (b = -3.85, p = .49) after controlling for sociodemographic covariates. Differences in consumption were observed by age, gender,

and race/ethnicity in which younger adults consumed the highest added sugar quantities (b = -17.63, p < .01), males consumed more added sugar than females, and non-Hispanic Whites (b = 20.6, p < .01) and non-Hispanic Blacks (b = 18.8, p < .01) consumed more added sugar than the lowest consumer group Other Race. Overall, the study findings suggested adults aware of having prediabetes are no more likely than unaware individuals to engage in dietary risk-reduction behaviors by reducing their added sugar. Future research is recommended to identify specific barriers that prevent engagement in dietary-risk reduction behaviors, including reductions in added sugar, in adults with prediabetes.

Manuscript 3: Total Added Sugar Consumption is not Associated with Risk for Prediabetes Among U.S. Adults: National Health and Nutrition Examination Survey, 2013-2018

Manuscript three examined the associations between added sugar consumption and risk for prediabetes in U.S. adults. A secondary, cross-sectional analysis was conducted using NHANES data collected between 2013-2018 and included a total of 13,406 adults (≥20 years); 4,501 with prediabetes (mean HgbA1c of 5.91%) and 8,905 with normoglycemia. The purpose of the study was to examine whether total added sugar consumption was associated with prediabetes and if the probability (i.e., risk) of having prediabetes differed by the amount consumed (< 10%, 10-15%, >15% added sugar calories/day). These associations were also individually examined by race/ethnicity status and a mediation analysis estimated the direct and indirect ‘effects’ of added sugar on prediabetes, with body mass index (BMI) as a mediator.

Survey-weighted logistic regression indicated that usual mean intake for total added sugar (g/day) and percent intakes of added sugar were not significantly associated with having an increased odds of prediabetes (total added sugar intake- unadjusted: OR: 1.001, 95% CI: .99 - 1.003, p = .62; adjusted: OR: 1.001, 95% CI: .99 - 1.006, p = .58 and percent added sugar intakes- [unadjusted: < 10%: (ref); 10 - 15%: OR: 1.119, 95% CI: .938 - 1.334, p = .206; >15%: OR: 1.057, 95% CI: .886 - 1.262, p = .531]; [adjusted: <10%: (ref); 10-15%: OR: 1.026, 95% CI: .827 - 1.273, p = .812; >15%: OR: 1.061, 95% CI: .835 -1.347, p = .623]). Sensitivity analyses indicated that total and percent intakes of added sugar were not significantly associated with an increased risk for prediabetes by race/ethnicity for non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and Other Race categories (Type 3 tests for interaction of race/ethnicity by total added sugar: unadjusted model [p = .65]; adjusted model [p = .51] and percent intake of added sugar: unadjusted model [p = .12]; adjusted model [p = .24]). Lastly, a mediation analysis indicated that that direct (.0074; p = .59) and indirect (0079; p = .06) associations of total usual intake of added sugar (g/day) on HgbA1c were not statistically significant. Overall, the study findings suggest that total added sugar consumption, including differing percent intakes, does not significantly increase the odds for having prediabetes. Similar findings were observed when comparing differences in risk by race/ethnicity status. Due to the lack of significant associations observed for added sugar consumption and prediabetes risk in our study, follow-up observational and experimental studies are needed to clarify added sugar's direct relationship to prediabetes risk.

Summary and Integration of Dissertation Findings

Findings from this body of research add new knowledge to our scientific understanding of added sugar's role on prediabetes in adults ≥20 years. Manuscript one used a novel concept analysis approach to explore what is known about added sugar in the context of T2D risk and identified a conceptual definition for added sugar. Manuscripts two and three analyzed cross-sectional, population based NHANES data collected from U.S. adults ≥20 years of age. Manuscript two examined the associations between prediabetes awareness and total added sugar consumption in adults with prediabetes using four years of survey data (2013-2016). Manuscript three examined associations between total and percent intakes of added sugar on prediabetes risk in adults ≥20 years with normoglycemia and prediabetes using six years of survey data (2013-2018).

Findings from the concept analysis (manuscript one) provided a rationale for the necessity of this dissertation study. The analysis revealed that substantial evidence exists that suggests added sugar likely increases the risk for T2D. However, unanimous scientific consensus for a strong, causal relationship was considered lacking, though could be partially explained by differences in the operationalization of added sugar (Sneed et al., 2019). For example, the analysis reported that studies in populations with T2D risk have consistently isolated added sugars by their type (i.e., HFCS, fructose, sucrose) or source (e.g., SSBs) and have not examined total consumption from all dietary sources. Furthermore, the analysis found that current evidence has not determined a specified "amount" for added sugar (including total intake) that drives metabolic change

and causes risk for T2D (Sneed et al., 2019). Another important issue (though not extensively discussed in the concept analysis) is that most individuals with prediabetes (85%) are unaware of their condition (Centers for Disease Control and Prevention [CDC], 2020) and therefore, are less likely to participate in dietary modifications to reduce their risk for developing T2D (Gopalan et al., 2015). Due to added sugar's link to prediabetes (Allister & Stanhope, 2016) and a significant number of individuals being unaware of their condition (CDC, 2020), studying whether prediabetes awareness influences an individual's decision to modify their total added sugar intake was prioritized to advance this concept within the scientific literature. To address these persistent gaps, two cross-sectional studies were conducted for this dissertation which examined associations between "total" added sugar consumption and prediabetes.

A plethora of observational studies that have examined the relationship between added sugar and risk for prediabetes (i.e., insulin resistance, dysglyemica, reduced insulin sensitivity) have done so using added sugar proxies such as SSBs containing HFCS (Barrio-Lopez et al., 2013; Dhingra et al., 2007; Green et al., 2014; Lana et al., 2014; J. Ma et al., 2016; Teshima et al., 2015). In experimental and observational studies, individual sugar types such as fructose, sucrose, or HFCS have predominately been examined (Aeberli et al., 2013; Biggelaar et al., 2017; Black et al., 2006; Brynes et al., 2003; Faeh et al., 2005; Lê et al., 2009; Lecoultre et al., 2013; Lewis et al., 2013; Lowndes et al., 2015; Raben et al., 2001; Stanhope et al., 2009; Weber et al., 2018). Yet, added sugars are consumed from a variety of sources including SSBs, fruit drinks, sweets and desserts, candies, cereals (U.S. Department of Agriculture and U.S. Department of Health and Human Services [USDA and HHS], 2020), and consist of a combination of

monosaccharide sugars (i.e., fructose, glucose) ingested mainly in the form of sucrose or HFCS (Malik & Hu, 2015). Added sugars such as fructose and glucose are not consumed in isolation as part of a usual diet (Fitch & Keim, 2012; Stanhope, 2016). Therefore, due to the lack of studies assessing the relationship between total dietary intake of added sugars (from all dietary sources) and prediabetes, this dissertation examined only total added sugar consumption. Total added sugar consumption was evaluated in the context of prediabetes awareness for manuscript two. In manuscript three, differences in amounts of total added sugar consumed (i.e., <10%, 10-15%, >15% total energy intake) were evaluated in the context of prediabetes risk.

Results from manuscript two and three resulted in non-significant associations which was in contrast to each study's hypotheses: a) prediabetes awareness would be significantly associated with reduced consumption of added sugar (manuscript two); and b) total added sugar consumption would be associated with risk for prediabetes, with risk increasing at higher percent intakes (>10-15%, >15% total calories) compared to lower percent intakes (<10% total calories); associations between total and percent intakes for prediabetes risk would differ by race/ethnicity status (manuscript three). Manuscript two revealed that prediabetes awareness did not significantly influence consumption of total added sugars in U.S. adults. Manuscript three found that in adults, added sugar consumption was not significantly associated with an increased risk for prediabetes, including at greater percent intakes and by race/ethnicity status.

As previously mentioned, the operationalization of added sugar has been shown to influence associations observed in relation to risk for T2D (Sneed et al., 2019). For our studies, we assessed total added sugar from all dietary sources. Therefore, it is possible

that examination of only "total added sugars" influenced study findings, particularly in manuscript three. However, because the study aim for manuscript two was to compare differences in comsumption by awareness status and not assess the odds (i.e., risk) of having prediabetes, it is unlikely that our examination of total added sugar influenced manuscript two's results.

To our knowledge, no studies have examined if individuals aware of their prediabetes status modify their consumption of added sugars. Due to this gap in the literature and the need to advance our scientific understanding of added sugar in the context of prediabetes (Sneed et al., 2019), a study was conducted for this dissertation to examine if prediabetes awareness influences consumption of added sugar in U.S. adults. Manuscript two revealed that individuals aware of having prediabetes were no more likely than unaware individuals to engage in dietary risk-reduction behaviors since they did not significantly alter their added sugar consumption. This lack of associations was possibly attributed to: a) the classification of prediabetes as a T2D risk factor and not a disease (American Diabetes Association [ADA], 2020); b) a lack of healthcare provider dietary counseling (Karve & Hayward, 2010) and/or dietetic referrals (Tseng et al., 2019); c) and a lack of awareness about the metabolic consequences of added sugar consumption on prediabetes (Allister & Stanhope, 2016; Malik & Hu, 2015). Since this is the first known study that has examined these associations, the rationale for why prediabetes awareness did not result in reduced intake of added sugar remains unclear and additional follow-up studies are needed to identify barriers that prevent engagement in dietary-risk reduction behaviors. The study did, however, provided important details about the characteristics of added sugar consumers by awareness status and included comparisons

by age, sex, and race/ethnicity status. These findings provide important details about high-risk groups with prediabetes and can be useful to inform T2D prevention health and policy initiatives.

Experimental and observational studies examining added sugar's causal links to prediabetes have been mixed with some studies supporting that added sugars increase the risk for prediabetes (Faeh et al., 2005; Green et al., 2014; Lana et al., 2014; Lê et al., 2009; Lecoultre et al., 2013; J. Ma et al., 2016; Teshima et al., 2015; Weber et al., 2018) and others reporting no relationship (Biggelaar et al., 2017; Black et al., 2006; Brynes et al.; Lewis et al., 2013; Lowndes et al., 2015; Matikainen et al.; Raben et al.). Observational studies of adults have reported significant associations between consumption of added sugar and risk for prediabetes through the use of added sugar proxies such as SSBs (Barrio-Lopez et al., 2013; Dhingra et al., 2007; Green et al., 2014; Lana et al., 2014; Y. Ma et al., 2016; Teshima et al., 2015). Moreover, experimental studies have found that consuming high concentrations of fructose from added sugars (>15% total calories) impair insulin resistance (Faeh et al., 2005; Lê et al., 2009; Lecoultre et al., 2013), increase fasting plasma glucose concentrations (Stanhope et al., 2009), and decrease insulin sensitivity (Lê et al., 2009; Lecoultre et al., 2013; Stanhope et al., 2009). Yet, no studies (to our knowledge) have examined whether total added sugar consumption (from all dietary sources) is associated with risk for prediabetes or if greater consumption (10-15% and/or >15% compared to <10% total calories) is associated with greater risk for prediabetes. These associations were also tested by race/ethnicity status to improve the generalizability of our study findings and a mediation analysis was used to

estimate the direct and indirect 'effects' of added sugar on prediabetes, with body mass index (BMI) as a mediator.

The results of manuscript three reveled that total added sugar consumption is not significantly associated with an increased risk for prediabetes and does not appear to increase the risk with greater consumption of total added sugars. Similar non-significant associations were observed by race/ethnicity status and results of the mediation analysis indicated no significant 'effects' of total usual intake of added sugar (g/day) on HgbA1c. The operationalization of added sugar between studies has varied widely (Sneed et al., 2019) and has likely confounded the effects of added sugar on risk for prediabetes making it difficult to make meaningful between study comparisons, including our own. It is possible that our use of *total* added sugars in lieu of examining added sugars by type (i.e., fructose, glucose, sucrose, HFCS) and/or source (liquid versus solid) may have contributed to our null findings.

As mentioned above, factors such as how much added sugar (e.g., <10% vs >25%) and what types are consumed (e.g., sucrose, fructose) appear to exert differing effects on prediabetes risk (Stanhope, 2016; Tsilas et al., 2017). For example, multiple randomized intervention studies in normoglycemic adults (*n*= 13 to 152) consuming sucrose for up to 12 weeks have consistently reported that sucrose (upwards of ~25% total energy intake) does not increase insulin resistance or reduce insulin sensitivity (Aeberli et al., 2013; Black et al., 2006; Brynes et al., 2003; Lewis et al., 2013; Lowndes et al., 2015; Raben et al., 2001). Similar associations have been observed in prospective cohort and cross-sectional studies which have suggested that sucrose consumption (upwards of 60 g/day) does not increase the risk for prediabetes (Biggelaar et al., 2017)

or T2D (Janket et al., 2003; Montonen et al., 2007). Yet, in short-term (<12 weeks) randomized intervention studies of normoglycemic adults (*n* = 7 to 55), greater fructose consumption (15% to ≥25% of total energy) has been shown to impair insulin resistance (Faeh et al., 2005; Lê et al., 2009; Lecoultre et al., 2013), increase fasting plasma glucose concentrations (Stanhope et al., 2009), and decrease insulin sensitivity (Lê et al., 2009; Lecoultre et al., 2013; Stanhope et al., 2009). Similar associations have also been observed in observational studies (Barrio-Lopez et al., 2013; Dhingra et al., 2007; Goran et al., 2013; Green et al., 2014; Lana et al., 2014; Y. Ma et al., 2016; Teshima et al., 2015). For example, in an ecological analysis, higher availability of HFCS was associated with significantly greater fasting glucose (mmol/L) concentrations and population prevalence of T2D, independent of BMI (Goran et al., 2013).

Added sugar's link to metabolic conditions, including prediabetes risk, is primarily due to the determinantal effects of fructose (Macdonald, 2016). However, fructose is not consumed in isolation as part of an ad libitum diet (Allister & Stanhope, 2016) and added sugars contain both glucose and fructose, often in an equal or close to equal ratio of 50/50 (for sucrose) to 55/45 (for HFCS) (Fitch & Keim, 2012). As such, the purpose of the dissertation study was to examine the role of *total* added sugar consumption on prediabetes since this represents actual intake for the majority of the U.S. population (Bailey et al., 2018; Bowman, 2017). It is possible that we did not observe a significant association between added sugar and risk for prediabetes because we did not delineate added sugars by their glucose and fructose form, but rather examined effects of total added sugar on prediabetes risk by tertiles (<10%, 10-15%, >15%). Furthermore, evidence suggests that insulin resistance develops when fructose consumption totals

≥15% of an individual's total energy intake (Aeberli et al., 2013; Faeh et al., 2005; Lê et al., 2009; Lecoultre et al., 2013; Stanhope et al., 2009) which is equivalent to about ≥30% of total calories from added sugars based on the assumption of 50/50 glucose to fructose (as part of a 2,000 kcal diet) (Bowman, 2017; Fitch & Keim, 2012; USDA and HHS, 2020). In manuscript three, approximately 18.4% of the total sample (including adults with normoglycemia and prediabetes) reported consumed >15% of their total calories from added sugar and of those at the 90th percentile, average consumption was estimated at 90 g/day (results not shown). These amounts of added sugars contain fructose concentrations well below quantities that have been shown to promote insulin resistance which may also explain why we did not observe a significant association with prediabetes risk in manuscript three.

Though it was beyond the scope of this dissertation research, a lack of comparisons between added sugar sources (i.e., liquids vs solids) in manuscript three may have also contributed to the lack of significant associations observed for the study. Evidence suggests consuming added sugars in liquid form (e.g., SSBs, fruit drinks) versus solid form (e.g. food products) is attributed to insulin resistance, likely due to the rapid digestion and hepatic metabolism of fructose at high concentrations (Sundborn et al., 2019; Tsilas et al., 2017). Data in adults is sparse; however, a recent cross-sectional study found that added sugars consumed as liquids (e.g., SSBs, coffee, tea) were positively associated with insulin resistance (via HOMA-IR), a trend not observed for solid added sugar foods (O'Connor et al., 2018). Similar associations have also been observed in children ages 8-10 years (Wang et al., 2013). Moreover, observational studies have consistently linked SSBs to prediabetes (Ma et al., 2016) and T2D (de Koning et al.,

2011; Drouin-Chartier et al., 2019; Montonen et al., 2007; O'Connor et al., 2015), irrespective of body weight gain (Drouin-Chartier et al., 2019; Y. Ma et al., 2016; Montonen et al., 2007; O'Connor et al., 2015). This evidence is currently evolving and future studies assessing these differences in populations with prediabetes are warranted.

Lastly, results from the mediation analysis in manuscript three indicated that both the direct and indirect effects (via the BMI pathway) of total added sugar consumption on HgbA1c were of small magnitude and not statistically significant. The lack of direct 'effects' observed for total added sugar on HgbA1c mirrored the null results of the primary study findings (total added sugar consumption was not associated with an increased risk for prediabetes) and were likely non-significant for similar reasons addressed above. Additionally, results of the mediation analysis did not support an association between total added sugar consumption and prediabetes through indirect BMI pathway. As such, the results of the mediation analysis of this study neither support nor refute added sugar's direct association with risk for prediabetes. However, there is substantial scientific evidence which indicates that added sugar does in fact, directly promote hepatic and whole-body insulin resistance through dysregulation of fructose metabolism which occurs independent of body weight gain (Black et al., 2006; Lewis et al., 2013; Stanhope, 2016; Swarbrick et al., 2008). At what amount of consumption this occurs for *total* added sugar intake was not determined by this dissertation study and remains unknown. Therefore, future observational and experimental studies are needed that examine the direct effects of total added sugar consumption on prediabetes risk, independent of overweight and obesity status.

Since manuscript three is the first known study to have examined associations between total added sugar and prediabetes risk, a clear rationale for why total added sugar consumption did not increase the risk for prediabetes could not be determined. Future observational and experimental studies should be conducted to examine the relationship between total added sugar consumption and risk for prediabetes in adult populations to confirm or disprove our findings.

Strengths and Limitations

First, this dissertation study had some major strengths. To our knowledge, manuscript two and manuscript three were the first studies that have examined associations between added sugar consumption and prediabetes (awareness and risk respectively) in a large, nationally representative U.S. adult sample. Secondly, we examined important differences in added sugar consumption and prediabetes by race and ethnicity status due to a current lack of representation of different racial and ethnic groups in the present literature on this subject. This allowed our findings to be more generalizable to a broader U.S. population. Thirdly, we were able to capture usual intake of added sugar and total energy intake for our study sample in manuscript three by using steps outlined by the robust National Cancer Institute (NCI) dietary recall method (National Cancer Institute, 2020) which accounts for between- and within-person variation in intake (National Cancer Institute; Tooze et al., 2010).

This dissertation study also had some limitations which are inherent to the use of secondary data. First, NHANES is a cross-sectional survey that captures single time points of data collection (Ahluwalia et al., 2016). Therefore, it was not possible to

identify temporal associations or determine causal effects attributed to added sugar consumption and prediabetes for this dissertation study. Specifically, findings from manuscript three revealed that overall consumption of added sugar in the study population was 10.2% of total daily calories which was lower than the 13% average for the entire U.S. population, but mirrored current dietary guidelines recommendations (<10% total daily energy intake) (USDA and HHS, 2020; USDA and HHS, 2015). Due to the cross-sectional nature of the study, we were unable to determine if reduced intake over time contributed to the lack of significant associations observed for added sugar consumption and risk for prediabetes in manuscript three.

Second, added sugar and total energy intake were collected using a self-reported, 24-hour dietary recall method. The use of this method (along with all self-reported estimates of dietary intake) is subject to measurement error due to recall bias (e.g., imperfect short-term memory, inaccurate portion size estimates) and can result in under- or over-reporting of dietary intake (Kirkpatrick & Raffoul, 2017). Additionally, misreporting due to social desirability, interview, and self-monitoring bias are pertinent issues to consider when using 24-hour dietary recall data (Kirkpatrick & Raffoul, 2017) collected from NHANES since participants are told they will undergo dietary questioning (Ahluwalia et al., 2016). It is also possible that individuals with prediabetes consciously underreport their energy intake similar to what has been observed in overweight, obese, or weight-conscious individuals (Moshfegh et al., 2008; Nielsen & Popkin, 2003). This phenomenon was not observed in manuscript two of this dissertation since prediabetes awareness did not appear to significantly alter an individual's consumption of added sugar. Nonetheless, NHANES has taken steps to reduce the incidence of measurement

errors during their 24-hour dietary recall collection by using the Automated Multiple-Pass Method (AMPM). The AMPM is a standardized method conducted by trained staff that has been found to accurately estimate total energy intake (Moshfegh et al., 2008) and usual nutrient intakes (i.e., sodium) in adults at both the population and group level (Rhodes et al., 2013). Therefore, use of the AMPM method may have mitigated some of the measurement error inherent with the collection of self-reported, 24-hour dietary data.

Additionally, we estimated the usual mean intake of added sugar and total energy intake for manuscript three of our study and used the steps outlined by the NCI method (National Cancer Institute, 2020). The NCI method provides a SAS macro consisting of a two-part model that allows for assessment of the "probability" of food consumption on a given day as well as the "amount" consumed. The model also controls for covariates and can be performed in specific subgroups (Tooze et al., 2010). For the purposes of the study, we were only interested in evaluating usual intake for added sugar and total energy intake. Therefore, we followed the steps outlined in part two of the NCI method and did not use the complex SAS macro (National Cancer Institute, 2020). It is possible that our estimates for usual added sugar and total calorie intake may differ compared to estimates produced using the NCI SAS macro. However, usual intakes for added sugar in our study was similar to previous population-reported estimates from NHANES (Bowman et al., 2017) emphasizing the soundness of our dietary assessment methods.

Third, the use of HgbA1c as the primary estimate for prediabetes could have contributed to the null findings of our study. Evidence suggests numerous methodological issues are attributed to the use of HgbA1c as a primary measure for prediabetes. For example, HgbA1c has a lower sensitivity at cut-points of 5.7-6.4% and is associated with

greater diagnostic inaccuracy in the presence of certain medical conditions that increase red blood cell turnover (e.g., sickle cell disease, pregnancy, erythropoietin therapy). Also, differences by race and ethnicity status have been observed with HgbA1c levels registering higher in non-Hispanic Blacks compared to non-Hispanic Whites with similar fasting glucose levels (ADA, 2020). Moreover, some studies have reported a lack of significant associations between added sugar consumption and HgbA1c while simultaneously observing significant associations with measures of insulin resistance (HOMA-IR) (Lana et al., 2014; O'Connor et al., 2018), though others have not found similar associations (Chen, 2018). Nonetheless, the American Diabetes Association cites important advantages of using HgbA1c as a singular diagnostic test for prediabetes including its use in non-fasting states and its ability to reflect glycemic control long-term (i.e., ~3 months) with limited influences by day-to-day factors attributed to stress, diet, or illness (ADA, 2020). Due to these advantages, as well as it's routine use in clinical settings (Watson, 2017), HgbA1c was considered an appropriate method for estimating prediabetes in our studies.

Another important methodological limitation was our categorization of prediabetes awareness status (manuscript two) which may have resulted in recall bias. Awareness was based on a self-reported question (yes/no) asking participants if they had ever been told by a healthcare professional that they had the following conditions: "prediabetes, impaired fasting glucose, impaired glucose tolerance, borderline diabetes or [a] blood sugar … higher than normal but not high enough to be called diabetes or sugar diabetes? ". However, we were able to ensure only participants with prediabetes were

included in our sample population through the use of laboratory estimated prediabetes (HgbA1c).

Lastly, our analyses categorized race/ethnicity status using four groups: non-Hispanic White, non-Hispanic Black, Hispanic, and Other Race. While NHANES categorizes certain groups into additional categories (i.e., Mexican American, Other Hispanic, and non-Hispanic Asian), we included only four groups in our study to ensure that we had a sufficient sample size to detect statistically significant differences by race/ethnicity for all analyses. Generalizability of our findings is therefore limited to the aforementioned groups only.

Advancement of Nursing and Health Science and Implications for Future Research

This dissertation has potential to advance nursing and health science through the dissemination of three manuscripts which describe the relationship between added sugar consumption and prediabetes in a nationally representative U.S. adult sample. Results from each study provided significant insights on added sugar influence on prediabetes in a large sample that is representative of over 88 million U.S. adults living with the condition (CDC, 2020).

The concept analysis for this dissertation (manuscript one) identified that excessive intake from various types (e.g., fructose, HFCS) and sources (e.g., SSB) of added sugar increases the risk for T2D. Yet, the analysis also revealed that the concept has not been previously described within the nursing literature (Sneed et al., 2019). Dissemination of this work, in the form of a peer-reviewed publication, has allowed for advancement of this important topic in nursing through the systematic appraisal of 35

peer-reviewed articles that provided a conceptual definition of added sugar in the context of T2D risk. The manuscript provides scholarly information for nurses interested in understanding the concept added sugar and can serve as an empirical resource for nurses practicing in a variety of clinical settings who provide counseling to adult patients with prediabetes.

This dissertation will also advance nursing research through the examination of added sugar's association with prediabetes in U.S. adults ≥ 20 years. Manuscripts two and three are the first studies that have examined associations between total added sugar consumption and prediabetes awareness (manuscript two) and risk (manuscript three) using a nationally representative U.S. adult sample. Additionally, this dissertation study examined differences in added sugar consumption and prediabetes (awareness status and risk) using four racial/ethnic groups to ensure that the study findings were generalizable to a broad U.S. adult population.

The knowledge generated from both cross-sectional studies of this dissertation provide important insights about added sugar's association with prediabetes in a nationally representative adult population. Manuscript two revealed that ~16% of adults with prediabetes were aware of their condition, however, they did not report reducing their consumption of added sugar. These findings suggests that individuals aware of their prediabetes status either lack knowledge about the health implications of their condition (Allister & Stanhope, 2016; Malik & Hu, 2015) or have not received appropriate dietary counseling by a health professional about reducing their added sugar consumption (Karve & Hayward, 2010; Tseng et al., 2019). Manuscript three found that total and percent intakes of added sugar did not increase the risk of prediabetes, even for different

racial/ethnic minority groups. Explanations for this lack of significant associations may be due to the operationalization of added sugar in the study (i.e., total added sugar) since additional factors shown to influence the risk of prediabetes include the type of added sugar (e.g., fructose, sucrose, HFCS) and the source consumed (i.e., beverages or solid-food sources) (Malik & Hu, 2015; Stanhope, 2016; Sundborn et al., 2019).

Study limitations, including the cross-sectional design and a singular definition for added sugar (i.e., total added sugar) illustrate the need for additional research in this area. Future studies using longitudinal prospective cohort and/or experimental designs are needed to examine what effects, if any, total added sugar consumption has on risk for prediabetes or prediabetes awareness. These studies are missing within the current literature and though they were beyond the scope of this dissertation, findings from manuscript two and three indicate they are necessary to advance our current understanding of added sugar's influence on risk for prediabetes. Advancement of this research in nursing and other health-related disciplines will provide clinicians with empirical evidence that allows for effective patient engagement in dietary risk-reduction behaviors for promotion of disease management and T2D prevention.

Conclusions

This dissertation will contribute to existing knowledge about added sugar's role in adults with prediabetes through the dissemination of three manuscripts. Added sugar's association with prediabetes is likely the result of overconsumption of added sugar, though whether total added sugar consumption directly influences risk for prediabetes is still unclear. Additionally, low rates of prediabetes awareness in adults undoubtedly

prevents engagement in dietary-risk reduction behaviors, including reductions to added sugar consumption. Overall, the findings from the three manuscripts of this dissertation add new knowledge to this growing body of literature. However, due to the lack of significant associations observed in manuscripts two and three of this dissertation, additional prospective cohort and experimental studies are needed to confirm or disprove our findings.

References

Aeberli, I., Gerber, P. A., Hochuli, M., Kohler, S., Haile, S. R., Gouni-Berthold, I., Berthold, H. K., Spinas, G. A., & Berneis, K. (2011). Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: a randomized controlled trial. *American Journal of Clinical Nutrition, 94*(2), 479-485. https://doi.org/10.3945/ajcn.111.013540

Aeberli, I., Hochuli, M., Gerber, P. A., Sze, L., Murer, S. B., Tappy, L., Spinas, G. A., & Berneis, K. (2013). Moderate amounts of fructose consumption impair insulin sensitivity in healthy young men: A randomized controlled trial. *Diabetes Care, 36*(1), 150-156. https://doi.org/10.2337/dc12-0540

Ahluwalia, N., Dwyer, J., Terry, A., Moshfegh, A., & Johnson, C. (2016). Update on NHANES dietary data: Focus on collection, release, analytical considerations, and uses to inform public policy. *Advances in Nutrition, 7*(1), 121-134. https://doi.org/10.3945/an.115.009258

Allister, P. C., & Stanhope, K. L. (2016). Understanding the Impact of added sugar consumption on risk for type 2 diabetes. *Journal - California Dental Association, 44*(10), 619-626.

American Diabetes Association. (2019a). Classification and diagnosis of diabetes: Standards of medical care in diabetes—2019. *Diabetes Care, 42*(Supplement 1), S13. https://doi.org/10.2337/dc19-S002

American Diabetes Association. (2019b). Lifestyle management: Standards of medical care in diabetes—2019. *Diabetes Care, 42*(Supplement 1), S46. https://doi.org/10.2337/dc19-S005

American Diabetes Association. (2019c). Prevention or delay of type 2 diabetes: standards of medical care in diabetes—2019. *Diabetes Care, 42*(Supplement 1), S29. https://doi.org/10.2337/dc19-S003

American Diabetes Association. (2020). 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2020. *Diabetes Care, 43*(Suppl 1), S14.

Bailey, R. L., Fulgoni, V. L., Cowan, A. E., & Gaine, P. C. (2018). Sources of added sugars in young children, adolescents, and adults with low and high intakes of added sugars. *Nutrients, 10*(1). https://doi.org/10.3390/nu10010102

Bardenheier, B. H., Cogswell, M. E., Gregg, E. W., Williams, D. E., Zhang, Z., & Geiss, L. S. (2014). Does knowing one's elevated glycemic status make a difference in macronutrient intake? *Diabetes Care, 37*(12), 3143-3149. https://doi.org/10.2337/dc14-1342

Barrio-Lopez, M. T., Martinez-Gonzalez, M. A., Fernandez-Montero, A., Beunza, J. J., Zazpe, I., & Bes-Rastrollo, M. (2013). Prospective study of changes in sugar-sweetened beverage consumption and the incidence of the metabolic syndrome and its components: The SUN cohort. *British Journal of Nutrition, 110*(9), 1722-1731. https://doi.org/10.1017/S0007114513000822

Biggelaar, L. J., Eussen, S. J., Sep, S. J., Mari, A., Ferrannini, E., Dongen, M. C., Denissen, K. F., Wijckmans, N. E., Schram, M. T., Kallen, C. J., Koster, A., Schaper, N., Henry, R. M., Stehouwer, C. D., & Dagnelie, P. C. (2017).

Associations of dietary glucose, fructose, and sucrose with beta-cell function, insulin sensitivity, and type 2 diabetes in the Maastricht Study. *Nutrients, 9*(4). https://doi.org/10.3390/nu9040380

Bhargava, A., & Amialchuk, A. (2007). Added sugars displaced the use of vital nutrients in the National Food Stamp Program Survey. *Journal of Nutrition, 137*(2), 453-460. https://www.scopus.com/inward/record.uri?eid=2-s2.0-33846838628&partnerID=40&md5=43b6256a50de79312b1acdc655b8245b

Black, R. N., Spence, M., McMahon, R. O., Cuskelly, G. J., Ennis, C. N., McCance, D. R., Young, I. S., Bell, P. M., & Hunter, S. J. (2006). Effect of eucaloric high- and low-sucrose diets with identical macronutrient profile on insulin resistance and vascular risk: A randomized controlled trial. *Diabetes, 55*(12), 3566-3572. https://doi.org/10.2337/db06-0220

Bowman, S. A., Clemens, J. C., Martin, C. L., Anand, J., Steinfeldt, L. C., & Moshfegh, A. J. (2017). *Added Sugars Intake of Americans: What We Eat in America, NHANES 2013-2014.* Food Surveys Research Group. Retrieved April 18, 2020 from https://www.ars.usda.gov/ARSUserFiles/80400530/pdf/DBrief/18_Added_Sugars_Intake_of_Americans_2013-2014.pdf

Bray, G. A., & Popkin, B. M. (2014). Dietary sugar and body weight: Have we reached a crisis in the epidemic of obesity and diabetes?: Health be damned! Pour on the sugar. *Diabetes Care, 37*(4), 950-956. https://doi.org/10.2337/dc13-2085

Brynes, A. E., Mark Edwards, C., Ghatei, M. A., Dornhorst, A., Morgan, L. M., Bloom, S. R., & Frost, G. S. (2003). A randomised four-intervention crossover study

investigating the effect of carbohydrates on daytime profiles of insulin, glucose, non-esterified fatty acids and triacylglycerols in middle-aged men. *British Journal of Nutrition, 89*(2), 207-218. https://doi.org/10.1079/bjn2002769

Centers for Disease Control and Prevention. (2020). National diabetes statistics report, 2020. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services. Retrieved August 27, 2020 from https://www.cdc.gov/diabetes/data/statistics-report/index.html

Chen, S. (2018). Consumer behaviors, added sugar intake, diet quality, inflammation and metabolic syndrome risks among adults from the National Health and Nutrition Examination Survey 2007-2010.

Choo, V. L., Viguiliouk, E., Blanco Mejia, S., Cozma, A. I., Khan, T. A., Ha, V., Wolever, T. M. S., Leiter, L. A., Vuksan, V., Kendall, C. W. C., de Souza, R. J., Jenkins, D. J. A., & Sievenpiper, J. L. (2018). Food sources of fructose-containing sugars and glycaemic control: Systematic review and meta-analysis of controlled intervention studies. *BMJ, 363*, k4644. https://doi.org/10.1136/bmj.k4644

Cohen, E., Cragg, M., deFonseka, J., Hite, A., Rosenberg, M., & Zhou, B. (2015). Statistical review of US macronutrient consumption data, 1965-2011: Americans have been following dietary guidelines, coincident with the rise in obesity. *Nutrition, 31*(5), 727-732. https://doi.org/10.1016/j.nut.2015.02.007

de Koning, L., Malik, V. S., Rimm, E. B., Willett, W. C., & Hu, F. B. (2011). Sugar-sweetened and artificially sweetened beverage consumption and risk of type 2 diabetes in men. *American Journal of Clinical Nutrition, 93*(6), 1321-1327. https://doi.org/10.3945/ajcn.110.007922

Dhingra, R., Sullivan, L., Jacques, P. F., Wang, T. J., Fox, C. S., Meigs, J. B., D'Agostino, R. B., Gaziano, J. M., Vasan, R. S., Dhingra, R., Sullivan, L., Jacques, P. F., Wang, T. J., Fox, C. S., Meigs, J. B., D'Agostino, R. B., Gaziano, J. M., & Vasan, R. S. (2007). Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. *Circulation*, *116*(5), 480-488. https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.107.689935

Diabetes Prevention Program Research Group. (2002). The Diabetes Prevention Program (DPP): Description of lifestyle intervention. *Diabetes Care*, *25*(12), 2165-2171.

DiMeglio, D. P., & Mattes, R. D. (2000). Liquid versus solid carbohydrate: Effects on food intake and body weight. *International Journal of Obesity and Related Metabolic Disorders*, *24*(6), 794-800. https://doi.org/10.1038/sj.ijo.0801229

Drouin-Chartier, J. P., Zheng, Y., Li, Y., Malik, V., Pan, A., Bhupathiraju, S. N., Tobias, D. K., Manson, J. E., Willett, W. C., & Hu, F. B. (2019). Changes in consumption of sugary beverages and artificially sweetened beverages and subsequent risk of type 2 diabetes: Results from three large prospective U.S. cohorts of women and men. *Diabetes Care*. https://doi.org/10.2337/dc19-0734

Faeh, D., Minehira, K., Schwarz, J. M., Periasamy, R., Park, S., & Tappy, L. (2005). Effect of fructose overfeeding and fish oil administration on hepatic de novo lipogenesis and insulin sensitivity in healthy men. *Diabetes*, *54*(7), 1907-1913. https://doi.org/10.2337/diabetes.54.7.1907

Fitch, C., & Keim, K. S. (2012). Position of the Academy of Nutrition and Dietetics: Use of nutritive and nonnutritive sweeteners. *Journal of the Academy of Nutrition and Dietetics, 112*(5), 739-758. https://doi.org/10.1016/j.jand.2012.03.009

Gaillard, T. R. (2018). The metabolic syndrome and its components in African-American women: Emerging trends and implications. *Frontiers in Endocrinology, 8*(383). https://doi.org/10.3389/fendo.2017.00383

Gopalan, A., Lorincz, I. S., Wirtalla, C., Marcus, S. C., & Long, J. A. (2015, Oct). Awareness of prediabetes and engagement in diabetes risk-reducing behaviors. *American Journal of Preventive Medicine, 49*(4), 512-519. https://doi.org/10.1016/j.amepre.2015.03.007

Goran, M. I., Ulijaszek, S. J., & Ventura, E. E. (2013). High fructose corn syrup and diabetes prevalence: A global perspective. *Global Public Health, 8*(1), 55-64. https://doi.org/10.1080/17441692.2012.736257

Gower, B. A., & Fowler, L. A. (2020). Obesity in African-Americans: The role of physiology. *Journal of Internal Medicine, 288*(3), 295-304. https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/joim.13090?download=true

Green, A. K., Jacques, P. F., Rogers, G., Fox, C. S., Meigs, J. B., & McKeown, N. M. (2014). Sugar-sweetened beverages and prevalence of the metabolically abnormal phenotype in the Framingham Heart Study. *Obesity, 22*(5), E157-E163. https://doi.org/10.1002/oby.20724

Hite, A. H., Feinman, R. D., Guzman, G. E., Satin, M., Schoenfeld, P. A., & Wood, R. J. (2010). In the face of contradictory evidence: report of the Dietary Guidelines for Americans Committee. *Nutrition, 26*(10), 915-924.

Hu, F. B. (2013). Resolved: There is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obesity Reviews, 14*(8), 606-619. https://doi.org/10.1111/obr.12040

Institute of Medicine. (2005). Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. *The National Academies Press*. https://doi.org/doi:10.17226/10490

Iranfar, N., & Smith, T. C. (2018). When Should "pre" carry as much weight in the diabetes comorbidity debate? Insights From a population-based survey. *Preventing Chronic Disease, 15*, E36. https://doi.org/10.5888/pcd15.170158

Janket, S.-J., Manson, J. E., Sesso, H., Buring, J. E., & Liu, S. (2003). A prospective study of sugar intake and risk of type 2 diabetes in women. *Diabetes Care, 26*(4), 1008. http://care.diabetesjournals.org/content/diacare/26/4/1008.full.pdf

Johnson, R. J., Sanchez-Lozada, L. G., Andrews, P., & Lanaspa, M. A. (2017). Perspective: A historical and scientific perspective of sugar and its relation with obesity and diabetes. *Advances in Nutrition, 8*(3), 412-422. https://doi.org/10.3945/an.116.014654

Johnson, R. K., Appel, L. J., Brands, M., Howard, B. V., Lefevre, M., Lustig, R. H., Sacks, F., Steffen, L. M., & Wylie-Rosett, J. (2009). Dietary Sugars intake and cardiovascular health. *Circulation, 120*(11), 1011. http://circ.ahajournals.org/content/circulationaha/120/11/1011.full.pdf

Juul, F., Martinez-Steele, E., Parekh, N., Monteiro, C. A., & Chang, V. W. (2018). Ultra-processed food consumption and excess weight among US adults. *British Journal of Nutrition*, 1-11. https://doi.org/10.1017/s0007114518001046

Karve, A., & Hayward, R. A. (2010). Prevalence, diagnosis, and treatment of impaired fasting glucose and impaired glucose tolerance in nondiabetic U.S. adults. *Diabetes Care, 33*(11), 2355-2359. https://doi.org/10.2337/dc09-1957

Kirkpatrick, S., & Raffoul, A. (2017). Measures registry user guide: Individual diet. *Washington DC: National Collaborative on Childhood Obesity Research*.

Khan, T. A., & Sievenpiper, J. L. (2016). Controversies about sugars: Results from systematic reviews and meta-analyses on obesity, cardiometabolic disease and diabetes. *European Journal of Nutrition, 55*(Suppl 2), 25-43. https://doi.org/10.1007/s00394-016-1345-3

Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., Nathan, D. M., & Diabetes Prevention Program Research, G. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine, 346*(6), 393-403. https://doi.org/10.1056/NEJMoa012512

Kristal, A. R., Shattuck, A. L., & Henry, H. J. (1990). Patterns of dietary behavior associated with selecting diets low in fat: Reliability and validity of a behavioral approach to dietary assessment. *Journal of the American Dietetic Association, 90*(2), 214-220.

Kritchevsky, D. (1998). History of recommendations to the public about dietary fat. *The Journal of Nutrition, 128*(2), 449S-452S. https://doi.org/10.1093/jn/128.2.449S

Lana, A., Rodríguez-Artalejo, F., & Lopez-Garcia, E. (2014). Consumption of sugar-sweetened beverages is positively related to insulin resistance and higher plasma leptin concentrations in men and nonoverweight women. *Journal of Nutrition, 144*(7), 1099-1105. https://doi.org/10.3945/jn.114.195230

Lê, K. A., Ith, M., Kreis, R., Faeh, D., Bortolotti, M., Tran, C., Boesch, C., & Tappy, L. (2009). Fructose overconsumption causes dyslipidemia and ectopic lipid deposition in healthy subjects with and without a family history of type 2 diabetes. *American Journal of Clinical Nutrition, 89*(6), 1760-1765. https://doi.org/10.3945/ajcn.2008.27336

Lecoultre, V., Egli, L., Carrel, G., Theytaz, F., Kreis, R., Schneiter, P., Boss, A., Zwygart, K., Le, K. A., Bortolotti, M., Boesch, C., & Tappy, L. (2013). Effects of fructose and glucose overfeeding on hepatic insulin sensitivity and intrahepatic lipids in healthy humans. *Obesity (Silver Spring), 21*(4), 782-785. https://doi.org/10.1002/oby.20377

Lewis, A. S., McCourt, H. J., Ennis, C. N., Bell, P. M., Courtney, C. H., McKinley, M. C., Young, I. S., & Hunter, S. J. (2013). Comparison of 5% versus 15% sucrose intakes as part of a eucaloric diet in overweight and obese subjects: Effects on insulin sensitivity, glucose metabolism, vascular compliance, body composition and lipid profile. A randomised controlled trial. *Metabolism: Clinical and Experimental, 62*(5), 694-702. https://doi.org/10.1016/j.metabol.2012.11.008

Lowndes, J., Sinnett, S. S., & Rippe, J. M. (2015). No effect of added sugar consumed at median american intake level on glucose tolerance or insulin resistance. *Nutrients, 7*(10), 8830-8845. https://doi.org/10.3390/nu7105430

Ma, J., Jacques, P. F., Meigs, J. B., Fox, C. S., Rogers, G. T., Smith, C. E., Hruby, A., Saltzman, E., & McKeown, N. M. (2016). Sugar-sweetened beverage but not diet soda consumption is positively associated with progression of insulin resistance and prediabetes. *Journal of Nutrition, 146*(12), 2544-2550. https://doi.org/10.3945/jn.116.234047

Maersk, M., Belza, A., Stødkilde-Jørgensen, H., Ringgaard, S., Chabanova, E., Thomsen, H., Pedersen, S. B., Astrup, A., & Richelsen, B. (2011). Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: A 6-mo randomized intervention study. *The American Journal of Clinical Nutrition, 95*(2), 283-289. https://doi.org/10.3945/ajcn.111.022533

Malik, V. S., & Hu, F. B. (2015, Oct 06). Fructose and cardiometabolic health: What the evidence from sugar-sweetened beverages tells us. *Journal of the American College of Cardiology, 66*(14), 1615-1624. https://doi.org/10.1016/j.jacc.2015.08.025

Marriott, B. P., Hunt, K. J., Malek, A. M., & Newman, J. C. (2019). Trends in intake of energy and total sugar from sugar-sweetened beverages in the United States among children and adults, NHANES 2003–2016. *Nutrients, 11*(9), 2004. https://www.mdpi.com/2072-6643/11/9/2004

Matikainen, N., Söderlund, S., Björnson, E., Bogl, L. H., Pietiläinen, K. H., Hakkarainen, A., Lundbom, N., Eliasson, B., Räsänen, S. M., Rivellese, A., Patti, L., Prinster, A., Riccardi, G., Després, J. P., Alméras, N., Holst, J. J., Deacon, C. F., Borén, J., & Taskinen, M. R. (2017). Fructose intervention for 12 weeks does not impair glycemic control or incretin hormone responses during oral glucose or mixed

meal tests in obese men. *Nutrition, Metabolism & Cardiovascular Diseases, 27*(6), 534-542. https://doi.org/10.1016/j.numecd.2017.03.003

Macdonald, I. A. (2016). A review of recent evidence relating to sugars, insulin resistance and diabetes. *European Journal of Nutrition, 55*(Suppl 2), 17-23. https://doi.org/10.1007/s00394-016-1340-8

Monteiro, C. A., Moubarac, J.-C., Cannon, G., Ng, S. W., & Popkin, B. (2013). Ultra-processed products are becoming dominant in the global food system. *Obesity Reviews, 14*(S2), 21-28. https://doi.org/10.1111/obr.12107

Montonen, J., Järvinen, R., Knekt, P., Heliövaara, M., & Reunanen, A. (2007). Consumption of sweetened beverages and intakes of fructose and glucose predict type 2 diabetes occurrence. *Journal of Nutrition, 137*(6), 1447-1454. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L46855484

Moshfegh, A. J., Rhodes, D. G., Baer, D. J., Murayi, T., Clemens, J. C., Rumpler, W. V., Paul, D. R., Sebastian, R. S., Kuczynski, K. J., & Ingwersen, L. A. (2008). The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *The American Journal of Clinical Nutrition, 88*(2), 324-332. https://doi.org/ 10.1093/ajcn/88.2.324

National Cancer Institute. (2020). Usual dietary intakes: The NCI method. Retrieved February 22, 2021 from https://epi.grants.cancer.gov/diet/usualintakes/method.html

National Center for Chronic Disease Prevention and Health Promotion. (2020). Diabetes and prediabetes. Centers for Disease Control and Prevention. Retrieved February

3, 2021 from https://www.cdc.gov/chronicdisease/resources/publications/factsheets/diabetes-prediabetes.htm

National Center for Health Statistics. (2017). Dietary intake for adults aged 20 and over. Centers for Disease Control and Prevention. Retrieved March 19, 2020 from https://www.cdc.gov/nchs/fastats/diet.htm

Nielsen, S. J., & Popkin, B. M. (2003). Patterns and trends in food portion sizes, 1977-1998. *JAMA, 289*(4), 450-453. https://jamanetwork.com/journals/jama/articlepdf/195813/jbr20367_450_453_1602622700.97607.pdf

O'Connor, L., Imamura, F., Lentjes, M. A. H., Khaw, K. T., Wareham, N. J., & Forouhi, N. G. (2015). Prospective associations and population impact of sweet beverage intake and type 2 diabetes, and effects of substitutions with alternative beverages [Article]. *Diabetologia, 58*(7), 1474-1483. https://doi.org/10.1007/s00125-015-3572-1

O'Connor, L., Imamura, F., Brage, S., Griffin, S. J., Wareham, N. J., & Forouhi, N. G. (2018). Intakes and sources of dietary sugars and their association with metabolic and inflammatory markers. *Clinical Nutrition, 37*(4), 1313-1322. https://doi.org/10.1016/j.clnu.2017.05.030

Okosun, I. S., & Lyn, R. (2015). Prediabetes awareness, healthcare provider's advice, and lifestyle changes in American adults. *International Journal of Diabetes Mellitus, 3*(1), 11-18. https://doi.org/https://doi.org/10.1016/j.ijdm.2010.12.001

Owei, I., Umekwe, N., Ceesay, F., & Dagogo-Jack, S. (2019). Awareness of prediabetes status and subsequent health behavior, body weight, and blood glucose levels. *Journal of the American Board of Family Medicine, 32*(1), 20-27. https://doi.org/10.3122/jabfm.2019.01.180242

Pan, X. R., Li, G. W., Hu, Y. H., Wang, J. X., Yang, W. Y., An, Z. X., Hu, Z. X., Lin, J., Xiao, J. Z., Cao, H. B., Liu, P. A., Jiang, X. G., Jiang, Y. Y., Wang, J. P., Zheng, H., Zhang, H., Bennett, P. H., & Howard, B. V. (1997). Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care*, *20*(4), 537-544. https://www.ncbi.nlm.nih.gov/pubmed/9096977

Penrod, J., & Hupcey, J. E. (2005). Enhancing methodological clarity: Principle-based concept analysis. *Journal of Advanced Nursing, 50*(4), 403-409. https://doi.org/10.1111/j.1365-2648.2005.03405.x

Perez-Pozo, S. E., Schold, J., Nakagawa, T., Sánchez-Lozada, L. G., Johnson, R. J., & Lillo, J. L. (2010). Excessive fructose intake induces the features of metabolic syndrome in healthy adult men: Role of uric acid in the hypertensive response. *International Journal of Obesity (2005), 34*(3), 454-461. https://doi.org/10.1038/ijo.2009.259

Raben, A., Holst, J. J., Madsen, J., & Astrup, A. (2001). Diurnal metabolic profiles after 14 d of an ad libitum high-starch, high-sucrose, or high-fat diet in normal-weight never-obese and postobese women. *American Journal of Clinical Nutrition, 73*(2), 177-189.

http://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=107020468&site=ehost-live

Rhodes, D. G., Murayi, T., Sebastian, R. S., Clemens, J. C., Baer, D. J., & Moshfegh, A. J. (2013). The USDA Automated Multiple-Pass Method accurately assesses population sodium intakes. *The American Journal of Clinical Nutrition, 97*(5), 958-964. https://doi.org/10.3945/ajcn.112.044982

Schulze, M. B., Manson, J. E., Ludwig, D. S., Colditz, G. A., Stampfer, M. J., Willett, W. C., & Hu, F. B. (2004). Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. *Journal of the American Medical Association, 292*(8), 927-934. https://doi.org/10.1001/jama.292.8.927

Slining, M. M., & Popkin, B. M. (2013). Trends in intakes and sources of solid fats and added sugars among U.S. children and adolescents: 1994-2010. *Pediatric Obesity, 8*(4), 307-324. https://doi.org/10.1111/j.2047-6310.2013.00156.x

Sneed, N. M., Patrician, P. A., & Morrison, S. A. (2019). Influences of added sugar consumption in adults with type 2 diabetes risk: A principle-based concept analysis. *Nursing Forum, 54*(4), 698-706. https://doi.org/10.1111/nuf.12399

Sobal, J., Khan, L. K., & Bisogni, C. (1998). A conceptual model of the food and nutrition system. *Social Science and Medicine, 47*(7), 853-863.

Stanhope, K. L. (2016). Sugar consumption, metabolic disease and obesity: The state of the controversy. *Critical Reviews in Clinical Laboratory Sciences, 53*(1), 52-67. https://doi.org/10.3109/10408363.2015.1084990

Stanhope, K. L., Medici, V., Bremer, A. A., Lee, V., Lam, H. D., Nunez, M. V., Chen, G. X., Keim, N. L., & Havel, P. J. (2015). A dose-response study of consuming high-

fructose corn syrup-sweetened beverages on lipid/lipoprotein risk factors for cardiovascular disease in young adults. *American Journal of Clinical Nutrition, 101*(6), 1144-1154. https://doi.org/10.3945/ajcn.114.100461

Stanhope, K. L., Schwarz, J. M., Keim, N. L., Griffen, S. C., Bremer, A. A., Graham, J. L., Hatcher, B., Cox, C. L., Dyachenko, A., Zhang, W., McGahan, J. P., Seibert, A., Krauss, R. M., Chiu, S., Schaefer, E. J., Ai, M., Otokozawa, S., Nakajima, K., Nakano, T., Beysen, C., Hellerstein, M. K., Berglund, L., & Havel, P. J. (2009). Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *Journal of Clinical Investigation, 119*(5), 1322-1334. https://doi.org/10.1172/JCI37385

Strodel, R. J., Chang, C. H., Khurana, S. G., Camp, A. W., Magenheimer, E. A., & Hawley, N. L. (2019). Increased awareness, unchanged behavior: Prediabetes diagnosis in a low-income, minority population. *Diabetes Educator, 45*(2), 203-213. https://doi.org/10.1177/0145721719826578

Sundborn, G., Thornley, S., Merriman, T. R., Lang, B., King, C., Lanaspa, M. A., & Johnson, R. J. (2019). Are liquid sugars different from solid sugar in their ability to cause metabolic syndrome? *Obesity (Silver Spring), 27*(6), 879-887. https://doi.org/10.1002/oby.22472

Swarbrick, M. M., Stanhope, K. L., Elliott, S. S., Graham, J. L., Krauss, R. M., Christiansen, M. P., Griffen, S. C., Keim, N. L., & Havel, P. J. (2008). Consumption of fructose-sweetened beverages for 10 weeks increases postprandial triacylglycerol and apolipoprotein-B concentrations in overweight

and obese women. *British Journal of Nutrition, 100*(5), 947-952. https://doi.org/10.1017/s0007114508968252

Tabak, A. G., Herder, C., Rathmann, W., Brunner, E. J., & Kivimaki, M. (2012). Prediabetes: A high-risk state for diabetes development. *Lancet, 379*(9833), 2279-2290. https://doi.org/10.1016/s0140-6736(12)60283-9

Te Morenga, L., Mallard, S., & Mann, J. (2012). Dietary sugars and body weight: Systematic review and meta-analyses of randomised controlled trials and cohort studies. *BMJ, 346*, e7492. https://doi.org/10.1136/bmj.e7492

Teff, K. L., Grudziak, J., Townsend, R. R., Dunn, T. N., Grant, R. W., Adams, S. H., Keim, N. L., Cummings, B. P., Stanhope, K. L., & Havel, P. J. (2009). Endocrine and metabolic effects of consuming fructose- and glucose-sweetened beverages with meals in obese men and women: Influence of insulin resistance on plasma triglyceride responses. *Journal of Clinical Endocrinology and Metabolism, 94*(5), 1562-1569. https://doi.org/10.1210/jc.2008-2192

Teshima, N., Shimo, M., Miyazawa, K., Konegawa, S., Matsumoto, A., Onishi, Y., Sasaki, R., Suzuki, T., Yano, Y., Matsumoto, K., Yamada, T., Gabazza, E. C., Takei, Y., & Sumida, Y. (2015). Effects of sugar-sweetened beverage intake on the development of type 2 diabetes mellitus in subjects with impaired glucose tolerance: The Mihama diabetes prevention study. *Journal of Nutritional Science and Vitaminology, 61*(1), 14-19. https://doi.org/10.3177/jnsv.61.14

Tooze, J. A., Kipnis, V., Buckman, D. W., Carroll, R. J., Freedman, L. S., Guenther, P. M., Krebs-Smith, S. M., Subar, A. F., & Dodd, K. W. (2010). A mixed-effects model approach for estimating the distribution of usual intake of nutrients: The NCI

method. *Statistics in Medicine, 29*(27), 2857-2868. https://doi.org/10.1002/sim.4063

Tsilas, C. S., de Souza, R. J., Mejia, S. B., Mirrahimi, A., Cozma, A. I., Jayalath, V. H., Ha, V., Tawfik, R., Di Buono, M., Jenkins, A. L., Leiter, L. A., Wolever, T. M. S., Beyene, J., Khan, T., Kendall, C. W. C., Jenkins, D. J. A., & Sievenpiper, J. L. (2017). Relation of total sugars, fructose and sucrose with incident type 2 diabetes: A systematic review and meta-analysis of prospective cohort studies. *CMAJ: Canadian Medical Association Journal, 189*(20), E711-E720. https://doi.org/10.1503/cmaj.160706

Tseng, E., Greer, R. C., O'Rourke, P., Yeh, H.-C., McGuire, M. M., Albright, A. L., Marsteller, J. A., Clark, J. M., & Maruthur, N. M. (2019). National survey of primary care physicians' knowledge, practices, and perceptions of prediabetes. *Journal of General Internal Medicine, 34*(11), 2475-2481.

U.S. Department of Health and Human Services and U.S. Department of Agriculture. (2015). *2015 - 2020 Dietary Guidelines for Americans* (8th ed.). Retrieved April 20, 2021 from https://health.gov/our-work/food-nutrition/previous-dietary-guidelines/2015.

United States. Congress. Senate. Select Committee on Nutrition and Human Needs (1977). Dietary goals for the United States (2nd ed.)

Wang, J., Light, K., Henderson, M., O'Loughlin, J., Mathieu, M.-E., Paradis, G., & Gray-Donald, K. (2013). Consumption of added sugars from liquid but not solid sources predicts impaired glucose homeostasis and insulin resistance among

youth at risk of obesity. *The Journal of Nutrition*, *144*(1), 81-86. https://doi.org/10.3945/jn.113.182519

Watson, C. S. (2017). Prediabetes: screening, diagnosis, and intervention. *The Journal for Nurse Practitioners*, *13*(3), 216-221.e211. https://doi.org/https://doi.org/10.1016/j.nurpra.2016.08.005

Weber, K. S., Simon, M.-C., Markgraf, D. F., Szendroedi, J., Müssig, K., Roden, M., Strassburger, K., & Buyken, A. E. (2018). Habitual Fructose intake relates to insulin sensitivity and fatty liver index in recent-onset type 2 diabetes patients and individuals without diabetes. *Nutrients*, *10*(6), 774. https://doi.org/10.3390/nu10060774

World Health Organization. (2015). *Guideline: Sugars intake for adults and children*. World Health Organization. http://apps.who.int/iris/bitstream/handle/10665/149782/9789241549028_eng.pdf;jsessionid=8DB31E3E739C06316556991E93EFC326?sequence=1

World Health Organization. (2016). *Global Report on Diabetes*. World Health Organization. https://books.google.com/books?id=tNsEkAEACAAJ

Yang, Q., Zhang, Z., Gregg, E. W., Flanders, W. D., Merritt, R., & Hu, F. B. (2014). Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Intern Med*, *174*(4), 516-524. https://doi.org/10.1001/jamainternmed.2013.13563

Zhu, Y., Sidell, M. A., Arterburn, D., Daley, M. F., Desai, J., Fitzpatrick, S. L., Horberg, M. A., Koebnick, C., McCormick, E., Oshiro, C., Young, D. R., & Ferrara, A. (2019). Racial/ethnic disparities in the prevalence of diabetes and prediabetes by

bmi: Patient Outcomes Research To Advance Learning (PORTAL) Multisite cohort of adults in the U.S. *Diabetes Care*, *42*(12), 2211. https://doi.org/10.2337/dc19-0532

Zhuo, X., Zhang, P., Barker, L., Albright, A., Thompson, T. J., & Gregg, E. (2014). The lifetime cost of diabetes and its implications for diabetes prevention. *Diabetes Care*, *37*(9), 2557-2564. https://doi.org/10.2337/dc13-2484