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Consumer Behaviors, Added Sugar Intake, Diet Quality, Inflammation and Metabolic Syndrome Risks among Adults from the National Health and Nutrition Examination Survey 2007-2010

Shanshan Chen

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**CONSUMER BEHAVIORS, ADDED SUGAR INTAKE, DIET QUALITY,
INFLAMMATION AND METABOLIC SYNDROME RISKS AMONG ADULTS
FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION
SURVEY 2007-2010**

A Dissertation Presented

by

SHANSHAN CHEN

Submitted to the Graduate School of the
University of Massachusetts Amherst in partial fulfillment
of the requirements for the degree of

DOCTOR OF PHILOSOPHY

May 2018

Nutrition
Public Health and Health Sciences

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Approved as to style and content by:

Richard J. Wood, Chair

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Richard J. Wood, Department Head
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DEDICATION

To my dearest family.

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First and foremost, I would like to express my appreciation to Dr. Alayne Ronnenberg, Dr. Richard Wood, Dr. Zhenhua Liu, and Dr. Daniel Gerber, who have guided and supported me throughout this project. They have not hesitated to share their expertise and experiences which inspired me and kept me on the right track. Without their support I believe I could not complete my dissertation. I also thank Dr. Elena Carbone for her thoughtful advice along this journey.

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ABSTRACT

CONSUMER BEHAVIORS, ADDED SUGAR INTAKE, DIET QUALITY, INFLAMMATION AND METABOLIC SYNDROME RISKS AMONG ADULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2007-2010

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Consumption of added sugar has substantially increased in the American diet over the past few decades and has become a growing public health concern. As evidence indicates that consumer behaviors may contribute to dietary practices, it is important to understand related risk factors for high added sugar intake. However, the links between consumer behaviors and added sugar consumption remain unknown. In addition, it was reported that high added sugar intake reduces diet quality and nutrient intakes, and it may be associated with health outcomes such as inflammation and metabolic syndrome. However, the impact of added sugar intake on diet quality and adverse health outcomes is still controversial. The purpose of this research was to investigate the associations between consumer behaviors and added sugar consumption, further to examine the impact of excess added sugar intake on diet quality, nutrient intakes, as well as its relationship with health indicators including inflammatory biomarker high sensitivity C-reactive protein (hs-CRP) and a series of cardio-metabolic markers.

We carried out a secondary data analysis of adults aged ≥ 20 years from the National Health and Nutrition Examination Survey (NHANES) 2007-2010. All analyses were weighted using NHANES sample weights to account for the complex survey design, survey non-response, and post-stratification. Added sugar intake was calculated based on the 24-hour dietary recall, using the datasets of Food and Nutrient Database for Dietary Studies 4.1 (FNDDS 4.1) and the Food Patterns Equivalent Database (FPED) to convert foods and beverages to respective number of teaspoon equivalents of added sugar. Added sugar intake was further presented as continuous variable (gram/day), binary variable ($\leq 10\%$ of calories from added sugar, $>10\%$ of calories from added sugar) based on the USDA/HHA recommendation, tertiles ($\leq 10\%$ of calories from added sugar, 10-25% of calories from added sugar, $>25\%$ of calories from added sugar), as well as quintiles (“1” to “5”, representing the lowest to the highest intake). Overall, majority of our population (60.4%) exceeded the USDA/HHS recommendation on added sugar consumption.

In the first study, soft drink availability at home was positively associated with added sugar intake ($p < 0.001$), whereas cooking frequency in the past 7 days and the use of food label were negatively associated with added sugar intake ($p = 0.03$, $p < 0.001$, respectively), after adjustments for demographics, energy intake, and body mass index (BMI). Reducing soft drink availability at home ($p < 0.001$), increasing cooking frequency ($p = 0.002$), and increasing the use of nutrition label ($p < 0.001$) were all associated with lower added sugar intake ($\leq 10\%$ of calories). Noticeably, major grocery shopping frequency was not associated with added sugar intake.

In the second study, added sugar intake was negatively associated with diet quality determined by Healthy Eating Index (HEI) 2015, after adjusting for demographic and

anthropometric characteristics ($p<0.001$). With regards to energy and nutrient intakes, excess added sugar intake was significantly related to high energy intake and compromised intakes of most macro- and micro-nutrients. Interestingly, excess added sugar intake was significantly associated with reduced sodium consumption, even after adjusting for energy intake ($p<0.001$).

In our third study, after adjusting for demographics, energy intake, BMI, lifestyle factors, and recent use of medication, individuals consuming more than 25% of calories from added sugar in the diet had nearly 4-times likelihood of having low HDL-cholesterol, compared to those consuming $\leq 10\%$ of calories from added sugar (OR=3.68 among men, $p=0.01$; OR=3.88 among women, $p<0.001$). Positive association was seen between added sugar intake and levels of serum triglycerides ($\beta=0.19$ among men, $p=0.006$; $\beta=0.17$ among women, $p=0.007$). However, no relationship was observed between added sugar intake and hs-CRP levels.

Together, the results of these studies suggest that certain consumer behaviors may be related to added sugar intake. Consuming excess amount of added sugar in the diet may play a complicated role in affecting diet quality, and in the risks of developing cardio-metabolic abnormalities. Our findings provide evidences for future intervention and policy changes in terms of reducing added sugar intake, to aid in efforts to promote healthy eating and overall health among adults.

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CHAPTER 1

INTRODUCTION

Consumption of added sugar has substantially increased in the American diet over the last few decades.^{1,2} In 2016, the Centers for Disease Control and Prevention (CDC) reported that added sugar contributed to an average of 13% of total calories intake in adults and 16% in children nationwide.³ Although consuming added sugar to less than 10% of daily calories is a key recommendation from the 2015-2020 Dietary Guidelines for Americans, reaching this goal may be difficult for many people because sugar is not only the most popular ingredient added to foods and beverages in the US,⁴ but also one of the cheapest sources of calories.⁵

Consumer behaviors are important determinants of health and may contribute to the individual dietary practices.⁶ However, evidence of associations between food-related consumer factors and added sugar intake remains inconsistent.^{7,8} Therefore, investigating consumer behaviors and their relationships with added sugar intake may help us understand those potential risk factors for excess added sugar intake, and may guide future intervention and policy changes aimed at improving food choices. In addition, increased added sugar intake has been linked to reduced diet quality, mostly by contributing to excess calories intake and potentially displacing nutrient-dense foods from the diet.⁹ Others have highlighted the harmful associations between added sugar consumption and adverse health outcomes such as obesity, type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD).¹⁰ However, no link has been clearly established between added sugar intake and inflammation, dyslipidemia or other indicators for metabolic syndrome.^{11, 12, 13}

The first goal of this study was to assess how consumer behaviors were related to individual added sugar intake, while accounting for sociodemographic status and other confounders. For the second goal of the study, we examined the impact of added sugar intake on diet quality determined by the Healthy Eating Index (HEI) 2015, as well as the energy and nutrient intakes. Our last goal was to evaluate the associations between added sugar intake and circulating hs-CRP as an inflammatory biomarker, and risks of developing metabolic syndrome and related cardio-metabolic anomalies. This dissertation study analyzed nationally representative data from 3,233 adults 20 years or older from the National Health and Nutrition Examination Survey (NHANES) 2007-2008 and 2009-2010 cycles. We evaluated the relationships between consumer behaviors, added sugar intake, diet quality, as well as inflammatory and cardio-metabolic indicators. The study findings will shed light on a better understanding of the roles of consumer behaviors in influencing added sugar intake, also to add literature to the effect of added sugar on diet quality and adverse health outcomes. Our findings provide evidences for future intervention and policy changes in terms of reducing added sugar intake, to aid in efforts to promote healthy eating and health among American adults.

CHAPTER 2

ADDED SUGAR

2.1 Definition

Sugar is a ubiquitous component of the diet, in either naturally occurring forms (i.e. fructose in the fruit and lactose in the milk) or as additions to foods and beverages during processing and preparation (i.e. high fructose corn syrup). Sugar that is artificially added to foods and beverages is called “added sugar”.¹⁴ There is no universally accepted definition for added sugar yet. The U.S. Food and Drug Administration (FDA) defines added sugar as “sugars that are either added during the processing of foods, or are packaged as such, and include sugars, sugars from syrups and honey, and sugars from concentrated fruit or vegetable juices that are in excess of what would be expected from the same volume of 100 percent fruit or vegetable juice of the same type”.¹⁵ More examples of added sugar include sucrose, fructose, glucose, high-fructose corn syrup, maple syrup, molasses, anhydrous dextrose, crystal dextrose, and dextrin. Sugar alcohols are not considered as added sugar.¹⁵

Sugars are added to foods and beverages for various reasons, including adding sweetness and improving desirable sensory effects, and promoting the palatability of product.¹⁶ Sugars may also be added for texture enhancement such as introducing a tender texture in baked products and inhibiting crystallization in frozen products.¹⁶

2.2 Guidelines on Added Sugar Intake

There are no chemical differences between the same types of naturally occurring sugar and added sugar, thus human body cannot distinguish the source of sugar.¹⁷

Nevertheless, regardless of the purpose of adding sugar in foods and beverages, added sugars are considered as “empty calories”, meaning that little or no nutritional value is provided.¹⁸ A large body of literature has suggested an association between added sugar intake and diet-related health problems such as weight gain and obesity, T2DM, hypertension, and CVD.^{19,20,21,22,23}

Therefore, the United States Department of Agriculture (USDA) has been using the term of “added sugar” since 2000 in the Dietary Guidelines for Americans (DGAs) to raise awareness among the consumers, and to aid consumers in limiting the intake of foods and beverages that are high in added sugar.²⁴ For example, the most recent 2015-2020 DGAs recommend that Americans limit their added sugar intake to less than 10% of daily calories.²⁵ It should be noted that there are different guidelines on added sugar intake from other organizations. For example, the American Heart Association (AHA) recommends that added sugar in the diet supplies no more than 150 calories for men and 100 calories for women per day.²⁶ The Institute of Medicine (IOM) recommends that less than 25% of total calories come from added sugar,²⁷ whereas the World Health Organization (WHO) recommends that less than 10% of total calories should come from free sugars,²⁸ defined as “all monosaccharides and disaccharides added to foods by the manufacturer, cook or consumer, plus sugars naturally present in honey, syrup and fruit juices”.²⁹

To help consumers make informed dietary choices, FDA introduced the Nutrition Facts label in 1994 to provide point-of-purchase nutrition information such as calories, nutrient contents, and serving sizes.³⁰ In 2008, about 54% of US adults reported using the Nutrition Facts label for information,³⁰ indicating this standardized food label has been

playing an important role in affecting people's dietary choices, public health education and policy. However, for over 20 years, only "sugars" are included on the label, as a sum of naturally occurring sugars and added sugars.³¹ Due to the identical chemical structure of sugars from different sources, missing information of "added sugar" on the Nutrition Facts Label makes it difficult for consumers to distinguish those with high amount of added sugar.³¹ Therefore, meeting the USDA/DGA added sugar intake recommendation by using such Nutrition Facts label is not feasible.

This situation will be changed in the future since FDA announced the new Nutrition Facts label in May, 2016 and required that added sugar be clearly labeled on food and beverage packages, both in grams and as a percent Daily Value (%DV).³¹ The DV is calculated based on the USDA/DGA recommendation, which is 200 calories from added sugar based on a 2,000-calorie diet. Currently, both previous and new Nutrition Fact labels can be seen on the market, because manufacturers are required to use the new label by July 26, 2018, and small businesses will have an additional year to comply.³¹

2.3 Food Sources of Added Sugar in the US

It is known that US is one of the largest sugar consumers worldwide, ranking the third after India and EU.³² Therefore, limiting added sugar intake may be of difficulty for many Americans, particularly due to the fact that sugar is the most popular ingredient added to foods and beverages in the US.³³ After the World War II, the American food environment shifted remarkably, with one critical change being the increased use of sugar.³⁴ During 2010-2012, over 10 million metric tons of sugar were used in the US, enabling sugar-loaded foods and beverages widely available to the American people.³⁵

The increased consumption of soda and soft drinks contributed the most to this sugar-heavy dietary shift.³⁶ Han and Powell recently reported that soda was the most heavily consumed sugar sweetened beverages (SSBs) in all age groups except for children.³⁷ According to the findings from NHANES 2003-2006, the top 10 food sources of added sugar in the U.S. diet were “soft drinks and soda”, “candy and sugary foods”, “cake, cookies, quick bread, pastry and pie”, “fruit drinks”, “milk desserts”, “ready-to-eat cereals”, “yeast bread and rolls”, “milk drinks”, “yogurt”, and “condiments and sauces”.³⁸ These 10 food categories accounted for approximately 93% of added sugar intake among the American population.³⁸ Based on NHANES 2009-2010, Steele et al. found that ultra-processed foods comprised 57.9% of caloric intake and provided 89.7% of added sugar intake in the diet.³⁹ It was also reported that the content of added sugar in ultra-processed foods was eightfold higher than that in normally processed foods (21.1% and 2.4% of calories, respectively),³⁹ indicating the potential effectiveness of reducing the consumption of ultra-processed foods in lowering the excess intake of added sugar.

Children are also exposed to a variety of foods and drinks containing added sugar. Based on NHANES 2003-2004 and 2005-2006, Reedy et al. reported that the top sources of calories for 2-18 years old in the US were grain desserts (138 kcal/day), pizza (136 kcal/day), and soda (118 kcal/day), of which, soda and fruit drinks together, counted for 173 kcal/day of calories.¹⁸ In addition, as a common breakfast choice, ready-to-eat cereals are frequently consumed by Americans, especially children.⁴⁰ It was reported that breakfast cereals contributed 8-9% of added sugars in children’s diet.⁴⁰ In fact, about 75% of all foods and beverages in the US contain added sugar in a variety of forms,³² making it almost unrealistic to bypass added sugar for consumers. It is believed that the

top five food sources of added sugar provide little or no nutritional value with very few exceptions. However, limiting consumption of certain food items, such as “milk drinks” and “yogurt”, may lead to potential under-consumption of nutrients including calcium.³⁸ Thus, consumers may be confused to make healthy dietary choices.

2.4 Epidemiology of Added Sugar Consumption in the US

A recent study revealed that American adults have increased their added sugar intake by about 20% from 1970-1974 to 2000, with added sugar consumption per capita being 31.4 teaspoons per day in 2000.⁴¹ From 1977 through 2000, added sugar contributed a 22% increased proportion of calories to the American diet.⁴² In 2010, an average American consumed 78 pounds of added sugar per year.⁴³ Despite a recent decline in consumption of added sugar since 2003 in the US, the mean adjusted added sugar intake remains to be above the USDA/DGA recommended level.⁴⁴

Based on NHANES 2003-2006, over 65% of the US population consumed added sugar higher than 10% of total calories, with no appreciable difference between men and women.⁴⁵ It was reported that added sugar contributed to an average of 13% of total caloric intake in adults and 16% in children nationwide between 2005 and 2010.³ Using data from 1999 to 2002, Cook and Friday reported that an average of 22.9 teaspoons of added sugar (about 359 kcals or 16.6% of daily caloric intake) were consumed per day for individuals 2 years and older.⁴⁶ Between 2013 and 2014, the estimated mean intake of added sugar was 17.4 teaspoon equivalents or 73 grams daily, for American adults and children older than 2 years.⁴⁷ In addition, based on the data of adolescents aged 12-19 years from NHANES 2005-2010, another study revealed that the average usual percent of

calories from added sugar was 16%, with 88% of adolescents having usual intake of added sugar $\geq 10\%$ of total calories.⁴⁸ It was found that, as a major contributor to the added sugar in the diet, the consumption of soft drinks had risen from 10 gallons per person per year to just over 50 gallons per year from 1950 to 2000.⁴⁹ It was also reported that fructose and glucose in soft drinks and fruit drinks contribute to nearly 50% of added sugar in the US.⁴⁹

2.5 Factors Related to Excess Added Sugar Intake

2.5.1 Sociodemographic Characteristics

It is known that the intake of added sugar is excessive for most Americans,^{3,47} thus it is important to understand which factors are related to added sugar intake in order to formulate effective nutrition policies, education or intervention programs.⁵⁰ Dietary intake of added sugar can be affected by a variety of factors, even though the exact predictors of added sugar intake remain unclear.⁵⁰ Based on NHANES 2003-2004, Asian Americans and Hispanics were the two groups consuming the lowest, and the second lowest amount of added sugar, respectively,⁵⁰ whereas Black males had the highest intake compared to all other ethnicity populations.⁵⁰ Using the data from NHANES 1999-2008, it was reported that Black children and adolescents showed a higher odds of heavy fruit drink consumption compared to whites.³⁷ Non-Hispanic Blacks were also more likely to consume excess added sugar compared to the overall population (15.1% versus 12.5%).⁴⁵ Most American adults and children consume excess calories from added sugar, regardless of income and race/ethnicity.⁵¹ However, there are still disparities including the disproportionate consumption of SSBs among young people. Using data from NHANES

1999-2004, youth aged 12-19 years consumed about 16% of total calories from SSBs.⁵² Between 2003 and 2006, more American children 9-13 years than any other age group consumed 15-20% of total calories from added sugar.⁴⁵ Nearly one third of adults older than 51 years consumed more than 15% of their calories from added sugar.⁴⁵

According to the findings from the National Health Interview Survey 2005, researchers concluded that added sugar intake was higher among males than females and was inversely associated with age, educational status, and family income.⁵⁰ Another study found that more women than men 14-30 years were having more than 25% of calories from added sugar (19.8% versus 17.1%), both were higher than any other life stage group.⁴⁵ Lower socioeconomic status was reported to be associated with higher odds of heavy consumption of total SSBs, soda, and fruit drinks among adults.³⁷ It was also found that children of low and mid-low educated mothers were more likely to consume excessive amounts of high-calorie snacks and sugar-containing beverages compared with children of higher educated mothers.⁵³

Furthermore, Sharkey et al. found that the prevalence of any consumption of SSBs and the prevalence of high consumption of SSB were substantially higher among rural adults compared to their urban counterparts, indicating a need for understanding associations among multiple eating behaviors among economically and geographically disadvantaged adults in the US.⁵⁴

2.5.2 Food Environment

According to USDA, limited access to supermarket, supercenters, grocery stores, or other sources of healthy and affordable food outlets may make it harder for some

Americans to consume less added sugar.⁵⁵ Thus, food environmental factors are believed to play huge roles in affecting individual food choices and dietary practices. In the past decade, researchers have been paying attention to the retail food environment as a determinant of dietary intake and weight status.⁷ Yet, there appears to be no definitive conclusion of how the retail food environment is associated with dietary pattern or intake, such as the consumption of SSBs.^{56,57} Both cross-sectional and longitudinal studies have found varied outcomes.⁷ For example, some studies revealed that residents from neighborhoods with fewer supermarkets had unhealthy dietary habits and higher rates of obesity,^{58,59,60} while others reported that living closer to a supermarket was not related to fruit and vegetable consumption, dietary habits, or obesity.^{61,62} Interestingly, despite that the typical perception of grocery stores as healthy food resources, grocery stores can also serve as an important source of obtaining sugar-heavy foods and drinks. In a cross-sectional survey among adults in Kentucky, Gustafson et al. reported that individuals shopping frequently at a supermarket had significantly higher odds of consuming SSBs compared with those who shopped at a farmer's market and specialty stores at least once a week.⁷

According to several surveillance studies, SSBs are widely available in American schools nationwide.^{63,64,65} For example, the US National School Lunch Program recently banned whole milk but allows sugar-sweetened chocolate skim milk.⁶⁶ In addition, the foods and beverages sold outside of federal school meal programs are not required to meet federal nutrition standards.⁶⁷ Therefore, the Healthy, Hunger-Free Kids Act (HHFKA) of 2010 requires USDA to develop regulations governing foods and beverages sold in schools.⁶⁷ The Institute of Medicine (IOM) also recommended that all SSBs be

banned in schools.⁶⁸ Currently, many states have passed laws to regulate competitive foods at schools,⁶⁹ even though the effectiveness of such policies remain questionable. In a study of public schools in 40 states that have banned SSBs during 2006 and 2007, Taber et al. found that state policies banning all SSBs in middle schools appeared to reduce access to and purchasing of SSBs in school among adolescents but did not reduce their overall consumption of SSBs.⁷⁰

Limited access to healthy foods is a known risk factor for poor diet,⁵⁵ thus food deserts have achieved more attention in the recent years. Food deserts are defined as areas with limited access to healthy foods, usually in impoverished areas.⁵⁵ Therefore, placing full-service supermarkets has been proposed as an important policy strategy to confront the overly availability of SSBs and other sugar-containing foods and drinks.⁸ However, the recent Pittsburgh Hill/Homewood Research on Eating, Shopping and Health study has revealed that, after placing a full-service supermarket in one neighborhood (while the comparable one did not change in food environment), use of the new supermarket was not related to dietary changes including lower intake of SSBs.⁸

2.5.3 Health Literacy

Health literacy refers to the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions.⁷¹ In fact, people generally underestimate the number of calories and amount of added sugar in the foods and drinks they consume, which may restrict their abilities to make healthy food choices.⁷² A study reported that about 90% of participants underestimated the caloric content of nine restaurant entrees by an average of

more than 600 calories.⁷² There is empirical evidence suggesting that consumers' choices are markedly influenced by information.⁷³ However, according to a systematic review, the effect of caloric information and added sugar on food consumption and purchase is weak or inconsistent.⁷⁴ This finding may be partly due to the way the nutrition information is presented, such as the missing information of added sugar on the currently used nutrition labels in the US.³¹

The revised Nutrition Facts label with information of added sugar will be used beginning July, 2018 in the US,³¹ to help consumers obtain clear information on the amount of added sugar in their chosen foods and beverages. With regards to restaurant foods, even though current law remains ambiguous about how dietary calories must be reported, all the fast food restaurants in the US have been required by the Patient Protection and Affordable Care Act (PPACA) to provide "clear and conspicuous" caloric information on menu boards since mid 2012.⁷⁵ The policy makers and nutrition experts believed that creating such opportunities will improve the effectiveness of caloric information on purchasing behavior, particularly among those at the highest risk for excessive consumption of added sugar and calories.⁷⁶

In a case-crossover study conducted in a predominantly Black neighborhood in Baltimore, researchers found that exposure to any caloric information among Black adolescents significantly reduced the odds of SSB purchases relative to the baseline.⁷⁶ It was also found that the most easily understandable caloric information was provided in a physical activity equivalent format.⁷⁶ Another study conducted in rural Mississippi revealed that health literacy significantly predicted consumption of SSBs, with one-point increase in health literacy score associated with 34 fewer calories from SSBs per day,

after controlling for demographic variables.⁷⁷ Park et al. reported that knowledge about the adverse effects of SSBs was significantly associated with SSBs consumption and lower added sugar intake.⁷⁸ A recent study reported that by providing a 20-month comprehensive, multi-component education as a school-based randomized trial, favorable effects in favor of the intervention group were found for intake of SSBs and fruit among the adolescents, particularly for children of parents with low and medium educational level who had reduced their intake of SSBs the most.⁷⁹

2.5.4 Food Insecurity

Food insecurity is defined as a household level economic and social condition of limited or uncertain access to adequate food.⁸⁰ In 2016, about 12.3% of American households were food insecure,⁸⁰ including the most vulnerable populations such as families with children, women, elderly, minority groups, and those from low-income households.⁸⁰ Because calorie-dense foods and drinks such as SSBs and sugary snacks cost significantly less per calories than nutrient-dense ones, and low-income households with children place greater importance on the convenience in food preparation and longer food shelf life,⁸¹ food insecure individuals consume SSBs and other calorie-dense foods and drinks more frequently versus those who experience food security.^{82,83} Nevertheless, there is still limited evidence that can demonstrate an association between household food insecurity and increased added sugar, processed foods, or caloric intake.^{84,85,86}

A study among Mexican-origin children in Texas indicated that children from food insecure families were more likely to have greater percent of calories from added sugar.⁵⁴ Another study in Canadian Arctic communities revealed that significantly higher intake

of high-sugar snacks and foods, as well as lower consumption of fruit and vegetables and dairy were seen among adults from food insecure household versus food secure households.⁸⁷ A Minnesota parents study discovered that food insecure parents consumed almost an additional full serving of SSB each day compared to parents from food secure households.⁸⁸ A recent study showed that the Supplemental Nutrition Assistance Program (SNAP) participants with any level of food insecurity had a significantly higher intake of added sugar (22.0 vs 18.7 teaspoons) and higher intake of empty calories (787.9 vs 731.5 kcals) compared to those with full food security.⁸⁹

Based on a 3-month longitudinal study in Massachusetts, it was also reported that SNAP participants consumed high intake of SSBs at baseline compared to the 2010-2015 Dietary Guidelines for Americans.⁹⁰ After the initiation of benefits, they still consumed almost 1.5 servings of SSBs and fruit juices per day, and the SNAP participation was not associated with improved household food security status.⁹⁰ In a maternal feeding study among urban Black mothers, researchers found that the odds of adding sugars to beverages served to children was elevated among food insecure households, even though it did not reach statistical significance.⁹¹

2.6 Added Sugar and Diet Quality

The increased consumption of added sugar has been linked to an overall decrease in diet quality.⁹ Added sugar influences diet quality mostly by contributing to excess calories intake and potentially displacing nutrient-dense foods from the diet.²⁵ Based on NHANES 1999-2000, adults with highest intake of SSBs had a higher intake of calories, carbohydrates, as well as a lower intake of fiber, orange juice, and low-fat milk.⁹² A recent systematic review based on 52 studies stated that higher intake of added sugar is

associated with poorer diet quality, after adjusting for total caloric intake,⁹³ and a negative association was observed between added sugar and micronutrient intake.⁹³ In addition, Marriott et al. reported that overall nutrient intake was lower with increased added sugar intake for all life stage groups, and the median estimated nutrient intake was lowest among those who consumed greater than 25% of total calories from added sugar.⁴⁵

In addition, it is believed that added sugar may affect diet quality by playing a role in the regulation of appetite and eating behaviors.⁹⁴ Added sugar can interrupt the secretion of ghrelin and leptin, leading to cravings for more foods and excessive caloric intake.⁹⁴ “Sugar addiction” is a relatively new term which may explain people’s cravings for added sugar upon habitual exposure.⁹⁵ This term was invented by several researchers, mostly neuroscientists.⁹⁶ The strong argument is that the highly palatable foods with high amount of added sugar could be genuinely addictive, among a significant proportion of people.^{97,98} Also, foods rich in added sugar may trigger brain activity by stimulating certain cells in the digestive process,⁹⁹ and involving brain mechanism to regulate glucose signaling.¹⁰⁰ These combined effects from added sugar on the nervous system are drug-like (but at a significantly lower level), and may partially explain why many people seek sweet foods for their comforting and mood-altering psychoactive effects.¹⁰¹ Together, these findings may explain why a number of people have difficulty in cutting added sugar intake after being habitually exposed to it.⁹⁵

2.7 Public Health Impacts of Added Sugar Intake

2.7.1 Systemic Inflammation

Systemic inflammation is characterized by high levels of circulating inflammatory cytokines and increased macrophage infiltration in peripheral tissues.¹⁰² There have been strong evidences showing that low-grade systemic inflammation is related to the development of obesity and cardio-metabolic diseases.¹⁰² Added sugar intake may play a role in the development of systemic inflammation, especially via SSB consumption.^{103,104} Malik et al. reported that excess added sugar intake increased the risk for metabolic syndrome and CVD by stimulating the inflammation.¹⁰⁵ Researchers also found that consuming sugar-loaded beverages induced the transcription and activation of multiple monocyte inflammatory cytokine-related genes via key signaling pathways.¹⁰⁶ According to a randomized controlled crossover dietary intervention study, excessive consumption of SSBs over 8 days affected low-grade chronic systemic inflammation among normal-weight to obese adults, with no difference detected among difference sources of added sugar.¹⁰⁷

Even though the exact mechanism of the potential association between added sugar intake and inflammation remains unknown, researchers have looked at advanced glycation end products (AGEs) as a key modulator. AGEs are a heterogeneous group of molecules formed from non-enzymatic reaction of reducing sugars with amino groups of proteins, lipids, and nucleic acids.¹⁰⁸ Increased added sugar intake results in an excessive amount of glucose, further converted into AGEs via three pathways including Millard reaction, Oxidation of glucose, and polyol pathway.¹⁰⁹ Circulating AGEs are positively correlated with high levels of CRP.¹¹⁰

2.7.2 Overweight/Obesity

Obesity is an enormous public health issue in the US, affecting more than one third of adults and about 17% of children.¹¹¹ Even though the etiology of obesity remains not fully understood, the development of obesity essentially involves an excess of caloric intake over caloric expenditure. It is known that the primary drivers of obesity are calorie-dense diets and a lack of physical activity, thus added sugar may increase obesity risk by increasing the caloric density of the diet or promoting the enjoyment of calorie-dense foods and beverages.¹¹²

Soft drink consumption has increased fivefold since 1950.³² A typical 20-ounce bottle of regular soda in the US contains 15 to 18 teaspoons of sugar, providing 250 to 300 calories, which by itself, already exceeds the daily limit of added sugar as recommended by USDA/DGA. It is believed that the rising consumption of SSBs has been a major contributor to the obesity epidemic.¹¹¹ Furthermore, a close parallel between the increased SSBs consumption and the obesity epidemic in the US has been provided using time-trend data in the past three decades.¹¹³ Based on NHANES 1999-2000, researchers found that increased consumption of SSBs was also associated with total and abdominal obesity in US adults aged 20–39 years.⁹²

Children are also affected. According to the Infant Feeding Practices Study II in 2005-2007, American children who consumed SSBs during infancy had higher odds of being obese at 6 years than non-consumers during infancy.¹¹⁴ Fox et al. reported in the third School Nutrition Dietary Assessment Study that among middle-school aged children, the availability of vending machines that sold low-nutrient and calorie-dense

foods and drinks in or near the cafeteria was significantly associated with higher BMI z-score,¹¹⁵ and this finding was consistent with another study which found that children in middle schools that did not having pouring rights contrasts consumed considerably fewer calories from SSBs than their counterparts.¹¹⁶ It has been well documented that obese children are more likely to become obese adults,¹¹⁷ suggesting the importance of cutting SSBs consumption among children and adolescents.

In 2012, Morenga et al. analyzed 30 randomized controlled trials and 38 prospective cohort studies, and concluded that SSBs consumption is a determinant of body weight.¹¹⁸ Another systematic review stated that, large cross-sectional studies, in conjunction with well-powered prospective cohort studies with long periods of follow-up, showed a positive association between greater consumption of SSBs and weight gain and obesity among both children and adults.¹¹⁹ A third systematic review of six randomized controlled trials also indicated that decreasing SSBs consumption reduces the prevalence of obesity.¹²⁰ In addition, findings from the Framingham Offspring Study reported that, after a 4-year follow up, those who consumed at least one soft drink per day had a 37% higher risk of developing obesity compared to non-consumers.¹²¹ A trial study among US adults found that reducing SSBs intake by one serving daily was linked to a weight loss of 0.49 kg at 6 months and 0.65 kg at 18 months.¹²² A meta-analysis of seven studies that added SSBs to persons' diets showed dose-dependent increased weight, whereas an updated meta-analysis of eight studies attempting to reduce SSB consumption showed an ambiguous effect on body weight composition.¹²⁰ Furthermore, if limited to only overweight subjects at baseline, there was a roughly 0.25 standard deviation of more weight loss or less weight gain relative to control groups.¹²⁰ In 2013, Hu et al. concluded

that there was sufficient scientific evidence that reducing SSBs consumption will reduce the prevalence of obesity and obesity-related diseases and suggested public health action to be taken before absolute adverse outcomes occur.¹²³

2.7.3 Insulin Resistance and Diabetes

Insulin resistance is defined as “a state when a normal or elevated serum insulin level produces an attenuated biological response, leading to impaired sensitivity to insulin mediated glucose metabolism”.¹²⁴ Insulin resistance is associated with many abnormalities such as diabetes, hypertension, dyslipidemia and CVD.¹²⁵ These abnormalities and related physical outcomes, as a cluster, constitute the insulin resistance syndrome.¹²⁶ In fact, insulin resistance is closely related to the development and progression of T2DM.¹²⁷

As a serious and rapidly growing chronic health condition in the US, diabetes affected more than 30 million Americans in 2015, with nearly one fourth of them not knowing it.¹²⁸ Majority (about 90-95%) of people with diabetes are estimated to have T2DM.¹²⁹ In fact, more than a third of US adults are affected by prediabetes,¹²⁸ a health condition characterized by a higher than normal blood glucose level, but not yet within the diabetes range. Prediabetes is not known by approximately 90% of patients.¹²⁸ Without intervention, people with prediabetes will progress to T2DM at a rate of 10% per year.¹²⁸

Many epidemiological and mechanistic studies have found that excessive added sugar consumption affects human and animal health beyond merely adding “empty calories”. Importantly, added sugar intake can be linked to insulin resistance and other

chronic conditions.¹³⁰ As the top food source of added sugar, SSBs has been found to be associated with higher risk of insulin resistance and diabetes by a growing body of evidence, through increased adiposity and other metabolic effects.¹³⁰ Two short-term randomized trials have shown increased serum levels of glucose and insulin in participants.^{131,132}

Based on NHANES 1999-2004, increased SSBs intake was also associated with adverse metabolic parameters among adolescents 12-19 years, and the significance of the associations differed by race and gender,¹³³ affecting non-Hispanic white females and non-Hispanic white males the most. It was reported that low to moderate intake of SSBs among a group of healthy young men impaired glucose metabolism by increasing fasting glucose level significantly.¹³⁴ A recent Canadian study revealed that liquid added sugar (i.e. syrups) was a risk factor for developing insulin resistance among youth over 2 years old who were at risk of obesity.¹³⁵ Through a 15-year cohort study, researchers found that the consumption of a diet containing high amount of added sugar was linked to increased risk for diabetes, independent of weight changes.¹³⁶ Schulze et al. also reported that consumption of SSBs may contribute to a high glycemic load (GL) diet, increase T2DM and cardiovascular risk independently of obesity.¹⁰³ The intake of added sugars was also found to be positively associated with insulin resistance among a group of overweight/obese US adolescents.¹³⁷ Similar results were found by Stanhope et al., that consuming fructose-sweetened beverages specifically increased insulin resistance among overweight/obese adults.¹³¹ In animal models, it was reported that added sugar intake (in the form of fructose) induced insulin resistance, impaired glucose tolerance, and

hyperinsulinemia.¹³⁸ Another animal study also indicated that sucrose-sweetened water induced insulin resistance in mice.¹³⁹

There is also mounting evidence showing the connection between added sugar intake and T2DM. A large prospective cohort study in Europe found that consumption of SSBs was closely related to the risk of T2DM.¹⁴⁰ A Japanese study revealed that soft drink consumption was associated with increased risk of T2DM among women.¹⁴¹ Another study analyzed research data from both developed and developing countries, and concluded that soft drink consumption was significantly associated with diabetes independent of total caloric intake worldwide.¹⁴² Based on the Nurses' Health Study II 1991-1999, Hu et al. reported that SSBs contributed to the development of T2DM, not entirely mediated through weight gain.¹⁴³ In a prospective cohort study among African American women, researchers found that the incidence of T2DM was higher in those who had higher intake of two sugar-sweetened soft drinks.¹⁴⁴ Analysis of over 20 years of data among healthy men from the Health Professional Follow-Up Study indicated that SSBs consumption was associated with an increased risk of T2DM, with a reduced risk by 17% after replacing one serving of SSB with coffee.¹⁴⁵ A recent systematic review of 17 cohort studies concluded that habitual consumption of SSBs was associated with a greater risk of T2DM, independent of adiposity.¹⁴⁶

2.7.4 Cardiovascular Disease (CVD)

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality among American adults, accounting for 23.4% of the deaths in the US in 2015.¹⁴⁷ Lifestyle factors including food choices have been a central focus of CVD risk.¹⁴⁸ Based on

NHANES 1999-2004, consumption of added sugar among US adolescents was positively associated with multiple measures known to increase cardiovascular risk, including triglycerides, LDL, and HDL.¹³⁷ Yang et al. analyzed NHANES data during 1988-2006 and reported that most US adults consumed more added sugar than the recommended level for a healthy diet, and a significant relationship was observed between added sugar consumption and increased risk for CVD mortality.¹⁴⁹ Evidence from epidemiological studies and experimental trials in animals and humans have also suggested that added sugar, particularly fructose, may increase blood pressure (BP), BP variability, heart rate, and myocardial oxygen demand, and other metabolic dysfunction.¹⁵⁰ A recent meta-analysis found that consumption of SSBs may increase the risk of CVD, especially among men and American populations.¹⁵¹ As a main type of added sugar, another study found that fructose intake higher by 2 standard deviations (5.6% kcal) was associated with significant higher systolic/diastolic blood pressure, after adjusting for weight and height.¹⁵²

It is believed that reducing the consumption of foods containing added sugar and refined grains would reduce CVD risk, by improving blood lipid profiles, reducing body weight, and improving insulin sensitivity,¹⁵³ even though there are inconsistent findings. In 2016, a group of researchers called for an action in urging policymakers to consider giving less weight to food industry-funded studies as well as include studies appraising the effect of added sugar on multiple CVD biomarkers and disease development.¹⁵⁴ However, in a randomized prospective parallel group blinded study, it was reported that when consumed as part of a normal diet, common fructose-containing sugars did not raise

blood pressure, even at five times the upper level recommended by the AHA and three times the upper level recommended by WHO.¹⁵⁵

Cardiovascular health outcomes among children can also be affected by added sugar consumption. In a cross-sectional study conducted in Alabama, researchers found that added sugar intake was positively associated with diastolic BP and serum triglycerides among a group of children aged 7-12 years, indicating its effect on adverse cardiovascular outcomes.¹⁵⁶ Kosova et al. reported in a young children study that increased SSBs intake was independently associated with decreased HDL.¹⁵⁷ A recent scientific statement from AHA stated that strong evidence supports the association between added sugar and increased CVD risk in children through increased caloric intake, increased adiposity, and dyslipidemia.¹⁵⁸ The AHA committee suggested that it is reasonable to recommend that children consume ≤ 25 g (about 6 teaspoons) of added sugar per day and to avoid added sugar for children younger than 2 years,¹⁵⁸ even though few children actually achieve such levels of added sugar consumption. In an Australian study among adolescents, it was found that both girls and boys in the top tertile of SSB intake group showed increases in triglycerides, and boys showed reductions in HDL independent of BMI.¹⁵⁹ Prasad and Dhar recently reported that oxidative stress may be a mechanism of added sugar-induced CVD, that various sources of sugar-induced generation of reactive oxygen species (ROS) such as mitochondria, nicotinamide adenine dinucleotide phosphate-oxidase, advanced glycation end products, insulin and uric acid.¹⁰⁹

2.7.5 Metabolic Syndrome (MetS)

According to NHANES 1999-2006, among the 6113 adults consuming less than 5%, 5%-10%, 10-17.5%, 17.5-25%, and 25% and above of total calories as added sugar, adjusted mean HDL levels were 58.7, 57.5, 53.7, 51.0, and 47.7 mg/dL, respectively ($p < 0.001$).¹⁶⁰ Among US adolescents aged 12-19 years from NHANES 2005-2015, added sugar was significantly associated with MetS, independent of total caloric intake, physical activity or BMI z-score.¹⁶¹ Another cross-sectional study in the US suggested that added sugar was positively associated with diastolic BP and serum triglycerides among children aged 7-12 years.¹⁵⁶ A recent study in Taiwan found that a high SSB intake was related to adolescent MetS among boys but not girls.¹⁶² Wang et al. reported in a cohort study that higher SSB consumption was associated with elevated systolic BP and greater insulin resistance among overweight/obese children whereas the associations were not evident among normal-weight children.¹⁶³ However, there have been different findings. Even though a recent state-of-the-art review article suggested that fructose is associated with the development of MetS,¹⁶⁴ based on NHANES 1999-2006, Sun et al. found that fructose, averaged 37% of total sugar intake, was not associated with indicators of MetS among participants 12-80 years old.¹⁶⁵ Another review paper stated that long term consumption of diet high in saturated fat, omega-6 fatty acids and sugar especially fructose, while low in omega-3 fatty acids contributes to the development of MetS,¹⁶⁶ it is noticeable though, that the influence of fructose on MetS is unclear.

Dekker et al. reported that fructose may play a role in the development of insulin resistance and MetS in animal models, possibly related to altered gene expression patterns, altered satiety factors in the brain, increased inflammation, higher ROS, and

portal endotoxin concentrations via toll-like receptors.¹⁶⁷ Another recent animal study revealed that endogenous fructose generation and metabolism in the liver represents an important mechanism whereas high serum glucose concentrations promote the development of MetS.¹⁶⁸ Khitan et al. reported possible mechanisms that fructose causes insulin resistance and other MetS symptoms.¹⁶⁹ It was also postulated that excessive fructose consumption may underlie the development of nonalcoholic fatty liver disease and MetS, with the same pathogenesis shared by alcoholic fatty liver disease.¹⁷⁰

CHAPTER 3

CONSUMER BEHAVIOR

3.1 Background

Consumers are the individuals who purchase products and services for personal consumption or to meet the collective needs of the family or household.¹⁷¹ Consumer behaviors refer to individual's specific behaviors in the decision-making process to spend their available resources such as time, money, and effort,¹⁷¹ such as grocery shopping, home cooking, and eating out. Consumer behavior is also defined as “the behavior that consumers display in searching for, purchasing, using, evaluating and disposing of products, services and ideas which they expect will satisfy their needs”.¹⁷² Due to the complexity of consumer behavior by its nature, it is almost impossible to predict with accuracy any consumer behavior in a given situation.¹⁷¹ With regards to dietary practices, understanding consumer behaviors and their impact on food choices are of great importance.

3.2 Factors Related to Food-Related Consumer Behaviors

3.2.1 Sociodemographics

Consumer behavior can be affected by a variety of factors such as age, gender, education, marital status, and income.¹⁷³ A study among 160 French adults aged 18-90 years revealed that younger consumers valued low prices more than suitability and other factors, compared to older individuals.¹⁷⁴ A recent study on online consumer behavior found that men were engaged in less exploratory behavior and developed less website involvement than women, indicating the gender difference as a driver of different attitudes

in consumption.¹⁷⁵ Therefore, it was suggested that a measure more relevant to gender-based consumer behaviors may be developed to increase the potential explanatory power of consumer behavior assessment.¹⁷⁶ With regards to income, a study on the relationship between consumer income and locus of control on financial behavior found that consumers' propensity to save, budget, and control spending depended partly on their income, along with their level of perceived control over outcome and knowledge.¹⁷⁷

A systematic review of 49 studies from 1966 to 2007 stated that low-income and racial/ethnic minority groups are more likely to be exposed to relatively poor food environments, characterized by a dearth of large grocery stores and high concentration of convenience stores.¹⁷⁸ A cross-sectional study conducted in Baltimore, MD revealed that the lowest healthy food availability was observed in 43% of predominantly black neighborhoods and 46% of lower-income neighborhoods, versus 4% of predominantly white neighborhoods and 13% of higher-income neighborhoods.¹⁷⁹ These differences were largely attributable to fewer supermarkets and more behind bullet-proof glass stores (a form of corner store) in the predominantly black neighborhoods and lower-income neighborhoods.¹⁷⁹ In 2012, Helen et al. reported that American young children who lived in residentially poor and minority neighborhoods were more likely to have greater access to convenience stores.¹⁸⁰ Based on NHANES 2009-2012, it was found that diet low in energy density can be obtained regardless of money spent at grocery stores, indicating that educating consumers regarding low-cost healthy food options may be a successful strategy in obesity prevention.¹⁸¹

3.2.2 Social/Environmental Factors

Consumer behavior is strongly influenced by cultural, social, environmental and psychological factors.¹⁷¹ A recent analysis paper on adolescents from NHANES 2007-2010 reported that both healthy food availability and an increase in supermarket spending were associated with a reduced prevalence of prediabetes and diabetes.¹⁸²

Food environment is critical to people's consumer behaviors. There are four major categories of commercial food store outlets for individuals to shop at, including grocery stores, supermarkets, and convenience/corner stores,¹⁸³ and farmer's markets.¹⁸⁴ Powell et al. reported that food outlets are more common in urban areas compared to suburban and rural areas in the US.¹⁸³ Furthermore, grocery stores and supermarkets are found to be more densely located in non-poor neighborhoods than poor neighborhoods,¹⁸⁵ with greater availability, and quality of healthier foods compared to convenience and corner stores.¹⁸⁵ Grocery store indoor environment may also play a role in influencing consumer behavior. A systematic review of supermarket-based nutrition intervention studies found that shelf labelling particularly using nutrition summary scores was the most effective and sustainable intervention in improving the healthiness of consumer purchases.¹⁸⁶ A recent study in Malaysia reported that the layout and store density had not significantly affected the consumer behavior in a supermarket. Instead, music and lighting were found to be dominant predictors.¹⁸⁷ A large-scale grocery chain study reported that the point-of-sale nutrition scoring system helped consumers make healthier food choices.¹⁸⁸ In addition, the same study revealed that consumers were more sensitive to promotion and less sensitive to price following the introduction of the food scoring system.¹⁸⁸

In addition, concerns with taste, nutrition, cost, and convenience are believed to be key influences on dietary choices. Based on NHANES 2007-2010, researchers found that even though majority of the US adults rated “taste” as “very important”, it had a weak relation with diet quality.¹⁸⁹ In this same study, it was reported that adults who prioritized nutrition during grocery shopping had higher diet quality regardless of gender, education and income.¹⁸⁹ Another study of 1,188 customers found that health value was the key factor in promoting healthy eating and increasing hedonic consumer expectations.¹⁹⁰

3.2.3 Health Literacy

Health and food literacy may play a role in shaping consumer behaviors. A recent systematic review of studies among adolescents reported that adolescents with greater food knowledge and frequent food preparation behaviors were more likely to adopt healthier dietary practices.¹⁹¹ Another study among adults aged 18-29 years found that health literacy was a predictor of food label use, which positively predicted food-related consumer behaviors.¹⁹² Based on a cross-sectional study among 1,012 consumers, it was found that a higher general health interest was associated with greater likelihood of strategy use in measuring, purchasing and eating.¹⁹³ Recent studies have identified various gaps in consumer behavior research. Front-of-package nutrition labeling system has been developed by both food retailers and manufacturers to help consumers identify more healthy choices at the point of purchase.¹⁹⁴ It was also reported that food-related attitudes have been known to affect diet quality and perceived value of cost over nutrition was associated with higher consumption of fats, added sugar and sodium.¹⁹⁵

3.2.4 Food Affordability

Starting 1974, USDA began implementing a federal production-oriented agricultural policy, encouraging farmers to produce commodity crops as much as possible.¹⁹⁶ This policy directly resulted in a 40% drop in the prices of commodity crops including corn, wheat, and soybeans by 2001.¹⁹⁷ As an effort to provide cheap food to Americans, this policy has been a success. However, this policy also directly causes high-sugar and high-fat foods, such as fast foods and SSBs, to become the least expensive foods in the American food environment.¹⁹⁸ In fact, unhealthy food loaded with sweets and fats are the most inflation-resistant part of the US diet,¹⁹⁹ especially when compared to fresh fruits and vegetables.¹⁹⁸ Between 1985 and 2000, the retail price of regular soda and sweets rose by 20% and 46%, respectively, whereas fresh fruits and vegetable retail price increased by 118% during the same time period.²⁰⁰

In contrast, even though commodity crops are in sufficient supply and of cheap prices in the US, the availability of healthy food such as fresh fruits and vegetables remains questionable.¹⁹⁸ USDA data indicate that there is a 24% supply shortfall per capita in the US in meeting the recommendations for five daily servings of vegetables on a 2,000-calorie diet.²⁰¹ Excluding starchy vegetables, the shortfall looks even worse, with only about half of recommended servings of dark green vegetables, one third of the orange vegetables, and a quarter of legumes being available.²⁰¹

It was reported that grains, sugar, and fats food groups supplied cheaper dietary calories, in comparison with fruits and vegetable groups.²⁰² This price difference may explain why calorie-dense and low nutritional-value foods are often low-cost, thus

affordable to most people. In another study, Aggarwal et al. found that higher intakes of added sugar and fats were associated with lower diet costs, whereas higher intakes of vitamins A, C, D, E and B12, folate, carotene, calcium, iron, magnesium, potassium, and dietary fiber were linked to higher diet costs.²⁰³ Affording healthy food can be an even bigger challenge for people who shop at convenience stores and gas stations since they tend to have higher prices for healthy food items versus grocery stores and supermarkets.^{204,205,206}

3.3 Consumer Behaviors and Dietary Practices

It should be noted that, even though 38 years have passed since the first version of DGAs was released, no substantial shift has been made in terms of consumer compliance, manifested as poor implementation of the recommendations as a result of a constellation of factors.²⁰⁷ Some of these factors include cultural and family influences, personal preferences, food availability and accessibility, food preparation skills, food marketing practices, time pressure, and food policies.²⁰⁷ According to the Office of Disease Prevention and Health Promotion, the typical dietary patterns consumed by Americans do not meet the recommendations stated by the 2015-2020 DGAs.²⁵ Instead, they are usually characterized by an abundance of processed foods and added sugar.^{39, 208} More importantly, these typical American dietary patterns are seen among all socio-demographic groups.²⁰⁹ Based on the findings from NHANES 2007-2010 and What We Eat in America, about three fourths of the American population was consuming a diet low in vegetables, fruits and dairy products,²⁵ and high in added sugar, saturated fats, and sodium.²⁵

Recently, more and more researchers have realized this huge gap and start to pay attention to the transition from consumer behavior to dietary practices. A recent cluster-randomized controlled trial among 2,714 students aged 5-12 years in Australia found that a consumer-behavior intervention using an online canteen infrastructure strongly improved purchasing behavior, as an effort to improve child public health nutrition.²¹⁰ It was also reported that greater likelihood of strategy usage in measuring, purchasing and eating contributed to smaller portion size of food.¹⁹³ Another study focusing on good practices in intervention and policy changes concluded that three domains of consumer behavioral factors, including main characteristics, monitoring/evaluation, and implementation worked in various populations in promoting healthy diet and physical activity.²¹¹

CHAPTER 4

C-REACTIVE PROTEIN (CRP)

4.1 Background

C-reactive protein (CRP) is an acute-phase plasma protein that serves as an early and sensitive marker of inflammation.²¹² It belongs to the calcium-dependent ligand-binding plasma protein family and is composed of five identical non-glycosylated polypeptide subunits.²¹³ CRP is currently considered as one of the best measures of nonspecific inflammation and tissue injury.²¹⁴ CRP was named for its capacity to precipitate the somatic C-polysaccharide of *Streptococcus pneumoniae*.²¹⁴ In the absence of infections, concentration of CRP in the blood is normally under 10 mg/L at 99th percentile value, with the median level of CRP being 0.8 mg/L among healthy young adults.²¹⁵ However, as it is massively induced as part of the innate immunity, CRP can rapidly reach 5 mg/L by roughly 6 hours and further rise to 350-400 mg/L within the first 48 hours during infection, or inflammation, or trauma.²¹² In response to serious infection or major tissue damage, CRP level may even spike up to 10,000-fold.²¹⁶

CRP is primarily produced in the liver, but recent studies have shown that non-hepatic tissues such as the renal epithelium and respiratory tract may also generate a small amount of CRP.²¹⁷ CRP synthesis starts rapidly after a single stimulus of infection, and this process is predominantly under transcriptional control by inflammation cytokine IL-6.²¹⁴ When such stimulus ceases, the blood CRP level falls quickly, at a rate of clearance²¹⁸ but the rate is constant, rendering CRP concentration as a reliable indicator of ongoing inflammation.²¹⁹ Importantly, acute-phase CRP values are not affected by diet and show no diurnal variation.²¹⁴ Dramatic elevations in blood CRP levels suggest acute

infections whereas in the absence of such apparent fluctuations, CRP concentration reflects the degree of background inflammation characteristic of an individual. It is much more accurate than other laboratory parameters of the acute-phase responses.²¹⁴

The serum half-life of CRP is approximately 19 hours and is constant under all health and disease conditions.²¹⁴ Therefore, CRP synthesis rate is used as the sole determinant of circulating CRP level because it directly reflects the intensity of the pathological process that stimulate CRP production.²¹⁹ It is noteworthy to mention that CRP concentration can stay relatively stable among people without serious infections, with minimal seasonal and year-to-year variations (self-correlation coefficient is about 0.5), similar to the levels of total cholesterol and systolic blood pressure.²²⁰ In fact, the sensitivity, speed, and range of CRP concentrations tend to be stable within each person, apart from occasional spikes due to minor or subclinical infections or inflammation.²¹⁴ CRP measurement, thereby, is a useful nonspecific serum biomarker of inflammation in screening for organic disease, assessing disease activity in inflammatory conditions, monitoring of the responses to infection treatment, and detecting inter-current infections in immunocompromised individuals.²¹⁴ Liver failure impairs CRP production, but no other pathologies and very few drugs can reduce CRP concentrations unless they also affect the underlying pathology providing the acute-phase stimulus.²¹⁴

4.2 Role of CRP in Inflammation

There are several mechanisms through which CRP activates the immune response and potentially worsens inflammation. As a product of acute-phase response upon being infected, human CRP binds with highest affinity to phosphocholine residues.²¹⁴ CRP also

binds to a variety of other autologous and extrinsic ligands such as native and modified plasma lipoproteins,²²¹ damaged cell membranes²²² and many phospholipids.²¹⁴ It can also aggregate or precipitate the cellular, particulate, or molecular structures bearing these ligands.²¹⁴ When aggregated or bound to macromolecular ligands, CRP can be recognized by C1q, the first subcomponent of the complement activation pathway, and potentially activates the pathway.²²² Following ligand binding, CRP also resembles some of the key properties of antibodies, suggesting its role under various circumstances as a contributor to host defense against infection, a pro-inflammatory mediator, or a participant in handling of autologous constituents.^{214, 223}

The capacity for CRP to bind different phosphocholine residues is important for both host defense and handling of autologous constituents.²²⁴ The activation of classic complement pathway by CRP may opsonize and enhance phagocytosis of the various residues or ligands, and mediate pro-inflammatory pathophysiological effects.²¹⁴ In fact, the spectrum of autologous ligands that recognize and bind CRP overlaps that of autoantibodies that are associated with early stages of cardiovascular disease in autoimmune syndromes.²¹⁴

4.3 Factors that can Impact CRP

4.3.1 Dietary Factors

Diet has been found to be related to inflammation due to several possible mechanisms. Part of this impact results from visceral adiposity because of the inflammatory effects of abdominal obesity, part of the impact can also be attributed to direct or indirect effects of nutrients and dietary pattern on inflammatory responses.¹¹ The

Health, Aging and Body Composition prospective cohort study in Pennsylvania and Tennessee revealed that a dietary pattern high in low fat dairy products, whole grains, fruit, vegetables, fish and poultry, may be associated with lower systemic inflammation and improved insulin sensitivity among older adults.²²⁵ Another study among 746 women post diagnosis of breast cancer found that better quality diet as recommended by DGAs was associated with lower levels of CRP and other chronic inflammatory biomarkers, indicating an improved survival.²²⁶ A recent review of 46 studies stated that even though the findings were inconsistent, interventions with presumed healthy diets such as diet that conforms with the DGAs recommendations, resulted in reductions in almost all measured inflammatory biomarkers.²²⁷ A recent study on Paleolithic diet and Mediterranean diet has shown that these two dietary patterns may be associated with lower levels of systemic inflammation, as measured by serum CRP.²²⁸

4.3.1.1 Added Sugar

There have been inconsistent findings on the relationship between added sugar intake and circulating CRP level. A recent study showed that free sugar, referring to all monosaccharides and disaccharides added to foods by the manufacturer, cook, or consumer, plus sugars naturally existent in honey, syrups and fruit juices,²⁹ were not related to CRP, when sugar from solids was not associated with any health outcome.¹² In the same study, sugar from liquids was positively associated with CRP.¹² In another study, SSB consumption was associated with the serum levels of several inflammatory markers including CRP.¹³ In a prospective randomized controlled trial among 29 healthy young men, Aeberli et al. reported that fasting glucose and CRP level increased significantly after all interventions on SSBs consumption after six 3-week

interventions.¹³⁴ Based on NHANES 1999-2004, among a total of 4,880 children aged 3 to 11 years, Kosova et al. found that increased consumption of SSBs was independently associated with increased CRP level.¹⁵⁷ Using data from NHANES 1999 to 2010, it was found that decreased SSB consumption significantly decreased CRP, independent of demographic and lifestyle factors.²²⁹ Raatz et al. recently reported that daily intake of 50 grams of carbohydrate from honey, sucrose, or high fructose corn syrup for 14 days resulted in similar effects on CRP.²³⁰ In a 24-30 year of follow up of Nurse's Health Study, it was reported that replacing saturated fats with carbohydrates from refined starches or added sugar was not associated with heart disease risk.²³¹

4.3.1.2 Fats

Dietary fatty acids are important modulators of inflammatory responses. For example, long-chain fatty acids are potent inflammatory mediators as shown in both in vivo and in vitro studies.²³² Many studies have suggested the inflammatory effect of saturated fat.^{233,234} It was found that the saturated fat stimulated inflammatory response involves a toll-like receptors (TLRs) pathway.²³⁵ Saturated fat serves as the acyl component of lipopolysaccharides, a ligand of TLR. Therefore, an excess intake of dietary saturated fat increases levels of TLRs.²³⁶ As a crucial mediator in the innate immune system, elevated levels of TLRs were seen in obese state and the expression was found in many insulin target tissues such as liver, and adipose tissue.²³⁶

n-6 polyunsaturated fat, known as linoleic acid (LA), may also contribute to pro-inflammatory effects.^{237, 238} The underlying mechanism is that LA can be converted into arachidonic acid (AA), a key substrate for eicosanoids production, which plays an

important role in the subsequent undesirable inflammation process.²³⁹ Furthermore, n-6 PUFA may compete for cyclooxygenase thus reducing the formation of anti-inflammatory mediators from n-3 PUFA.²⁴⁰ However, the findings are inconsistent. In 2012, Bjermo et al. reported that a high n-6 PUFA intake for 10 weeks did not cause any sign of inflammation or oxidative stress among abdominally obese individuals.²⁴¹ A randomized, double-blind, crossover study also revealed that among a small group of obese adult men (n=13), serum IL-6 and TNF- α dropped after n-6 PUFA meal, whereas the same biomarkers were increased after a saturated fat meal.²⁴² In a 3-week dietary intervention with predominant PUFA or saturated fats, Lesna et al. reported that a relatively high intake of PUFA decreased serum CRP levels compared to baseline.²⁴³ A systematic review of 15 randomized controlled trials found that no clinical evidence was able to suggest the pro-inflammatory effects of n-6 PUFA in healthy individuals except for infants.²⁴⁴

Polyunsaturated fats such as n-3 PUFA, including DHA and EPA, have shown anti-inflammatory properties in several animal studies.^{245,246} There is substantial evidence that these fatty acids are able to partly inhibit a number of aspects of inflammatory mediators such as leukocyte chemotaxis, adhesion molecule expression, production of prostaglandins and leukotrienes.²⁴⁷ In 2000, James reported that TNF- α and IL-1 β have shown $\leq 90\%$ inhibition of cytokine production after dietary supplementation with fish oil, containing high concentrations of n-3 PUFA.²⁴⁸ Due to the fact that n-3 PUFA has shown anti-inflammatory effects in both prospective epidemiological and in vitro studies, the anti-inflammatory potential of n-3 PUFA diet has been put to a rigorous test in clinical trials.²³⁵ Nevertheless, there is still a lack of evidence based on clinical studies.²³⁵

Three studies reported that n-3 PUFA had no favorable impact on the inflammatory responses when compared with saturated fats.^{249, 250} Another trial in 55 severely obese nondiabetic patients found that consuming 3.36g n-3 PUFA for 8 weeks remarkably decreased plasma IL-6 level, but not CRP concentration.²⁵¹

Nettleton et al. reported that higher intake of the fats and processed meats pattern was associated with higher levels of CRP, IL-6, and homocysteine.²⁵² The Diet and Exercise for Elevated Risk Trial at Stanford Medical School found that low-fat diet may be the most effective treatment for reducing CRP in women with metabolic syndrome.²⁵³ A randomized controlled clinical trial among women with PCOS found that consumption of the Dietary Approaches to Stop Hypertension (DASH) diet for 8 weeks resulted in the improvement of serum CRP levels, insulin resistance, and abdominal fat accumulation,²⁵⁴ but this finding only held for overweight and obese women. The Nurse's Health Study of 730 women found that trans fatty acid intake was positively related to serum CRP levels.²⁵⁵ A recent review looked at the underlying mechanism of the relationship between dietary fat and inflammation, and suggested that limiting total dietary fat intake, especially fat from animals or tropical oils (i.e. coconut or palm oil), and increasing sources of n-3 fatty acids, fiber and complex carbohydrate foods help promote healthy population of gut microbes, thereby improving intestinal health and reducing the risk of systemic inflammation and related diseases.²⁵⁶

4.3.1.3 Carbohydrates

Dietary glycemic index (GI) refers to the average propensity of carbohydrate in the diet to increase blood glucose compared to a reference food,²⁵⁷ as a measure of the blood

glucose-raising potential of the carbohydrate content of the food. Carbohydrate-containing foods can be classified into three categories: high (≥ 70), moderate (56-69), and low (≤ 55) compared to pure glucose (=100).²⁵⁸ Glycemic load (GL) is obtained by multiplying the quality of carbohydrate in a given food by the amount of carbohydrate in a serving of that food.²⁵⁹ It was reported that diets with high GI and high GL were associated with increased risk of heart disease, diabetes, and stroke, particularly among overweight individuals.²⁶⁰ However, observational studies have yielded inconsistent findings on the link between dietary GI, GL, the product of GI and quantity of carbohydrate, and the serum level of CRP,¹¹ suggesting that the relationship between carbohydrate quality and inflammation may only be measurable with relatively low GI diet.¹¹

The Harvard Women's Health Study reported that CRP concentrations showed a small but progressive increase across quintiles of dietary GI.²⁶⁰ Du et al. found that each 10 unit increase in dietary GI was associated with a 29% increase in serum CRP level in a Dutch population.²⁶¹ A 1-year prospective study conducted by UMass researchers revealed that no relationship was found between GI or GL and CRP among a population with a relatively high mean GI and GL.²⁶² In a Tufts University study among a group of healthy, overweight individuals through a weight loss program, a greater reduction in CRP was observed among those consuming the low GL diet, but not the high GL dieters.²⁶³ A randomized feeding study in Seattle suggested that low GI foods, independent of total calories, may reduce CRP and increase adiponectin among overweight and obese individuals.²⁶⁴

As a non-digestible type of carbohydrate, fiber content of the diet may also play a role in influencing the relationship between carbohydrate quality and the status of systemic inflammation.¹¹ A review on seven clinical trials stated that significantly greater reduction in CRP concentrations (25-54%) were seen with increased fiber intake (≥ 3.3 g/MJ) in six studies.²⁶⁵ A prospective case-control study in Italy suggested that the inverse association between fiber consumption and CRP level was independent of weight status but was associated with lower fasting glucose levels when fiber intake increases.²⁶⁶ Based on NHANES III, Krishnamurthy et al. reported that high dietary fiber intake was associated with lower risk of inflammation, especially in those with kidney disease.²⁶⁷ In the Women's Health Initiative observational study, researchers at UMass also found a significant inverse relationship between habitual dietary fiber intake and important mediators of inflammation including IL-6 and TNF- α among premenopausal women,²⁶⁸ but this relationship only occurred at relatively high fiber consumption (24g/day) and held for both soluble and insoluble fiber.²⁶⁸

4.3.1.4 Dietary Inflammatory Index (DII)

The dietary inflammatory index (DII) is a trademarked new tool, recently developed to provide an overall score for the inflammatory potential of the diet.²⁶⁹ DII is based upon an extensive literature search incorporating biological, animal, and epidemiological studies on the effect of diet on inflammation.²⁷⁰ The basis for the DII is the inflammatory effect scores, which are derived from data reported in 1,943 research articles examining the relationship between various dietary components and inflammatory biomarkers, based on 11 populations around the world.²⁶⁹ The food parameters used to calculate DII scores

include both macro- and micro-nutrients and even count in herbs and spices.²⁷¹ Higher scores of DII are more pro-inflammatory and lower scores are anti-inflammatory.

The original DII was created and validated in the longitudinal data of the SEASONS study with CRP, with results showing that the DII was able to significantly predict interval changes in CRP.²⁷² Tabung et al. reported in another validation study that the DII was significantly associated with inflammatory biomarkers including CRP, IL-6, and TNF- α .²⁷³ The DII was also found related to higher average BMI, waist circumference and waist: height ratio after adjusting for known risk factors.²⁷⁴ When using an adjusted DII (ADII) to conduct cross-sectional analysis of 2 Dutch cohort studies, it was found that a higher ADII was associated with a higher summary score for inflammation.²⁷⁵ Furthermore, when using DII to measure women's diet during pregnancy, it was reported that higher scored diet was associated with maternal systemic inflammation as measured by CRP and may also be associated with impaired fetal growth and breastfeeding failure.²⁷⁶ Overall, these findings reinforce the fact that different dietary components affect diet quality as a whole and play important roles in modifying inflammatory process in the body.²⁷⁷

4.3.2 Lifestyle Factors

4.3.2.1 Overweight/Obesity

Obesity is characterized by having a great number of adipose tissue and an increase in the size of adipocytes.²⁷⁸ Obesity has been found associated with elevated levels of CRP in many studies.^{279,280} It is believed that the obese condition may lead to oxygen depletion in adipose tissue hence causing adipocyte death,²³⁵ it can also result in excess

storage of triacylglycerols and an excessive influx of free fatty acids into circulation,²⁸¹ stimulating an overproduction of pro-inflammatory cytokines. A recent study in a group of morbid obesity patients revealed that white adipose tissue was a major contributor to increased CRP in obesity status.²⁸² It was found that this obesity-mediated inflammatory response was characterized by releasing a high amount of TNF- α and IL-6.²⁷⁸ It is known that the baseline levels of inflammatory markers including CRP are appreciably lower in lean healthy people versus an overweight population, hence the impact of dietary factors may virtually be negligible in lean healthy population.²³⁵ This may also explain the findings that beneficial effect of n-3 PUFA was mostly observed in severely obese patients, that the any impact of dietary fats may only contribute in addition to the high baseline levels of circulating inflammatory cytokines.²³⁵

Numerous studies have reported a link between elevated adiposity and increased pro-inflammatory cytokines.^{235,283} An Australian study found that high concentrations of CRP in indigenous participants were largely explained by abdominal obesity.²⁸⁰ A review of studies between 1990 and 2009 reported that abdominal adiposity was significantly associated with systemic inflammation as measured by CRP ($r=0.40-0.61$).²⁸⁴ Importantly, such association persists when taking into account body mass index. Increased CRP levels among abdominally obese individuals may be reversible with weight loss.²⁸⁴ A recent follow up study among children found that an obesity-related inflammation and high CRP level may be reversible by improving weight status.²⁸⁵

Even though the exact mechanism remains unclear, in the process of obesity-induced inflammation, two types of macrophages, M1 and M2, are believed to have played critical roles.²³⁵ M1 macrophages are classically activated macrophages that

produce high concentrations of pro-inflammatory cytokines such as TNF- α and IL-6, whereas M2 macrophages are known as alternatively activated macrophages, secreting anti-inflammatory cytokines such as IL-10.²³⁵ Mice models have shown that, instead of converting monocytes to M2 macrophages, the obesity-induced inflammatory response involves a phenotypic switch in adipose tissue macrophage from M2 to M1 state, resulting in a reduction of anti-inflammatory cytokines, in conjunction with an increase in pro-inflammatory cytokines.²⁸⁶ Asztalos et al. reported in a human study that adipose tissue produced a factor which influenced the formation of CRP molecular form-4, and this form might be used as an obesity-related inflammatory marker instead of regular CRP.²⁸⁷

4.3.2.2 Smoking

Current tobacco smoking is a known risk factor of inflammation and can lead to higher levels of pro-inflammatory markers including CRP.²⁸⁸ A British large prospective study among 2920 men aged 60-79 years found that increased CRP concentrations were among current smokers compared to those who had never smoked, even after controlling for other major cardiovascular risk factors.²⁸⁹ A Japanese study reported that cigarette smoking contributed to a high urinary protein associated with an increase in serum CRP level.²⁹⁰ Current smoking was also found related to higher systemic inflammation, measured by CRP and other biomarkers, among patients with COPD.²⁹¹

In addition to the positive relationship between current smoking and CRP, there is also a dose-response relationship between the number of past years of smoking and serum concentrations of CRP. Wannamethee et al. found that CRP level was lower in

previous light smokers (<20 cigarettes per day) versus previous heavy smokers (>20 cigarettes per day), even upon controlling for years since quitting and other confounders.²⁸⁹ A recent randomized trial of current and former heavy smokers failed to show similar findings, that CRP levels were not associated with measurements of smoking intensity,²⁹² even though IL-6 concentrations were found significantly associated with current smoking status.²⁹² Another large cohort study among 1504 current smokers also reported that smoking intensity was associated with increased WBC count, but not CRP levels, and smoking cessation did not reduce CRP.²⁹³

4.3.2.3 Physical Activity

It is well documented that physical activity is positively associated with a reduction in heart disease and other chronic diseases, partly due to its potential role in the inflammation process in the pathogenesis of cardiovascular disease.²⁹⁴ Balducci et al. reported in a randomized controlled trial that physical activity in T2DM patients with metabolic syndrome was associated with a significant reduction of CRP and insulin resistance biomarkers, independent of weight loss.²⁹⁵ Nevertheless, most research on this topic still only hypothesized that the association between physical activity and inflammation and inflammatory markers is independent of fatness, with only a few studies proving this,²⁹⁶ so it is not clear as to whether the anti-inflammatory health benefits of a physically active lifestyle are due to exercise itself or it is a result from favorable changes in the body composition.²⁹⁶ A systematic review in 2011 reported that significant reductions in CRP levels were noted in 11 of 25 trials of aerobic-based regimens, 2 of 5 combination protocol studies, but neither of two trials of resistance-based regimens.²⁹⁷ These results suggested that weight loss, or weight loss in conjunction

with exercise, instead of exercise itself, may be important in reducing inflammation.²⁹⁷ Another review stated that the combination of increased physical activity and exercise training, especially if combined with weight loss, was related to beneficial effects on systemic inflammation.²⁹⁸

Although it is still unclear how physical activity might influence inflammatory responses, researchers have considered several possible mechanisms. Pedersen et al. found that plasma IL-6 levels increased in an exponential fashion with exercise and was related to exercise duration, intensity, the mass of muscle recruited and individual's endurance capacity.²⁹⁹ The increase of IL-6 at the end of acute exercise is responsible for the elevated CRP levels during late recovery.²⁹⁶ However, by involving a mechanism that might include increased glycogen content, improved anti-oxidative capacity, and improved insulin sensitivity, regular exercise may decrease IL-6 at both baseline and post exercise levels.³⁰⁰ Regular physical activity might alleviate inflammation by improving insulin resistance, or by limiting the secretion of IL-1 and IL-6 as acute phase inflammatory cytokines by skeletal muscles.³⁰¹

A review stated that self-reported levels of physical activity was significantly linked to inflammatory biomarkers such as CRP in observational studies, the not significant, but promising findings in randomized controlled trials also indicated the effectiveness of increasing aerobic physical activity in reducing chronic inflammation.³⁰² Based on NHANES 2003-2004, objectively-measured physical activity was inversely associated with CRP in adults, but not children.³⁰³ A 10-year follow up study on from the Whitehall II cohort study also found that regular physical activity was associated with lower CRP and IL-6 and was an important factor in preventing the pro-inflammatory state with

aging.³⁰⁴ However, Stewart et al. reported in a randomized dose-response exercise training trial among a group of sedentary, overweight/obese postmenopausal women in Texas that despite increasing fitness, six months of aerobic exercise training did not improve the serum CRP level,³⁰⁵ the observed reduction in CRP concentrations was found associated with weight loss.

Regular physical activity is believed to be associated with lower levels of circulating CRP.²⁸⁸ High levels of strenuous aerobic activity were found to be associated with lower CRP levels among men.³⁰⁶ Donges et al. reported in a 10-week exercise training trial that only resistance exercise resulted in a significant reduction in CRP concentration.³⁰⁷ A systematic review on 42 studies concluded that exercises produces a short-term, inflammatory response, whereas habitual physical activity may contribute to a long-term anti-inflammatory effect according to cross-sectional studies and longitudinal training studies.²⁹⁴ Interesting, it was also reported that sedentary behaviors contributed to inflammation. An Australian study found that overall sitting time was positively associated with CRP levels in both men and women.³⁰⁸

CHAPTER 5

METABOLIC SYNDROME

5.1 Definition and Diagnosis

Metabolic syndrome (MetS) has become one of the major public health challenges worldwide and in the US,³⁰⁹ even though the pathophysiology remains largely unanswered. There has been growing interest in this constellation of closely related health conditions, especially with regards to its meaningfulness to help identify individuals at high risk of T2DM and CVD.³⁰⁹ There are two commonly used standards to diagnose MetS.

1) According to the National Cholesterol Education Program: Third Adult Treatment Panel (ATP III), presence of at least three of the following risk factors diagnose the MetS.³¹⁰

- Fasting plasma glucose ≥ 100 mg/dL (5.6mmol/L)
- Blood pressure $\geq 130/85$ mmHg
- Triglycerides ≥ 150 mg/dL (1.7 mmol/L)
- HDL: Men < 40 mg/dL (1.03 mmol/L); women < 50 mg/dL (1.29 mmol/L)
- Waist circumference: Men > 102 cm and women > 88 cm.

2) According to the International Diabetes Federation (IDF), the diagnosis of MetS is made when a participant has a waist circumference ≥ 94 cm in men and ≥ 80 cm in women, plus any two of the following risk factors.³⁰⁹

- Fasting plasma glucose ≥ 100 mg/dL (5.6mmol/L)

- Blood pressure $\geq 130/85$ mmHg
- Triglycerides ≥ 150 mg/dL (1.7 mmol/L)
- HDL: Men <40 mg/dL (1.03 mmol/L); women <50 mg/dL (1.29 mmol/L)

5.2 Visceral Obesity

Fat can be deposited in two compartments: subcutaneous and visceral. Visceral adipose tissue largely comprises omental adipose tissue and also includes other intra-abdominal fat sources including mesenteric fat, thus is more metabolically active than subcutaneous adipose tissue.³¹¹ It has been found that visceral adipose tissue has multiple endocrine, metabolic and immunological functions, and is believed to play a critical role in the pathogenesis of the MetS.³¹² It is noticeable that visceral obesity is more strongly associated with increased risk of insulin resistance, MetS and CVD, than BMI alone.³¹³ Furthermore, the importance of adipose tissue location is evident as an increased ratio of visceral fat area to subcutaneous fat has been significantly related to disorders of glucose and lipid metabolism in obese participants.³¹⁴ In a multi-center study among American women, researchers found that visceral obesity is a key marker of the inflammatory state, and they also suggest that carbohydrates, particularly added sugar, contribute to increased risk of visceral obesity and development of MetS.³¹⁵ Visceral fat, as well as other elements of the MetS, have been found to be independently associated with increased cancer risk, such as breast cancer and colorectal cancer.³¹⁶

Waist circumference measurement is an important indicator of visceral obesity, even though it is not a medical marker like blood pressure, but a surrogate marker of visceral fat accumulation. However, a recent systematic review and meta-analysis from studies,

involving more than 300,000 adults in several ethnic groups, has revealed the superior role of waist-to-height ratio over waist circumference for detecting cardio-metabolic risk factors in both genders.³¹⁷ Therefore, waist-to-height ratio may be considered as a screening tool for MetS.

5.3 Hypertension

Hypertension and vascular disorders are central to MetS. Essential hypertension is frequently associated with the several metabolic abnormalities such as obesity, glucose intolerance, and dyslipidemia.³¹⁸ Several mechanisms are believed to involve in the development of hypertension. One is that both hyperglycemia and hyperinsulinemia activate the renin-angiotensin system by increasing the expression of angiotensinogen, angiotensin II, and angiotensin I receptor, which together may contribute to the development of hypertension in patients with insulin resistance.³¹⁹ The other mechanism is due to increased sodium reabsorption as a result of sympathetic nervous system (SNS) activation following insulin resistance and hyperinsulinemia, thus the heart increases cardiac output and arteries respond with vasoconstriction resulting in hypertension.³²⁰ Accumulation of adipose tissue may also play a role in the development of hypertension because there is evidence that adipocytes produce aldosterone in response to angiotensin II and may be considered as a miniature renin-angiotensin system.³²¹ High circulating levels of free fatty acids in visceral obese individuals may also participate in the activation of the SNS, explaining the strong association between visceral obesity and increased sympathetic nerve outflow.³²² Overall, insulin, SNS, endothelium, and perivascular fat, and adipocytokines have been found related to vascular function and hypertension.

5.4 Dyslipidemia

Numerous metabolic processes are involved in the uptake, transport, and storage of lipids. Lipid metabolism is highly dynamic and depends on various factors including the postprandial state, triglyceride-rich lipoprotein concentrations, HDL levels, caloric expenditure, insulin levels and sensitivity, and adipose tissue function.³²³ The hallmark of dyslipidemia in MetS is elevated fasting triglycerides in combination with the preponderance of LDL and low HDL,³²³ out of which, hypertriglyceridemia may be the major cause of the other lipid abnormalities since it leads to delayed clearance of the triglyceride-rich lipoproteins and formation of LDL.³²⁴

HDL metabolism is strongly affected by obesity status because of the increased number of remnants of chylomicrons and VLDL together with impaired lipolysis.³²³ Therefore, exchange of cholesterol from HDL for triglycerides from VLDL and LDL,³²⁵ as well as lipolysis by hepatic lipase and reduced affinity for apo-A in HDL, will result in lower levels of HDL and a reduction in circulating HDL particles with impairment of reversed cholesterol transport.³²⁶

5.5 Insulin Resistance

Insulin resistance is closely related to the development and progression of T2DM,¹²⁷ and is frequently used as an indicator of MetS. It is known that chronic low-grade inflammation may induce insulin resistance, but the underlying mechanism remains unclear.³²⁷ More human studies have shown that obesity and the concomitant development of inflammation are major components of insulin resistance.³²⁸ Experiments in naturally occurring rodent models of obesity and studies of insulin signaling at the

molecular level have elucidated that obesity induces changes in skeletal muscles, adipose tissues and the liver, resulting in localized inflammation and insulin resistance through autocrine and paracrine signaling.³²⁸ This endocrine-mediated connection between insulin target tissues further contribute to insulin resistance in distant tissues.³²⁸

As early as 1950s, there was epidemiological evidence suggesting a correlation between inflammation and insulin resistance state.³²⁸ The inflammatory biomarker CRP is commonly elevated in human insulin resistance state.³²⁹ CRP was also found predictive of T2DM among obese individuals.³³⁰ Since CRP is currently the best epidemiological biomarker for T2DM-associated CVD,³²⁹ understanding the association between CRP and the development of T2DM and other chronic diseases is important. Interestingly, the circulating levels of CRP in obese individuals with prediabetes are similar to those in people with overt diabetes,³³¹ indicating that plasma CRP concentration may not reflect the severity of insulin resistance state.³³¹ Based on NHANES 1999-2004, Pande et al. reported that elevated CRP level (>3 mg/L) was strongly associated with peripheral arterial disease, and this association is modified by insulin resistance state.³³² Even though several population-based studies have shown an independent role of CRP in the development of insulin resistance, the uncertainty over adjustment for adiposity and other confounding factors is still the major barrier in understanding such association.³³³ Chung et al. reported that insulin resistance was independently associated with CRP and other inflammation markers among patients with rheumatoid arthritis.³³⁴ In a sample of adults screened for T2DM, CRP was linked to adiposity and insulin resistance among women, but not men, after adjusting for measured demographic variables, smoking, and medication status.³³⁵ In a Danish population-based study, both CRP and insulin resistance

were found to be independent predictors of CVD and that their hazard ratio did not change substantially after adjusting for additional MetS-associated variables.³³⁶ In fact, this finding held true when the researchers further restricted analyses solely to participants without diabetes.³³⁶

5.6 Added Sugar and Metabolic Syndrome (shown in 2.7.5)

5.7 Risk Factors for Metabolic Syndrome

5.7.1 Obesity

Obesity is a principal causative factor in the development of MetS. Increased oxidative stress in accumulated fat is suggested as an early instigator of MetS based on findings from obese mice model study.³³⁷ Overweight and obesity progress to MetS through pathophysiological mechanisms at the moment largely unknown. It has been hypothesized that the state of chronic low-grade inflammation associated with high weight status and excessive adipose tissue may explain the development of insulin resistance that triggers the associated comorbidity of MetS.³³⁸

5.7.2 Smoking

Smoking is an important cause of morbidity and mortality worldwide. It is also known to cause inflammation and chronic systemic inflammation contributes to a range of metabolic disorders, possibly due to the same pathway involved in the development of CVD.³³⁹ Current heavy smoking as measured by more than 20 cigarettes per day currently smoked showed a nonlinear association with most outcomes such as dyslipidemia, high serum glucose level and visceral obesity.³³⁹ Another recent study

reported that current smokers had higher risk of MetS versus nonsmokers and former smokers, after adjusting for BMI.³⁴⁰

Jia et al. reported that gender-specific differences may exist in the association between cigarette smoking and MetS development.³⁴¹ In men, most research supports a positive association between smoking and MetS risk, whereas such association has not been found among women in a meta-analysis study.³⁴¹

5.7.3 Physical Activity

A great number of studies have shown the relationship between physical activity (PA) and MetS, even though the results have been inconsistent. A meta-analysis of prospective cohort studies found that a high level of leisure time PA was statistically associated with decreased risk of MetS.³⁴² Another systematic review indicated that dynamic endurance training has a favorable effect on most of the CVD risk factors associated with MetS.³⁴³ A recent study among patients with COPD found that greater PA and less sedentary time are associated with lower rates of MetS.³⁴⁴ For example, according to NHANES 2005-2006, daily walking is one of the healthful ways to decrease the MetS and its risk components.²⁷⁹

With regards to the mechanism behind the relationship between PA and MetS, there have been different findings. There is evidence suggesting that resistance training may promote an increase in muscle mass and a reduction in body fat accumulation, therefore may be a key mediator leading to better metabolic control.³⁴⁵ It was also revealed that exercise increases secretion of anti-inflammatory cytokines and reduces pro-inflammatory cytokines and may reduce the risk of MetS.³⁴⁶

CHAPTER 6

RESEARCH GAP & PURPOSE OF THE STUDY

6.1 Specific Aims and Hypotheses by Manuscript Title

6.1.1 Study #1: Consumer Behaviors are Associated with Added Sugar Intake among Adults 20 Years or Older from NHANES 2007-2010

6.1.1.1 Specific Aim #1

To assess the association between individual consumer behaviors and added sugars intake among adults aged 20 years or older from NHANES 2007-2010.

6.1.1.2 Hypothesis #1a

Among adults aged 20 years or older, consumption of added sugars in the diet will be positively associated with soft drink availability at home.

6.1.1.3 Hypothesis #1b

Among adults aged 20 years or older, added sugars intake will be negatively associated with frequency of major food shopping, use of nutrition labels in food selection, and home cooking.

6.1.2 Study #2: High Added Sugar Intake is Associated with Low Measures of Overall Diet Quality among Adults 20 Years or Older from NHANES 2007-2010

6.1.2.1 Specific Aim #2

To assess the impact of added sugars in the diet on measures of overall dietary quality among US adults.

6.1.2.2 Hypothesis #2

High consumption of added sugars in the diet is associated with lower intakes of essential nutrients.

6.1.3 Study #3: High Intake of Added Sugar Increases Inflammatory Biomarker and the Risk of Metabolic Syndrome among Adults 20 Years or Older from NHANES 2007-2010

6.1.3.1 Specific Aim #3

To determine the association of added sugars in the diet on CRP as a biomarker of inflammation and the presence of Metabolic Syndrome in U.S. adults.

6.1.3.2 Hypothesis #3a

Added sugar intake will be positively associated with the concentration the inflammatory biomarker CRP.

6.1.3.3 Hypothesis #3b

High consumption of added sugars will be associated with a high risk of having the Metabolic Syndrome.

CHAPTER 7

STUDY DESIGN AND METHODS

7.1 Study Design and Population

This study employed a cross-sectional study design using data from the National Health and Nutrition Examination Survey (NHANES). NHANES is a survey designed to assess the health and nutritional status of adults and children in the U.S. NHANES is a major program of the National Center for Health Statistics as part of Center for Disease Control (CDC). Each year, approximately 5,000 individuals are randomly selected throughout the United States and invited to participate in NHANES. The survey is unique in that it combines interviews, questionnaires, physical examinations and laboratory results. The at-home interview includes demographic, socioeconomic, dietary, and health-related questions; whereas the physical examination component consists of medical, dental, and physiological measurements, as well as laboratory tests administered by highly trained medical personnel. The examination takes place in specially-designed and equipped mobile centers that travel throughout the country. The National Center for Health Statistics Research Ethics Review Board (ERB) has reviewed and approved the NHANES protocol.

NHANES uses a multistage, stratified, and clustered sampling method to recruit participants: All the counties in the US are divided into 15 groups based on their characteristics, such as metropolitan areas. One county is selected from each large group, and together they form the 15 counties in the NHANES surveys for each year. Within each county, smaller groups, comprised of a large number of households in each, are

formed and 20-24 of these small groups will be selected. All of the households or apartments within those selected small groups are identified and a sample of about 30 households are selected within each group. One person in the selected households is approached by NHANES interviewers at home and is asked about information (age, race, and gender) on all persons in the household, and a computer algorithm randomly selects some, all, or none of the household members. The sample for the survey is selected to represent the U.S. population of all ages. To produce reliable statistics, NHANES oversamples persons 60 and older, African Americans, and Hispanics. Details of the NHANES probability sampling and data collection procedures have been described extensively elsewhere.

To examine the association between consumer behaviors, added sugar, diet quality, inflammation and MetS risk, we used the 2007-2008 and 2009-2010 NHANES cycles. The survey sample of NHANES is meant to represent the US population of all ages. However, because there are markedly differences in food choices and subsequently added sugar intake among youths and adults, for this dissertation study, we limited the analysis to adults aged 20 years and older from NHANES 2007-2010.

7.2 Exposure Assessment

Consumer Behaviors module was first introduced to NHANES during 2007-2008, the consumer behavior section is part of the household interview, providing personal interview data on various dietary related consumer behavior topics at family level. A Flexible Consumer Behavior Survey (FCBS) module was added to NHANES in 2007, in order to collect information on people's knowledge, attitudes, and beliefs towards

nutrition and food choices. The FCBS module is composed of two elements: a core set of questions asked in the household interview, and a supplementary module, asked in a 15-minute telephone follow-up interview, which is specifically designed for each 2-year data collection cycle (CDC, 2010). Questions included in this section that will be used in the proposed study are: availability of certain types of foods in the family, family food expenditures, and time to get to grocery store for food shopping.

With regards to added sugar intake, NHANES uses 24-hour dietary recall method to collect data on the types and amounts of foods and beverages participants consume. The original Food and Nutrient Database for Dietary Studies 4.1 (FNDDS 4.1) is a tool to help provide nutrient composition of the over 7,000 food and beverages collected in NHANES (USDA ARS, 2017). However, many of the foods, such as pizza, fruit salad, and casseroles, are multi-ingredient foods consisting of ingredients from more than one food groups. Hence, the Food Patterns Equivalent Database (FPED) was created by USDA, Agricultural Research Service (ARS), and Food Surveys Research Group (FSRG) to disaggregate multi-ingredient foods to ingredients that can be assigned to a food pattern before computing the amount present in the food. The methodology used to develop the FPED has been described elsewhere.¹² For example, FPED converts FNDDS foods to the respective number of teaspoon-equivalents of added sugar. Foods like cane sugar, honey, and all types of syrups are examples of added sugar in their pure form. Ingredients that contain added sugar present in multi-ingredient foods, such as cakes, cookies, and ice cream, are also assigned an added sugar component. One teaspoon equivalent of added sugar in FPED is computed using the sugar content of foods and defined as “added

sugar”. One teaspoon equivalent of added sugar is defined as 4.2 grams of granulated sugar.¹²

7.3 Outcome Assessment

Assessment of added sugar intake has been described above.

To measure the diet quality: Healthy Eating Index (HEI) is a measure of diet quality, independent of quantity, that is designed to assess compliance with the Dietary Guidelines for Americans (DGAs). HEI emphasizes a variety of food groups and improving food and beverage choices within calorie needs.³⁴⁷ HEI-2015 is the latest version of the HEI. The main difference between HEI-2015 and the previous version (HEI-2010) is the introduction of the new aspect of the DGAs as the recommendation on limiting intake of added sugars to less than 10% of total caloric intake. The development and calculation of the HEI-2015 is described in detail elsewhere.³⁴⁷ The HEI 2015 scores were calculated based on the 24-hour dietary recall data. Food Patterns Equivalent Database (FPED) was used to compute various dietary constituents by disaggregating multi-ingredient foods to ingredients that can be assigned to a food pattern before computing the amount present in the food. The methodology used to develop the FPED has been described elsewhere.¹² HEI-2015 adequacy scores (with higher scores reflecting higher consumption) were for total fruit (5 points), whole fruit (5 points), total vegetables (5 points), greens and beans (5 points), whole grains (10 points), dairy (10 points), total protein foods (5 points), seafood and plant proteins (5 points) and the ratio of polyunsaturated and monounsaturated fatty acids to saturated fatty acids (10 points). Moderation scores (higher scores indicating lower consumption) included refined grains (10 points), sodium

(10 points), added sugars (10 points), and saturated fats (10 points). The HEI-2015 scores were adjusted for energy intake. Calculation methods of the HEI-2015 score methods were made available by the Division of Cancer Control and Population Sciences at National Cancer Institute.³⁴⁷ For each participant, daily total caloric and nutrient intakes from foods and beverages are included in the database. The Day 1 and Day 2 total nutrient intakes files provide a summary record of total nutrient intake for each individual, containing the following information: day of the week of the intake; total number of foods reported for the participant for that day's intake; the daily intake of water including all moisture present in foods and beverages; daily intake of food calories and 64 nutrients/food component from all foods, as calculated using FNDDS 4.1; in addition, whether the amount of food consumed was usual, much more than usual, or much less than usual was recorded. A complete list of information included in the total nutrient intake files is provided elsewhere. For the proposed study, only the above categories of information will be used.

For circulating CRP levels, blood specimens were collected and processed during the physical examination. Each biomarker in NHANES is assessed in different locations. For serum hs-CRP measurement, blood samples were stored and shipped to University of Washington, Seattle, WA for analysis. CRP was measured by latex- enhanced nephelometry. Particle-enhanced assays performed on a Behring nephelometer were also applied. These assays were based on the reaction between a soluble analyte and the corresponding antigen or antibody bound to polystyrene particles. For the quantification of CRP, particles consisting of a polystyrene core and a hydrophilic shell were used to link anti-CRP antibodies covalently. A dilute solution of test samples was

mixed with latex particles coated with mouse monoclonal anti-CRP antibodies. CRP present in the test sample forms an antigen antibody complex with the latex particles. An automatic blank subtraction was performed and CRP concentrations were computed by using a calibration curve.

Metabolic Syndrome: Several blood biomarkers and anthropometric measurements will be used in assessing the risk of metabolic syndrome in this dissertation study.

Metabolic syndrome state was determined by the criteria developed by the National Cholesterol Education Program: Third Adult Treatment Panel, with the presence of at least three of the following risk factors (NCEP, 2002): 1) Fasting plasma glucose ≥ 100 mg/dL (5.6 mmol/L); 2) Blood pressure $\geq 130/85$ mmHg; 3) Triglycerides ≥ 150 mg/dL (1.7 mmol/L); 4) HDL-cholesterol: Men < 40 mg/dL (1.03 mmol/L); women < 50 mg/dL (1.29 mmol/L); 5) Waist circumference: Men > 102 cm and women > 88 cm.

- **Fasting Glucose and Insulin Resistance:** For plasma fasting glucose and insulin, blood specimens were collected in the morning examination sessions only. Blood samples were later processed, stored and shipped to Fairview Medical Center Laboratory at the University of Minnesota, Minneapolis, MN for analysis. Using an enzymatic method, glucose is converted to glucose-6-phosphate (G-6-P) by hexokinase in the presence of ATP. G-6-P dehydrogenase then converts the G-6-P to gluconate-6-P in the presence of NADP⁺. As the NADP⁺ is reduced to NADPH during this reaction, the resulting increase in absorbance at 340 nm is measured. This is an endpoint reaction that is specific for glucose. For insulin measurements, the Merocodia Insulin ELISA was utilized. Insulin present in the sample binds to anti-insulin antibodies bound to the sample well, while the

peroxidase-conjugated anti-insulin enzyme-labelled antibodies also bind to the insulin at the same time. After washing to remove unbound enzyme-labelled antibodies, a labelled substrate is added and binds to the conjugated antibodies. Acid is added to the sample well to stop the reaction and the colorimetric endpoint is read on a microplate spectrophotometer set to the appropriate light wavelength.

- **Blood Lipid Profile:** Blood triglycerides, HDL, and LDL are measured for examinees that were examined in the morning session, who had fasted at least 8.5 hours or more but less than 24 hours. Blood specimens were processed, stored, and shipped to University of Minnesota, Minneapolis for analysis. 1) For triglycerides measurement, free glycerol is converted to glycerol-3-phosphate (G3P) by glycerol kinase. The hydrogen peroxide combines with 4-chlorophenol under the action of peroxidase to produce an oxidation product that does not react with the colorimetric component of reagent 2. After the initial reaction sequence is completed, the Mod P records a blank absorbance reading, then reagent 2 is added. The second reaction is driven when lipase is added in reagent 2 to convert triglycerides to glycerol, and 4-aminophenzone added to react with the hydrogen peroxide produced in the last reaction. The reaction is measured at 505 nm. 2) For HDL measurement, a magnesium/dextran sulfate solution is added to form water-soluble complexes with non-HDL cholesterol fractions. With addition of reagent 2, HDL-cholesterol esters are converted to HDL-cholesterol by PEG-cholesterol esterase. The HDL-cholesterol is acted upon by PEG-cholesterol oxidase, and the hydrogen peroxide produced from this reaction combines with 4-amino-antipyrine and HSDA under the action of peroxidase to form a purple/blue pigment that is

measured photometrically at 600 nm. 3) For LDL levels, LDL-cholesterol is calculated from measured values of total cholesterol, triglycerides, and HDL-cholesterol according to the Friedewald calculation:

$$[\text{LDL-cholesterol}] = [\text{total cholesterol}] - [\text{HDL-cholesterol}] - [\text{triglycerides}/5]$$

- **Blood Pressure:** In order to obtain accurate measurement of blood pressure (BP), the BP examiners are certified for BP measurement through a training program from Shared Care Research and Education Consulting. After participant been resting quietly in a sitting position for 5 minutes and determining the maximum inflation level, three consecutive BP readings are obtained. If a BP measurement is interrupted or incomplete, a fourth attempt may be made. All BP determinations (systolic and diastolic) are taken in the mobile examination center (MEC).
- **Waist Circumference:** The waist circumference measurement was conducted among participants aged 2 years of age and older. Data were collected by trained health technicians, assisted by a recorder during the body measurement examination. Participant gathers his or her gown shirt above the waist, cross the arms, and place the hands on opposite shoulders. If necessary, pants and underclothing need to be lowered slightly below the waist. Measuring tape is extended around the participant's waist, in a horizontal plane at the level of the measurement mark (just above the uppermost lateral border of the right ilium of the pelvis). The measurement is taken to the nearest 0.1 cm at the end of the participant's normal expiration.

7.3 Covariate Assessment

We considered as possible covariates a selected set of demographic and anthropometric, and lifestyle factors available through data collection during the demographic section and physical activity sections of the NHANES questionnaire, as well as the examination section. Gender was self-reported and was used as male or female. Age was classified into four categories: 20-29 years, 30-44 years, 45-64 years, and 65 years or older. According to the National Center for Health Statistics (NCHS) standard definitions for ethnicities, subjects were categorized as non-Hispanic whites, non-Hispanic blacks, Mexican-Hispanics, other Hispanics, and other race. Educational attainment was measured as the highest completed grade of school for those above the age of 20 and was categorized into four levels: less than high school, high school or equivalent, some college, and college graduate or above. Household income was calculated as the ratio of family income to the federal poverty threshold and was categorized as <1.5 (low income), $1.5-3.5$ (medium income), and >3.5 (high income).

Body mass index (BMI) was computed from height and weight measurements (kg/m^2) and was categorized into four standard categories: underweight ($\text{BMI} < 18.5 \text{ kg/m}^2$), normal weight ($18.5 \text{ kg/m}^2 \leq \text{BMI} < 25 \text{ kg/m}^2$), overweight ($25 \text{ kg/m}^2 \leq \text{BMI} < 30 \text{ kg/m}^2$), and obese ($\text{BMI} \geq 30 \text{ kg/m}^2$). Energy intake was categorized into tertile group, coded as “1-3” representing from the lowest to the highest daily caloric intake. Sedentary lifestyle covariate was assessed by asking participants about how many minutes they conduct sedentary activity on a typical day, including sitting or reclining at work, at home, or at school, but excluding time spent sleeping. This covariate was categorized into

tertiles. Current smoking and the use of medication in the past month were categorized as “0” and “1”, representing “no” and “yes”, respectively.

7.5 Statistical Analysis Plan

The multistage, stratified, and clustered sampling method used for NHANES data collection was incorporated into all data analyses using the “svy” command with appropriate weighting in Stata 15.0 (StataCorp LP, College Station, TX). Detailed information on the procedures for taking into account NHANES survey sampling weights have been described elsewhere.

General characteristics of our subjects will be presented as means +/- standard deviations, median, range for continuous variables such as age, body mass index (BMI), dietary added sugars intake, and serum CRP concentration. For categorical variables such as weight status group and household income categories, frequencies and percentages will be calculated. The normality of variables will be evaluated, and variables will be transformed if needed. For descriptive statistics, covariates will be plotted on an x-y scatter plot as well as cross-tabulated with continuous variables to evaluate potential confounders. Student’s t test will be used to assess potential confounders for continuous variables, whereas ANOVA and chi-square test will be used for categorical variables. P values will be evaluated to determine statistical significance at $p < 0.05$. shown to present the differences in distributions for all covariates.

For inferential statistics, unadjusted linear and logistic regression will be conducted to evaluate crude relationships between our exposures of interest and outcomes of interest. Multivariate analysis will be done for models without and with suspected

confounders to determine which covariates will be retained in the final multiple regression models. Risk factors and covariates that cause the regression coefficient for the exposure to change by 10% or greater will be retained in the final model. For linear regression, the regression coefficient (β) and standard error (SE) will be presented with the corresponding p-value. For logistic regression, the odds ratio (OR) and 95% confidence intervals will be presented. In order to assess moderation, dietary added sugar intake levels will be stratified into above and below the median, or above the recommended levels. Subsequent analysis will be carried out for each exposure and outcome variables by added sugars intake categories.

CHAPTER 8

“CONSUMER BEHAVIORS ARE ASSOCIATED WITH ADDED SUGAR INTAKE AMONG ADULTS 20 YEARS OR OLDER FROM NHANES 2007-2010”

8.1 Abstract

Excessive consumption of added sugar has become a public health concern during the last few decades. Social and environmental factors are important determinants of health and may contribute to individual dietary practices, including added sugar consumption. However, evidence of a solid link between social and environmental factors and added sugar intake remains inconsistent.

We conducted a secondary data analysis to evaluate the association between several consumer behaviors and added sugar intake among adults aged ≥ 20 years from the cross-sectional National Health and Nutrition Examination Survey (NHANES) 2007-2010. Based on the 24-hour dietary recall data, the datasets of Food and Nutrient Database for Dietary Studies 4.1 (FNDDS 4.1) and the Food Patterns Equivalent Database (FPED) were used to convert foods and beverages to respective number of teaspoon equivalents, further to grams of added sugar as granulated sugar. Added sugar intake were presented in the study as both continuous and binary (categorized as meeting or exceeding the recommendation level) variables. Consumer behaviors were assessed via household interview questionnaire on dietary related consumer behavior topics at family level, and the Flexible Consumer Behavior Survey (FCBS) module. All consumer behavior variables were coded as categorical variables.

To account for NHANES' complex survey design, we incorporated the sampling weights to analyze 3,233 observations. After adjusting for age, gender, race/ethnicity, education, household income, daily calories intake and BMI, soft drink availability at home was positively associated with added sugar intake ($p<0.001$), whereas cooking frequency in the past 7 days and the use of food label were negatively associated with added sugar intake ($p=0.03$, $p<0.001$, respectively). With regards to the likelihood of meeting the added sugar intake recommendation, multivariate logistic regression models show that reducing soft drink availability at home ($p<0.001$) was associated with higher chance of meeting the recommendations on added sugars intake; whereas increasing cooking frequency in the past 7 days ($p=0.002$) and the use of nutrition label ($p<0.001$) were positively associated with consuming recommended added sugar intake ($\leq 10\%$ of daily calories), after adjusting for covariates. Noticeably, major grocery shopping frequency is not associated with added sugar intake, suggesting its role in enabling increased exposure to both healthy and unhealthy food options. Further research is needed to determine whether changes in consumer behaviors predict added sugar intake in specific dimensions, and whether these findings can help us understand risk factors for excessive added sugar intake and may guide future intervention and policy efforts.

8.2 Introduction

The consumption of added sugar is excessive for most Americans.¹ According to recent statistics from the Centers for Disease Control and Prevention (CDC), added sugar intake contributed to an average of 13% of total calories for adults in the U.S. during 2005-2010, higher than the recommendation level ($\leq 10\%$).¹ Therefore, it is important to

understand which factors are related to added sugar intake in order to formulate effective nutrition policies, education or intervention programs.²

Researchers have reported that consumer behavioral factors may play huge roles in affecting individual food choices and dietary practices.³ Yet, there appears to be no definitive conclusion.^{4,5} A number of studies have reported that the increase of soda and soft drink consumption, as the most heavily consumed sugar sweetened beverages (SSBs) in all age groups except for children,⁶ contributed the most to increased added sugars intake.⁷ However, with regards to the sources of soda and soft drinks for consumers, researchers revealed that grocery stores, which we typically consider as healthy food outlets, may play an role in enabling increased exposure to SSBs and higher added sugars intake.³ In addition, according to NHANES 2009-2010, Steele et al. found that ultra-processed foods such as ‘mixtures of combined ingredients’ and ‘ready-to-eat’ foods contributed 89.7% of the caloric intake from added sugars,⁸ indicating the potentially protective role of home cooking in reducing added sugars intake. Due to the lack of information on added sugar on the current version of food labels (before July 26, 2018), the effect of reading food labels on food consumption and purchase is weak or inconsistent.⁹ Nevertheless, to the best of our knowledge, no studies have examined whether diet-related consumer behaviors, including soft drink availability, grocery shopping frequency, frequency of cooking, and the use of food label, are associated with added sugars intake among adults from NHANES. Therefore, assessing the association between these consumer behaviors and added sugars intake offers opportunities to investigate socially and environmentally appropriate interventions that may reduce individual added sugar consumption.

Our primary goal was to assess how consumer behaviors are related to individual added sugar intake, while accounting for social and demographic characteristics among 3,233 adults aged ≥ 20 years from the cross-sectional NHANES 2007-2010. Food environmental factors will be evaluated to determine how they may be contributing to excessive consumption of added sugar as well.

8.3 Methods

8.3.1 Study Design and Study Population

We analyzed the cross-sectional data from the 2007-2008 and 2009-2010 cycles of NHANES, which is a large nationally representative population-based study of risk factors, dietary status and health status in the US, from the National Center for Health Statistics as part of the CDC. The National Center for Health Statistics Research Ethics Review Board (ERB) has reviewed and approved the NHANES protocol.¹⁰

NHANES uses a multistage, stratified, and clustered sampling method to recruit participants who are representative of the US population. All the counties in the US are divided into 15 groups based on their characteristics such as metropolitan areas. One county is selected from each large group, and together they form the 15 counties in the NHANES surveys for each year. Within each county, smaller groups, comprised of a large number of households in each, are formed and 20-24 of these small groups will be selected. All of the households or apartments within those selected small groups are identified and a sample of about 30 households are selected within each group. One person in the selected households is approached by NHANES interviewers at home and is asked about information (age, race, and gender) on all persons in the household, and a

computer algorithm randomly selects some, all, or none of the household members. To produce reliable statistics, NHANES oversample persons 60 and older, African Americans, and Hispanics. Details of the NHANES probability sampling and data collection procedures are available at the NHANES website.¹⁰

Due to markedly differences in food choices and subsequent added sugars intake among youths and adults, we limited our study population to adults aged 20 years and older. We excluded those younger than 20 years; those who are pregnant; those who had missing data on dietary intakes, or consumer behaviors, and those who had missing data on blood biomarkers. The remaining sample contained 3,605 observations.

8.3.2 Assessment of Consumer Behaviors

The consumer behavior section is part of the household interview, providing personal interview data on various dietary related consumer behavior topics at family level. This is a new section for the NHANES 2007-2008. A Flexible Consumer Behavior Survey (FCBS) module was added to NHANES in 2007, in order to collect information on people's knowledge, attitudes, and beliefs towards nutrition and food choices. The FCBS module is composed of two elements: a core set of questions asked in the household interview, and a supplementary module asked in a 15-minute telephone follow-up interview with focuses specifically designed for each 2-year data collection cycle (CDC, 2010). Questions included in this section that were used in the study are: soft drink availability at home, cooking frequency during the past 7 days, frequency of major food shopping, and the frequency of using food labels.

All consumer behavior variables were coded as categorical variables. Soft drink availability at home was coded as “0” if rarely or never having soft drinks, fruit-flavored drinks, or fruit punch at home; “1” if having those beverages sometimes at home; “2” if always or most of time having the above drinks at home. With regards to cooking frequency during the past 7 days, those who cooked 0-1 time were coded as “0”, 2-4 times as “1”, 5-6 times as “2”, and at least 7 times as “3”. Grocery shopping frequency variable was coded as “0” if shopping once a month or less; “1” if shopping once every two weeks, “2” if shopping once a week, and “3” if shopping more than once a week. Last, frequency of using food label variable was coded as “0” if rarely or never using nutrition facts panel on food label, “1” if sometimes using nutrition facts label, “2” if always or most of the time using nutrition facts label. Variables including travel time to grocery store was recoded into tertiles.

8.3.3 Assessment of Added Sugar Intake

NHANES uses 24-hour dietary recall method to evaluate the types and amounts of foods and beverages participants consume. Two dietary recalls were collected for most participants, with the first one completed in-person at the Mobile Examination Center with a trained interviewer, whereas the second was completed over the telephone some days later. To calculate the amount of added sugar, we used the original Food and Nutrient Database for Dietary Studies 4.1 (FNDDS 4.1) as a tool to help provide nutrient composition of the over 7,000 food and beverages collected in NHANES (USDA ARS, 2017). This database converts single ingredient foods, including orange juice, cooked rice, or skim milk, into nutrient composition. However, many of the foods such as pizza, fruit salad, and casserole are multi-ingredient foods consisting of ingredients from more

than one food groups. Hence, we used another tool named the Food Patterns Equivalent Database (FPED) which was created by USDA, Agricultural Research Service (ARS), and Food Surveys Research Group (FSRG). FPED disaggregate multi-ingredient foods to ingredients that can be assigned to a food pattern before computing the amount present in the food. The methodology used to develop the FPED has been described elsewhere.¹¹

FPED converts FNDDS foods to the respective number of teaspoon equivalents of added sugars. For example, cane sugar, honey, and all types of syrups are examples of added sugars in their pure form. Ingredients that are considered added sugars present in multi-ingredient foods such as cakes, cookies, and ice cream are also assigned to the added sugars component. One teaspoon equivalent of added sugars in FPED is computed using the sugar content of foods defined as added sugars. One teaspoon equivalent of added sugars is defined as 4.2 grams of granulated sugar.¹¹

Daily added sugar intake was calculated by averaging the grams of added sugar consumed on two days, coded as a continuous variable (reflecting the exact amount of added sugar being consumed). In addition to the added sugar intake in grams, we coded added sugar intake as a binary variable as well, by calculating the percent of calories from added sugar and dichotomizing the variable using the USDA recommendation. Those with percent of calories from added sugar “10% or lower” was coded as “0”, whereas those with higher than 10% of daily calories from added sugar, indicating excessive consumption of added sugar, was coded as “1”.

8.3.4 Assessment of Covariates and Confounders

We considered as possible covariates a selected set of demographic and anthropometric, and lifestyle factors available through data collection during the demographic section and physical activity sections of the NHANES questionnaire, as well as the examination section. Gender was self-reported and was used as male or female. Age was classified into four categories: 20-29 years, 30-44 years, 45-64 years, and 65 years or older. According to the national Center for Health Statistics (NCHS) standard definitions for ethnicities, ethnicities were categorized as non-Hispanic whites, non-Hispanic blacks, Mexican-Hispanics, other Hispanics, and other race. Educational attainment was measured as the highest completed grade of school for those above the age of 20 and was categorized into four levels: less than high school, high school or equivalent, some college, and college graduate or above. Household income was calculated as the ratio of family income to the federal poverty threshold and was categorized as <1.5 (low income), 1.5-3.5 (medium income), and >3.5 (high income).

Body mass index (BMI) was computed from height and weight measurements (kg/m^2) and was categorized into four standard categories: underweight ($\text{BMI} < 18.5 \text{ kg/m}^2$), normal weight ($18.5 \text{ kg/m}^2 \leq \text{BMI} < 25 \text{ kg/m}^2$), overweight ($25 \text{ kg/m}^2 \leq \text{BMI} < 30 \text{ kg/m}^2$), and obese ($\text{BMI} \geq 30 \text{ kg/m}^2$). Sedentary lifestyle covariate was assessed by asking participants about how many minutes they conduct sedentary activity on a typical day, including sitting or reclining at work, at home, or at school, but excluding time spent sleeping. This covariate was categorized into three groups: the lowest (0-240 mins/day), medium (240-420 mins/day), and the highest tertile (420-1200 mins/day).

8.3.5 Data Analysis

The multistage, stratified, and clustered sampling method used for NHANES data collection was incorporated into all data analyses using the “svy” command with appropriate weighting in Stata 15.0 (StataCorp LP, College Station, TX). Detailed information on the procedures for taking into account NHANES survey sampling weights have been described elsewhere.

Descriptive statistics were calculated for the overall sample using means and standard errors for continuous variables and frequency distributions for categorical variables. Two-sample t tests, one-way ANOVAs and Pearson’s Chi square tests were carried out to assess crude differences in the added sugar intake as continuous variable (grams/day) and binary variable (meeting standards vs. exceeding standards), by various demographic indicators and consumer behaviors, as appropriate. Trend analyses were also conducted using Pearson’s correlation tests.

To explore the associations between different exposure variables and the two outcome variables, unadjusted linear and logistic regression were first performed for the continuous added sugar intake variable and binary added sugar intake variable, respectively, to evaluate crude relationships between individual exposure and the specific outcome variable. For all covariates that have a p value less than 0.2 in the adjusted regression analyses, they were retained in the multiple linear and logistic regression models. In addition, known risk factors for dietary intakes from the literature, such as gender and body mass index (BMI), were retained in the models. For linear regression, the regression coefficient (β) and standard error (SE) will be presented with the

corresponding p-value. For logistic regression, the odds ratio (OR) and 95% confidence intervals will be presented.

8.4 Results

The sociodemographic characteristics of the 3,233 adults who comprise our final sample are shown in table 1. The mean age of our sample was 47.4 years. There were 1,679 females (51.9%) and 1,554 males (48.1%). Majority of the population were non-Hispanic White (73.8%), married or living with a partner (65.7%), living in a small-medium size (2-4 persons) household (71.5%), had a high school or above degree (83.6%), and reported their household income equal to or above 150% of the federal poverty line (76.8%).

With regards to consumer behaviors, characteristics of the study population are presented in table 2. Majority of the population always or most of the time had soft drinks available at home (54.5%), reported cooking for at least 5 times during the past week (67.1%), and reported doing grocery shopping at least once a week (60.7%). 41.5% of the population always or most of the time read the nutrition label while grocery shopping whereas 21.8% of the population never or rarely use the food label.

The average daily calorie intake was 2110.5 kcals for the study population (2476.6 kcals among men and 1771.1 kcals among women). Added sugar intake by different characteristics are presented in table 3. The mean daily added sugar intake among males was 84.6 grams, which was 235% of the recommended amount for men (36 grams) by the American Heart Association (AHA). For females, the mean daily added sugar intake

was 61.9 grams, which was 248% of the amount recommended by the AHA (25 grams). Majority of the population (60.4%) exceeded the USDA/HHS recommended percent of calories from added sugars ($\leq 10\%$).

For the crude differences between added sugar intakes by demographic characteristics, the highest added sugar intake was observed among adults aged 20-29 years ($p < 0.001$), those with less than or equal to high school education ($p < 0.001$), single or never married ($p < 0.001$), and with household income less than 150% of federal poverty line ($p < 0.001$), as shown in Table 3. The added sugar intake among non-Hispanic Black was the highest (83.8g/day) compared to that of all other racial/ethnic groups (ranging from 52.6-72.9g/day). However, this difference was not statistically significant. With regards to the crude differences between added sugar intakes by consumer behaviors, the highest added sugar intake was reported by those individuals who always or most of the time had soft drink available at home ($p < 0.001$), did not cook or cooked for one time during the past 7 days ($p < 0.001$), did major grocery shopping once a month or less ($p < 0.001$), and those who never or rarely used nutrition labels ($p < 0.001$).

Table 1:
Sociodemographic characteristics of adults 20 years or older from NHANES 2007-2010

Sociodemographic variables	Categories	Mean / SE (range)	n	%
Total sample size			3233	
Age (years)	20-29	47.4 / 0.49 (20-80)	490	17.2
	30-44		803	27.1
	45-64		1180	39.2
	65 or older		760	16.6
Gender	Male		1554	48.1
	Female		1679	51.9
Race/ethnicity	non-Hispanic white		1707	73.8
	non-Hispanic black		539	9.3
	Mexican Hispanic		545	7.7
	Other Hispanic		321	4.3
	Other Race		121	5.0
Education	Less than high school		837	16.4
	High school or equivalent		753	22.7
	Some college		899	29.6
	College or above		741	31.1
Marital status	Single / never married		514	16.0
	Married / with partner		1980	65.7
	Divorced / separated / widowed		738	18.2
Household size	1 person		467	13.5
	2 persons		1040	35.4
	3-4 persons		1123	36.1
	5 or more persons		603	15.0
Household income	< 150% of federal poverty line		1149	23.2
	Between 150% and <300% of federal poverty line		1055	31.6

Table 2:
Distribution of consumer behaviors among adults 20 years or older from NHANES 2007-2010

Consumer behavior variables	Categories	n	%
Soft drink availability at home	Always or most of the time	1710	54.5
	Sometimes	542	15.9
	Rarely or never	981	29.6
# of times cooking in the past 7 days	0-1	220	6.6
	2-4	766	26.4
	5-6	877	31.9
	7 or more	1370	35.2
Frequency of doing major food shopping	More than once a week	446	13.2
	Once a week	1442	47.5
	Once every two weeks	858	26.9
	Once a month or less	485	12.4
Time to get to grocery store (min/trip)	1st tertiary (Mean=7.0)	1891	62.2
	2nd tertiary (Mean=14.9)	562	16.6
	3rd tertiary (Mean=33.4)	762	21.2
Use nutrition facts panel on food label	Always or most of the time	1377	41.5
	Sometimes	1125	36.7
	Rarely or never	727	21.8

Table 3:
Intake of added sugars across demographic and consumer behavior categories
among adults 20 years or older from NHANES 2007-2010

	Added sugars (g/d)			Percent of calories from added sugars			
	Mean	95% CI	p-value	Meeting guidelines (≤10%)		Exceeding guidelines (>10%)	
				n	%	n	%
Gender			<0.001*				0.5
Male	84.6	79.1, 90.0		626	40.5	928	59.5
Female	61.9	59.1, 64.7		646	38.7	1033	61.3
Age Group			<0.001**				<0.001**
20-29 (ref)	86.5	79.3, 93.7		132	31.2	358	68.8
30-44	81.2	74.6, 87.7		285	38.2	518	61.9
45-64	70.9	66.2, 75.6		488	40.5	692	59.5
65 or older	49.4	47.3, 51.5		367	48.4	393	51.6
<i>p-trend</i>			<0.001				
Education			<0.001**				<0.001**
Less than high school (ref)	75.6	69.3, 81.9		331	38.0	506	62.0
High school or GED	81.4	76.3, 86.6		267	33.1	486	66.9
Some college	74.7	69.3, 80.2		316	35.5	583	64.5
College or above	63.3	58.4, 68.2		356	48.8	385	51.2
<i>p-trend</i>			0.001				
Race/Ethnicity			<0.001**				<0.001**
Non-Hispanic White (ref)	72.9	68.7, 77.2		682	40.0	1025	60.0
Non-Hispanic Black	83.8	79.8, 87.8		163	29.1	376	70.9
Mexican Hispanic	72.9	64.9, 80.8		228	37.7	317	62.3
Other Hispanic	69.6	61.3, 77.7		135	37.0	186	63.0
<u>Other</u> Race	52.6	42.4, 62.9		64	57.5	57	42.5
Poverty Income Ratio category			<0.001**				<0.001**
<1.50 (ref)	80.3	75.1, 85.5		393	32.3	756	67.7
1.50 to <3.50	71.5	66.1, 76.8		422	39.0	633	61.0
≥ 3.50	69.8	64.5, 75.1		457	43.7	572	56.3
<i>p-trend</i>			0.008				
Soft drink availability at home			<0.001**				<0.001**
Rarely or never (ref)	58.5	54.4, 62.6		468	47.2	513	52.8
Sometimes	64.5	57.9, 71.1		230	44.8	312	55.3
Always or most of the time	83.0	78.1, 87.8		574	33.9	1136	66.1

# of times cooking in the past 7 days	<0.001**					0.003***
0-1 (ref)	82.1	69.0, 95.2	68	32.0	152	68.0
2-4	75.8	70.6, 81.1	284	36.0	482	64.0
5-6	70.8	66.6, 75.1	375	43.8	502	56.2
7 or more (only 3 participants cooked for more than 7 times)	70.5	66.2, 74.8	545	39.8	825	60.2
<i>p-trend¹</i>	0.2					
Major food shopping frequency	<0.001**					0.005***
Once a month or less (ref)	77.6	68.7, 86.5	172	35.1	313	64.9
Once every two weeks	78.2	74.0, 82.3	298	33.6	560	66.4
Once every week	70.3	66.0, 74.6	594	41.6	848	58.4
More than once a week	66.3	56.7, 75.8	208	48.7	238	51.3
<i>p-trend¹</i>	0.04					
Use nutrition labels while shopping	<0.001**					<0.001** *
Rarely or never (ref)	96.2	89.6, 102.7	213	29.3	514	70.7
Sometimes	74.9	70.0, 79.8	389	35.3	736	64.9
Always or most of the time	58.7	55.6, 61.9	667	48.6	710	51.4

* Independent t-test was conducted for continuous variables between two groups.

** One-way ANOVA was conducted for continuous variables among more than two groups.

*** Pearson's Chi-squared test was conducted for categorical variables across groups.

1. p-trend was calculated using Pearson's design-based correlation test.

The crude and adjusted associations between various exposures and continuous added sugar intake (g/d) are presented in table 4. The analysis revealed that, after adjusting for age, gender, race/ethnicity, education, household income, daily calories intake and BMI, higher soft drink availability at home from rarely or never to always or sometimes was associated with increased added sugar intake ($\beta=17.9$, $p<0.001$). After the adjustment, increasing cooking at home from 3-4 times to 5-6 times during the past week was significantly associated with lower added sugar intake ($\beta=-13.7$, $p=0.03$), whereas increasing the use of food label from rarely or never to sometimes, and from sometimes to always or most of the time was associated with lower added sugar intake, respectively

($\beta=-11.8$, $p=0.004$; $\beta=-19.3$, $p<0.001$). These results indicate the protective roles of reading food labels and home cooking in reducing added sugar intake. Noticeably, there was no significant association between frequency of major grocery shopping and added sugar intake ($p=0.13$).

In addition, results of logistic regression analysis testing the crude and adjusted associations between various exposures and binary added sugar intake are presented in table 4. After adjusting for age, gender, race/ethnicity, education, household income, BMI and physical inactivity, increasing soft drink availability at home from rarely or never to always or most of the time increased the likelihood of exceeding recommended added sugar intake by 61% among the study population (OR=1.61, $p<0.001$), whereas having soft drinks available sometimes at home was not related to higher added sugar intake compared to rarely or never having soft drinks at home. In contrast, increasing cooking frequency in the past 7 days from 0-1 time to 5-6 times and 7 or more times were both significantly associated with lower consumption of added sugar (OR=0.60, $p<0.001$; OR=0.69, $p=0.04$, respectively). Increasing the use of nutrition facts label from rarely or never to always or most of the time significantly reduced the likelihood of excess added sugar intake by 49%, respectively (OR=0.51, $p<0.001$). However, no relationship was found between major grocery shopping frequency and excess added sugar intake.

Table 4:
Linear and logistic regression of associations of consumer behaviors with added sugar intake
variable among adults 20 years or older from NHANES 2007-2010

	Added sugar intake (g/d)					
	Unadjusted		Model 1 ¹		Model 2 ²	
	β	P value	β	P value	β	P value
Soft drink availability at home (always or most of the time vs. rarely or never)	24.5	<0.001	19.4	<0.001	17.9	<0.001
Cooking frequency in the past 7 days (5-6 times vs. 0-1 time)	-11.2	0.08	-10.3	0.12	-13.7	0.03
Grocery shopping frequency (more than once a week vs. once a month or less)	-11.3	0.08	-5.6	0.33	-7.8	0.13
Use of nutrition label (always or most of the time vs. rarely or never)	-37.5	<0.001	-25.5	<0.001	-19.3	<0.001
1. Model 1 was adjusted for age, gender, race/ethnicity, education, and household income.						
2. Model 2 was adjusted for model 1 variables, daily calories intake, and BMI.						
	Exceeding recommended added sugar intake (>10% of daily calories intake)					
	Unadjusted		Model 1 ³		Model 2 ⁴	
	OR	P value	OR	P value	OR	P value
Soft drink availability at home (always or most of the time vs. rarely or never)	1.74	<0.001	1.61	<0.001	1.61	<0.001
Cooking frequency in the past 7 days (5-6 times vs. 0-1 time)	0.60	0.001	0.61	0.002	0.60	0.002
Grocery shopping frequency (more than once a week vs. once a month or less)	0.57	0.01	0.71	0.15	0.69	0.13
Use of nutrition label (always or most of the time vs. rarely or never)	0.44	<0.001	0.52	<0.001	0.51	<0.001
3. Model 1 was adjusted for age, gender, race/ethnicity, education, and household income.						
4. Model 2 was adjusted for model 1 variables, BMI, and physical inactivity.						

8.5 Discussion

In this large representative sample of American adults ≥ 20 years, we found that stocking soft drinks at home was positively associated with added sugar intake after adjustment for demographic and anthropometric characteristics. Furthermore, after adjusting for demographic and anthropometric factors, other consumer behaviors including the frequency of cooking at home and using food label were negatively associated with added sugar intake, suggesting these behaviors' protective roles in helping individuals meet the recommendation on added sugar intake. We failed to see an association between the frequency of major grocery shopping and added sugar intake, which was consistent with previous research.³ Although previous studies have also reported soft drink as the major source of added sugars, our study is the first to investigate how a number of consumer behaviors may influence the actual consumption of added sugar, while focusing on typical routine of lifestyle instead of single components of diet. Our findings are particularly meaningful since most current dietary guidelines recommend limiting added sugars consumption, but such guidelines are not always clear on how to put this recommendation into practice. Therefore, our findings provide evidences for future intervention and policy changes in terms of encouraging desirable behavioral changes towards lowering added sugars intake.

Our findings are largely consistent with previous literature.^{2,6,12,13,14} We observed that individuals at higher risk of consuming excessive added sugars were younger, less educated, single or never-married, and from the low-income households. We did not see a significant difference of added sugar intake between males and females, after counting in the impact of daily calories intake. Excessive added sugar intake was also found

prevalent across all categories of weight status, even though there was no significant association between body mass index (BMI) and added sugar intake. With regards to food environment, although it is commonly believed that limited access to grocery stores or other healthy and affordable food outlets make it harder for people to consume less added sugars as part of a healthy diet,¹⁵ some researchers revealed that grocery stores may also enable increased exposure to unhealthy choices such as soft drink, leading to higher added sugars intake.³ Yet, there appears to be no definitive conclusion of how the retail food environment is associated with added sugars intake.^{4,5} In this study, our findings reveal the ambiguous role of grocery stores in people's dietary practices, given that it provides access to healthy food choices as well as sugary foods and beverages.

It should be noted that, in reality, it may be unrealistic to bypass added sugar for most Americans since approximately 75% of foods and beverages in the U.S. contain added sugar in a variety of forms.¹⁶ Previous studies have pinpointed certain types of foods with high content of added sugars. It was reported that ultra-processed foods such as 'mixtures of combined ingredients' and 'ready-to-eat' foods had eightfold higher added sugars than that in normally processed foods,⁸ indicating the potential effectiveness of reducing the consumption of ultra-processed foods in lowering the intake of added sugars. However, while the evolution of human societies has turned more people into adopting a quick and convenient lifestyle, people spend less time in food preparation than a few decades ago. It was reported that U.S. consumers increasingly consume foods from away-from-home sources including fast food chains, cafeterias, and restaurants.¹⁷ Noticeable, carry-out and food deliveries are also popular, and it was estimated that half of all energy from fast food was consumed at home among children, suggesting that even

foods consumed at home are not necessarily home-cooked.¹⁸ Our findings emphasize the importance of home food preparation, and where intervention efforts for improving the American diet and reducing excess added sugars intake should be directed.

It is known that the effect of caloric information and added sugars on food consumption and purchase is weak or inconsistent,⁹ mainly due to the missing information of added sugars on the current version of nutrition labels in the U.S. However, despite the fact that revised food label with information of added sugar will not be used on food and beverage packages until July, 2018 in the US,¹⁹ current food label with information on total sugars (the sum of added sugars and naturally occurring sugars) may still be effective as a means of assisting consumers to moderate added sugars consumption.²⁰ A cross-sectional study in a predominantly Black neighborhood in Baltimore also found that exposure to any caloric information among Black adolescents significantly reduced the odds of soft drink purchases relative to the baseline,²¹ indicating the potential role of food label in reducing added sugars intake. Our findings support the protective role of nutrition facts label in lowering the consumption of added sugars, and we are optimistic that the magnitude of this association may be even stronger after the new version of food label being used.

Our study has important strengths, including a large and diverse sample of adult representatives of the US population, and the use of a validated measurement of added sugar intake as part of the dietary data collection and analysis. In addition, to the best of our knowledge, this study is the first analysis paper of NHANES using consumer behaviors to analyze added sugar intake. Our study also examined added sugar intake using two measures, as absolute amount of added sugar and categorical data as whether

the intake was meeting or exceeding the recommendation. Therefore, results based on these two measures of added sugar intake would allow for relevant interpretation.

Our findings should be interpreted in the context of several limitations. First, due to the cross-sectional nature of NHANES study design, we were unable to determine causality of the relationship between consumer behaviors and added sugar intake. Second, information bias may be a concern since both added sugar intake and consumer behaviors were self-reported using 24-hour dietary recall and questionnaire, respectively. However, all protocols are clearly specified and are administered systematically to all NHANES participants. Referring to the process of collecting dietary and consumer behaviors data, it was administered by trained staff during a structured in-person interview at the participants' homes for all NHANES participants. Therefore, the probability of non-differential misclassification of exposure occurring during the process of two-day dietary 24-hour dietary recall was highly unlikely. Additionally, participants were blinded to the hypothesis of our study as data was collected for general nutrition and health information and was for public use. It is believed that it was highly unlikely that interviewers would prompt selected participants to report added sugars intake differently than their counterparts.

8.6 Conclusion

In summary, we found that consumer behaviors are associated with added sugars intake among American adults 20 years or older. Our findings add literature to a better understanding of social and environmental elements associated with added sugars intake. Furthermore, the current study expands our knowledge of how food-related behaviors, as

part of a lifestyle routine, may contribute to added sugars intake among American adults. Our findings support the protective roles of reducing the frequency of stocking up soft drink, increasing the frequency of using food labels and preparing own foods in reducing added sugar intake. As a result, our findings underline the potential importance of future policy change and interventions such as education and skill training programs on informed food purchasing and food preparation.

8.7 References

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CHAPTER 9

“EXCESS ADDED SUGAR INTAKE COMPROMISES DIET QUALITY AND MOST NUTRIENT INTAKES, BUT REDUCES SODIUM INTAKE AMONG ADULTS 20 YEARS OR OLDER FROM NHANES 2007-2010”

9.1 Abstract

Consumption of added sugar has substantially increased in the American diet over the last few decades, and this trend has been linked to an overall reduction of diet quality. It was reported that high added sugar intake may influence diet quality by providing excess calories and potentially displacing nutrient-dense foods from the diet. Some researchers also believe that added sugar may play a role in the regulation of appetite and eating behaviors, leading to cravings for more foods and excessive caloric intake. However, the mechanism for the association between excess added sugar intake and low diet quality remains unclear.

We conducted a secondary data analysis among 3,233 adults aged ≥ 20 years from the cross-sectional National Health and Nutrition Examination Survey (NHANES) 2007-2010, to evaluate the associations between added sugar intake and diet quality and nutrient intakes. Based on the 24-hour dietary recall data, Food and Nutrient Database for Dietary Studies 4.1 (FNDDS 4.1) and Food Patterns Equivalent Database (FPED) were used to convert foods and beverages to respective number of teaspoon equivalents of added sugar. In our study, added sugar intake was determined by the percent of calories from added sugar in the diet, presented as binary (meeting or exceeding the recommendation level) and quintile (from lowest to the highest) variables. With regards

to diet quality measurements, the following information was used from the two day 24-hour dietary recall: total number of foods reported for the participant for that day's intake; daily aggregates of food calories and 64 nutrients/food component from all foods, as calculated using FNDDS 4.1. Diet quality variables in our study were presented as Healthy Eating Index (HEI) 2015 component scores and total score. Energy intake as well as macro- and micro-nutrient intakes were also calculated based on the 24-hour dietary recall. A complete list of information included in the total nutrient intake files is provided elsewhere.

To account for NHANES' complex survey design, we incorporated the sampling weights to analyze 3,233 observations. After adjusting for age, gender, race/ethnicity, education, household income, daily calories intake and BMI, added sugar intake was negatively associated with HEI-2015 score ($p < 0.001$). Excess added sugar intake significantly reduced consumption of food groups including total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein, and seafood and plant protein. Furthermore, excess added sugar intake was significantly associated with increased consumption of refined grains and saturated fat. With regards to energy and nutrient intakes, excess added sugar intake was significantly related to higher intakes of energy, carbohydrate, total sugar, and lower intakes of protein, dietary fiber, polyunsaturated fatty acids, copper, magnesium, phosphorus, potassium, selenium, zinc, vitamin A, beta-carotene, thiamin, niacin, total folate, vitamin B6, vitamin E and vitamin K. These findings were consistent with previous research to support the detrimental role of added sugar in influencing diet quality. Interestingly, excess added sugar intake was significantly associated with reduced sodium consumption, after adjusting for calories

($p < 0.001$), indicating a complicated relationship between added sugar intake and diet quality. Further research is needed to determine whether changes in added sugar intake predict food group consumption and nutrient intakes in specific dimensions, and whether these findings can help us understand the relationship between added sugar intake and overall dietary practices to help guide future intervention and policy efforts.

9.2 Introduction

The consumption of added sugar is excessive for most Americans.¹ According to recent statistics from the Centers for Disease Control and Prevention (CDC), added sugar intake contributed to an average of 13% of total calories for adults in the U.S. during 2005-2010, higher than the recommended level of added sugars in the diet ($\leq 10\%$).¹ The increased consumption of added sugar has been linked to an overall reduction in diet quality,² possibly by contributing to excess calories intake and potentially displacing nutrient-dense foods from the diet.³ Nevertheless, the impact of excess added sugar intake on diet quality, including changes in food group consumption and nutrient intakes, remain unclear.

Based on NHANES 1999-2000, adults with highest intake of sugar-sweetened beverages (SSBs) had a higher intake of calories, carbohydrates, as well as a lower intake of fiber, orange juice, and low-fat milk.⁴ A recent systematic review based on 52 studies stated that higher intake of added sugar is associated with poorer diet quality, after adjusting for total caloric intake,⁵ and a negative association was observed between added sugar and micronutrient intake.⁵ In addition, Marriott et al. reported that the median estimated nutrient intake was lowest among those who consumed greater than 25% of

total calories from added sugar.⁶ However, the mechanism for the potential impact of excess added sugar intake on diet quality including changes in food group consumption and nutrient intakes remain unclear. Therefore, assessing the associations between added sugar intake and measures of diet quality offers opportunities to examine related underlying factors, thus may guide future interventions in reducing added sugar consumption as a part of healthy dietary practice.

The HEI-2015 score captures all dietary components rather than a selected list of nutrients/food groups and also reflects the most up-to-date evidence on the components of a healthy diet.⁷ Along with the USDA food group recommendation, it is the ideal measure for evaluating healthy eating in a representative sample of US adults. The present study represents the first assessment of the relationship between added sugar intake and HEI-2015 components and total scores, based on the 2007-2008 and 2009-2010 NHANES. Our primary goal was to assess how added sugar intake is related to diet quality, determined by HEI-2015 component and total scores, as well as energy and nutrient intakes, among 3,233 adults aged ≥ 20 years from NHANES 2007-2010.

9.3 Methods

9.3.1 Study Design and Study Population

This cross-sectional study was based on data from adults aged ≥ 20 years from the 2007-2008 and 2009-2010 cycles of NHANES. NHANES is a large nationally representative population-based study of risk factors, dietary status and health conducted continuously in the United States. The National Center for Health Statistics Research Ethics Review Board (ERB) has reviewed and approved the NHANES protocol.⁸

NHANES uses a multistage, stratified, and clustered sampling method to recruit participants who are representative of the U.S. population. All the counties in the U.S. are divided into 15 groups based on their characteristics such as metropolitan areas. One county is selected from each large group, and together they form the 15 counties in the NHANES surveys for each year. Within each county, smaller groups, comprised of a large number of households in each, are formed and 20-24 of these small groups will be selected. All of the households or apartments within those selected small groups are identified and a sample of about 30 households are selected within each group. One person in the selected households is approached by NHANES interviewers at home and is asked about information (age, race, and gender) on all persons in the household, and a computer algorithm randomly selects some, all, or none of the household members. To produce reliable statistics, NHANES oversample persons 60 and older, African Americans, and Hispanics. Details of the NHANES probability sampling and data collection procedures are available at the NHANES website.⁸

Due to markedly differences in food choices and subsequent added sugars intake among youths and adults, we limited our study population to adults aged 20 years and older. We excluded those younger than 20 years; those who are pregnant; those who had missing data on dietary intakes, or consumer behaviors, and those who had missing data on serum biomarkers. The remaining sample contained 3,233 observations.

9.3.2 Assessment of Added Sugar Intake

The NHANES 24-h dietary recall utilized a multi-pass method, where respondents reported the types and amounts of all food and beverages consumed in the preceding 24-hours, from midnight to midnight. Two dietary recalls were collected for most

participants, with the first one completed in-person at the Mobile Examination Center with a trained interviewer, whereas the second was completed over the telephone some days later. To calculate the amount of added sugars intake, we used the original Food and Nutrient Database for Dietary Studies 4.1 (FNDDS 4.1) as a tool to help provide nutrient composition of the over 7,000 food and beverages collected in NHANES.⁹ This database converts single ingredient foods, including orange juice, cooked rice, or skim milk, into nutrient composition. However, many of the foods such as pizza, fruit salad, and casserole are multi-ingredient foods consisting of ingredients from more than one food groups. Hence, we used another tool named the Food Patterns Equivalent Database (FPED) which was created by USDA, Agricultural Research Service (ARS), and Food Surveys Research Group (FSRG). FPED disaggregate multi-ingredient foods to ingredients that can be assigned to a food pattern before computing the amount present in the food. The methodology used to develop the FPED has been described elsewhere.¹⁰

FPED converts FNDDS foods to the respective number of teaspoon equivalents of added sugar. For example, cane sugar, honey, and all types of syrups are examples of added sugar in their pure form. Ingredients that are added sugar present in multi-ingredient foods such as cakes, cookies, and ice cream are also assigned to the added sugar component. FPED uses the sugar content of foods defined as added sugar to compute teaspoon equivalent of added sugar. One teaspoon equivalent of added sugar is defined as 4.2 grams of granulated sugar.¹⁰ In our study, added sugar intake was further calculated as percent of calories from added sugar in the diet, and was presented as binary and quintile variables. For the binary variable, those with “10% or lower” percent of calories from added sugar in the diet was coded as “0”, whereas those with higher than

10% of calories from added sugar was coded as “1”. With regards to the quintile variable of added sugar intake, percent of calories from added sugar in the diet was categorized into quintiles, coded as “0-4” representing added sugar intake from the lowest to the highest.

9.3.3 Assessment of Diet Quality

Healthy Eating Index (HEI) is a measure of diet quality, independent of quantity, that is designed to assess compliance with the Dietary Guidelines for Americans (DGAs). HEI emphasizes a variety of food groups and improving food and beverage choices within calorie needs.⁷ HEI-2015 is the latest version of the HEI. The main difference between HEI-2015 and the previous version (HEI-2010) is the introduction of the new aspect of the DGAs as the recommendation on limiting intake of added sugars to less than 10% of total caloric intake. The development and calculation of the HEI-2015 is described in detail elsewhere.⁷

The HEI 2015 scores were calculated based on the 24-hour dietary recall data. Food Patterns Equivalent Database (FPED) was used to compute various dietary constituents by disaggregating multi-ingredient foods to ingredients that can be assigned to a food pattern before computing the amount present in the food. The methodology used to develop the FPED has been described elsewhere.¹⁰ HEI-2015 adequacy scores (with higher scores reflecting higher consumption) were for total fruit (5 points), whole fruit (5 points), total vegetables (5 points), greens and beans (5 points), whole grains (10 points), dairy (10 points), total protein foods (5 points), seafood and plant proteins (5 points) and the ratio of polyunsaturated and monounsaturated fatty acids to saturated fatty acids (10

points). Moderation scores (higher scores indicating lower consumption) included refined grains (10 points), sodium (10 points), added sugars (10 points), and saturated fats (10 points). The HEI-2015 scores were adjusted for energy intake. Calculation methods of the HEI-2015 score methods were made available by the Division of Cancer Control and Population Sciences at National Cancer Institute.⁷

9.3.4 Assessment of Covariates and Confounders

We considered as possible covariates a selected set of demographic and anthropometric, and lifestyle factors available through data collection during the demographic section and physical activity sections of the NHANES questionnaire, as well as the examination section. Gender was self-reported and was used as male or female. Age was classified into four categories: 20-29 years, 30-44 years, 45-64 years, and 65 years or older. According to the National Center for Health Statistics (NCHS) standard definitions for ethnicities, subjects were categorized as non-Hispanic whites, non-Hispanic blacks, Mexican-Hispanics, other Hispanics, and other races. Educational attainment was measured as the highest completed grade of school for those above the age of 20 and was categorized into four levels: less than high school, high school or equivalent, some college, and college graduate or above. Household income was calculated as the ratio of family income to the federal poverty threshold and was categorized as <1.5 (low income), 1.5-3.5 (medium income), and >3.5 (high income).

Body mass index (BMI) was computed from height and weight measurements (kg/m^2) and was categorized into four standard categories: underweight ($\text{BMI} < 18.5$ kg/m^2), normal weight ($18.5 \text{ kg}/\text{m}^2 \leq \text{BMI} < 25 \text{ kg}/\text{m}^2$), overweight ($25 \text{ kg}/\text{m}^2 \leq \text{BMI} < 30$

kg/m²), and obese (BMI \geq 30 kg/m²). Energy intake was categorized into tertile group, coded as “1-3” representing from the lowest to the highest daily caloric intake. Sedentary lifestyle covariate was assessed by asking participants about how many minutes they conduct sedentary activity on a typical day, including sitting or reclining at work, at home, or at school, but excluding time spent sleeping. This covariate was categorized into tertiles.

9.3.5 Data Analysis

The multistage, stratified, and clustered sampling method used for NHANES data collection was incorporated into all data analyses using the “svy” command with appropriate weighting in Stata 15.0 (StataCorp LP, College Station, TX). Detailed information on the procedures for taking into account NHANES survey sampling weights have been described elsewhere.

Descriptive analyses calculated mean HEI-2015 scores and percent of added sugar intake categories. Population subgroups were defined based on gender, age group (20-29 y, 30-44 y, 45-64 y, \geq 65 y), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican-American, other Hispanic and other race), family income-to-poverty ratio (<1.5, 1.5-3.5, >3.5); and education (<high school, high school graduate/equivalent, some college and college graduate). Survey-weighted tests were used to evaluate whether mean descriptive statistics were calculated for the overall sample using means and standard errors for continuous variables and frequency distributions for categorical variables. Two-sample t tests, one-way ANOVA and Pearson’s Chi square tests were carried out to assess crude differences in the added sugar intake, by HEI-2015 component values and total score. Trend analyses were also conducted using Pearson’s correlation tests.

To explore the associations between exposure and outcome variables, unadjusted linear regression models were first derived to evaluate crude relationships between exposure and individual outcome variables. For all covariates that have a p value less than 0.2 in the adjusted regression analyses, they were retained in the multiple linear regression models. In addition, known risk factors for dietary intakes from the literature, such as gender and body mass index (BMI) were retained in the models. The regression coefficient (β) and standard error (SE) will be presented with the corresponding p-value.

9.4 Results

The sociodemographic characteristics of the 3,233 adults who comprise our final sample are shown in Table 5. The mean age of our sample was 47.4 years. There were 1,679 females (51.9%) and 1,554 males (48.1%). Majority of the population were non-Hispanic White (73.8%), married or living with a partner (65.7%), living in a small-medium size (2-4 persons) household (71.5%), had a high school or above degree (83.6%), and reported their household income equal to or above 150% of the federal poverty line (76.8%).

The HEI-2015, which comprises a summary score out of 100 (higher = greater compliance with the 2015-2010 DGAs), is computed from the summation of scores from 13 food/nutrient categories (shown in Table 6). The mean HEI-2015 score for our sample was 54.91. A significant higher HEI-2015 score was observed between those who consumed $\leq 10\%$ of calories from added sugar and those who consumed $>10\%$ of

calories from added sugar in the diet (59.87 vs. 51.66, $p<0.001$). Similar differences in HEI-2015 component scores were found in the adequacy component groups including total fruits, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, with those who consumed $\leq 10\%$ of calories from added sugar having significantly higher scores compared to their counterparts ($p<0.001$ for all groups). In contrast, those who consumed $\leq 10\%$ of calories from added sugar had significantly lower scores compared to their counterparts for HEI-2015 moderation components, including refined grains ($p<0.001$) and saturated fats ($p<0.001$).

As shown in Table 8, higher percent of calories from added sugar in the diet were associated with lower HEI-2015 score and the individual component scores for total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein, and seafood and plant proteins ($p\text{-trend}<0.001$ for all). Higher percent of calories from added sugar in the diet were associated with higher HEI-2015 component scores in refined grains ($p\text{-trend}=0.02$), sodium ($p\text{-trend}<0.001$), and saturated fat ($p\text{-trend}<0.001$).

Mean intakes of energy and nutrient by levels of added sugar intake are presented in Table 7. The average energy intake was 2110.5 kcals for the study population, with significantly higher energy being consumed among higher added sugar intake group compared to lower added sugar intake group (2174.9 kcals vs. 2012.3 kcals, $p<0.001$). With regards to food groups, significantly lower intakes were observed among those who had excess added sugar intake ($>10\%$ of calories from added sugar in the diet) versus those who meet the recommendation on added sugar intake. These food groups included: total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total

protein, and seafood and plant protein. No statistically significant differences in the scores of fatty acids ratio, refined grains, and saturated fat were found between higher and lower added sugar intake groups.

In addition, as shown in Table 7, higher intakes of energy, carbohydrate, total sugar, and lower intakes of protein, dietary fiber, polyunsaturated fatty acids, copper, magnesium, phosphorus, potassium, selenium, zinc, vitamin A, beta-carotene, thiamin, niacin, total folate, vitamin B6, vitamin E and vitamin K were observed among those with higher added sugar intake versus those with lower added sugar intake. However, excess added sugar intake was associated with significantly lower sodium intake ($p<0.001$). Furthermore, Figure 1 illustrates that higher percent of dietary calories from added sugar was associated with significantly lower intake of sodium in a linear fashion across all energy intake tertiles ($p\text{-trend}<0.001$).

Table 5: Sociodemographic characteristics and average Healthy Eating Index-2015 (HEI-2015) scores among adults ≥ 20 years from NHANES 2007-2010 (n=3,233)

Sociodemographic variables	Categories	n	Weighted %	HEI-2015	
				Mean	SE
Total sample size		3233		54.9	0.39
Age (years)	20-29 (ref)	490	17.2	50.7	0.72
	30-44	803	27.1	53.4	0.48**
	45-64	1180	39.2	55.9	0.46**
	65 or older	760	16.6	59.4	0.67**
Gender	Male (ref)	1554	48.1	53.2	0.46
	Female	1679	51.9	56.5	0.51**
Race/ethnicity	non-Hispanic white (ref)	1707	73.8	53.4	0.61
	non-Hispanic black	539	9.3	51.7	0.50**
	Mexican Hispanic	545	7.7	53.4	0.52
	Other Hispanic	321	4.3	55.3	0.81
	Other Race	121	5.0	58.2	0.97
Education	Less than high school	837	16.4	52.2	0.45
	High school or equivalent (ref)	753	22.7	52.4	0.55
	Some college	899	29.6	54.6	0.46**
	College or above	741	31.1	58.5	0.61**
Marital status	Single / never married (ref)	514	16.0	52.5	0.80
	Married / with partner	1980	65.7	55.4	0.34**
	Divorced / separated / widowed	738	18.2	55.3	0.79*
Household size	1 person (ref)	467	13.5	57.1	0.98
	2 persons	1040	35.4	56.5	0.50
	3-4 persons	1123	36.1	53.4	0.48**
	5 or more persons	603	15.0	52.8	0.85**
Household income	< 150% of federal poverty line (ref)	1149	23.2	52.0	0.46
	Between 150% and <300% of federal poverty line	1055	31.6	54.7	0.58**
	$\geq 350\%$ of federal poverty line	1029	45.2	56.5	0.57**

*p<0.05

**p<0.001

Table 6: HEI-2015 score breakdown and differences between HEI-2015 score components by added sugar intake levels for adults ≥ 20 years from NHANES 2007-2010

HEI-2015 Components	Contribution to total score (Mean \pm SE)	Score by added sugars level (Mean \pm SE)	
		$\leq 10\%$ of calories	$>10\%$ of calories
Adequacy			
Total Fruits [5]	2.70 \pm 0.06	2.96 \pm 0.09	2.53 \pm 0.06**
Whole Fruits [5]	2.89 \pm 0.06	3.16 \pm 0.10	2.71 \pm 0.06**
Total Vegetables [5]	3.46 \pm 0.03	3.84 \pm 0.05	3.20 \pm 0.03**
Greens and Beans [5]	2.23 \pm 0.07	2.63 \pm 0.09	1.98 \pm 0.07**
Whole Grains [10]	3.38 \pm 0.07	3.97 \pm 0.09	3.00 \pm 0.08**
Dairy [10]	5.77 \pm 0.08	5.95 \pm 0.11	5.65 \pm 0.08*
Total Protein Foods [5]	4.39 \pm 0.03	4.53 \pm 0.04	4.30 \pm 0.03**
Seafood and Plant Proteins [5]	3.21 \pm 0.07	3.48 \pm 0.07	3.04 \pm 0.08**
Fatty Acids (ratio of poly- and monounsaturated fatty acids to saturated fatty acids) [10]	7.22 \pm 0.10	7.39 \pm 0.13	7.12 \pm 0.10
Moderation			
Refined Grains [10]	4.50 \pm 0.07	4.41 \pm 0.12	4.56 \pm 0.09
Sodium [10]	2.06 \pm 0.03	1.42 \pm 0.06	2.48 \pm 0.06**
Added Sugars [10]	5.82 \pm 0.09	8.99 \pm 0.05	3.74 \pm 0.07**
Saturated Fats [10]	7.28 \pm 0.05	7.15 \pm 0.09	7.36 \pm 0.07
Total Score [100]	54.91 \pm 0.39	59.87 \pm 0.40	51.66 \pm 0.36**

* $p < 0.05$

** $p \leq 0.001$

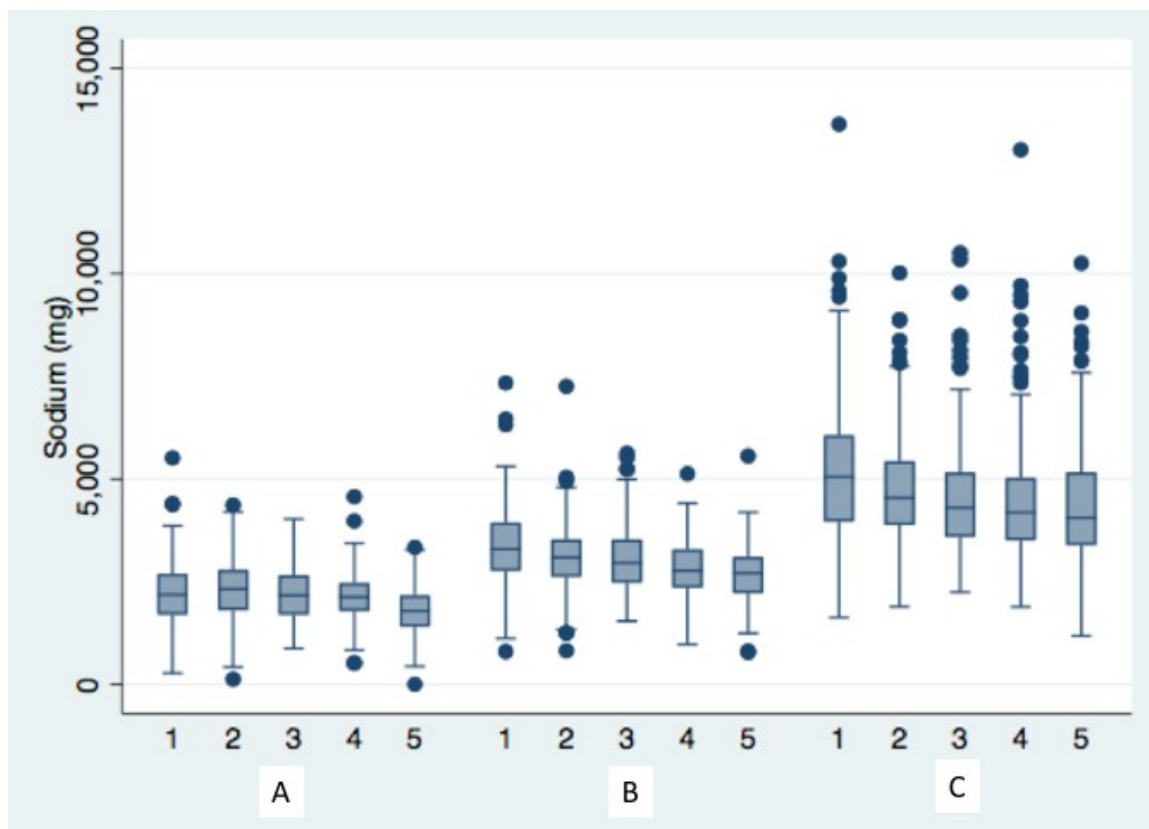
Table 7: Energy and nutrient intakes by meeting or exceeding added sugar recommendation for adults ≥ 20 years from NHANES 2007-2010

Variables	Added sugars $\leq 10\%$ of calories		Added sugars $> 10\%$ of calories		P-value
	Mean	SE	Mean	SE	
Energy (kcal)	2012.27	31.18	2174.87	26.54	<0.001
Protein (g)	87.93	1.39	80.17	1.01	<0.001
Carbohydrate (g)	220.04	3.76	279.70	3.44	<0.001
Dietary fiber (g)	18.87	0.54	16.03	0.28	<0.001
Total sugars (g)	75.86	1.48	139.27	2.36	<0.001
Added sugars (g)	31.12	0.63	100.06	2.32	<0.001
Total fat (g)	80.62	1.37	80.05	0.98	0.73
MUFA (g)	29.60	0.54	29.00	0.38	0.33
PUFA (g)	18.24	0.36	17.26	0.22	0.02
SFA (g)	25.50	0.47	26.67	0.40	0.06
Cholesterol (mg)	291.38	8.88	277.22	5.04	0.17
Calcium (mg)	984.75	17.89	975.48	17.47	0.61
Copper (mg)	1.42	0.03	1.29	0.02	<0.001
Iron (mg)	16.13	0.30	15.68	0.25	0.17
Magnesium (mg)	325.64	5.98	287.49	4.91	<0.001
Phosphorus (mg)	1441.51	23.14	1353.09	17.70	0.001
Potassium (mg)	2932.66	48.53	2630.62	31.72	<0.001
Selenium (μg)	118.62	1.87	108.26	1.76	<0.001
Sodium (mg)	3692.66	58.19	3447.90	34.93	0.001
Zinc (mg)	12.65	0.29	11.83	0.15	0.003
Vitamin A (μg)	687.53	20.82	632.55	13.92	0.004
Beta-carotene (μg)	2720.64	127.00	1938.93	77.77	<0.001
Thiamin (mg)	1.74	0.03	1.66	0.03	0.04
Riboflavin (mg)	2.26	0.04	2.21	0.04	0.26
Niacin (mg)	26.76	0.40	25.25	0.40	0.008
Total folate (μg)	438.64	8.90	404.94	8.46	0.003
Vitamin B6 (mg)	2.17	0.04	2.05	0.03	0.013
Vitamin B12 (μg)	5.53	0.20	5.57	0.13	0.80
Vitamin C (mg)	87.46	2.54	82.01	2.51	0.12
Vitamin D (μg)	5.19	0.21	4.81	0.15	0.11
Vitamin E (mg)	8.63	0.20	7.54	0.13	<0.001
Vitamin K (μg)	119.9	5.25	95.21	3.45	<0.001

Table 9. Estimated mean HEI-2015 components (and 95%CI) by weighted added sugar percentage quintiles among adults ≥ 20 years from NHANES 2007-2010

HEI-2015 components	Percent of calories from added sugar quintile					p-trend
	Q1(n=662)	Q2(n=725)	Q3(n=648)	Q4(n=610)	Q5(n=588)	
Total fruit [5]	3.0 (2.8, 3.2)	3.0 (2.8, 3.2)	2.8 (2.7, 3.0)	2.7 (2.5, 2.8)	1.9 (1.7, 2.1)	<0.001
Whole fruit [5]	3.2 (3.0, 3.4)	3.2 (3.0, 3.4)	3.0 (2.8, 3.2)	2.9 (2.7, 3.1)	2.0 (1.7, 2.2)	<0.001
Total vegetables [5]	4.0 (3.9, 4.1)	3.7 (3.5, 3.8)	3.6 (3.5, 3.7)	3.2 (3.1, 3.3)	2.8 (2.6, 2.9)	<0.001
Greens and beans [5]	2.7 (2.5, 2.9)	2.5 (2.3, 2.8)	2.4 (2.1, 2.6)	2.0 (1.7, 2.2)	1.4 (1.3, 1.6)	<0.001
Whole grains [10]	4.0 (3.7, 4.3)	3.9 (3.7, 4.2)	3.4 (3.2, 3.7)	3.1 (2.8, 3.3)	2.3 (2.0, 2.6)	<0.001
Dairy [10]	5.8 (5.4, 6.2)	6.1 (5.9, 6.3)	6.1 (5.9, 6.4)	5.7 (5.5, 6.0)	4.9 (4.7, 5.2)	<0.001
Total protein [5]	4.5 (4.4, 4.7)	4.5 (4.4, 4.6)	4.5 (4.4, 4.6)	4.4 (4.3, 4.5)	4.0 (3.9, 4.1)	<0.001
Seafood and plant protein [5]	3.5 (3.3, 3.8)	3.5 (3.3, 3.6)	3.3 (3.0, 3.6)	3.1 (2.9, 3.3)	2.5 (2.3, 2.7)	<0.001
Fatty acid ratio [10]	7.6 (7.3, 7.9)	7.2 (6.8, 7.6)	7.2 (6.9, 7.6)	7.3 (6.9, 7.6)	6.8 (6.4, 7.2)	0.01
Refined grains [10]	4.6 (4.2, 4.9)	4.3 (4.0, 4.7)	4.4 (4.0, 4.7)	4.4 (4.1, 4.8)	4.8 (4.6, 5.1)	0.02
Sodium [10]	1.4 (1.2, 1.5)	1.6 (1.4, 1.7)	1.9 (1.7, 2.0)	2.5 (2.3, 2.7)	3.2 (3.0, 3.5)	<0.001
Added sugar [10]	10 (10, 10)	7.6 (7.5, 7.7)	5.2 (5.2, 5.3)	3.8 (3.8, 3.8)	1.6 (1.4, 1.7)	<0.001
Saturated fat [10]	7.1 (6.8, 7.4)	7.1 (6.9, 7.3)	7.1 (6.8, 7.3)	7.1 (6.9, 7.4)	8.0 (7.8, 8.2)	<0.001
Total score [100]	61.3 (60.3, 62.3)	58.3 (57.0, 59.6)	55.0 (53.8, 56.2)	52.2 (51.2, 53.1)	46.3 (45.1, 47.4)	<0.001

Figure 1: Mean sodium intake by energy-adjusted added sugar intake quintiles among adults ≥ 20 years from NHANES 2007-2010



- A, B, and C represent tertiles of daily energy intake, from lowest to highest.
- 1, 2, 3, 4, and 5 represent quintiles of percent of calories from added sugar in the diet, from lowest to highest.

9.5 Discussion

In this large representative sample of American adults ≥ 20 years, we found that added sugar intake was negatively associated with diet quality, after adjusting for demographic and anthropometric characteristics. In addition, after adjusting for demographic and anthropometric factors, excess added sugar intake was related to low scores for HEI-2015 components that are considered as food groups “consumed in

adequacy”. This finding indicated the detrimental role of high added sugar intake in compromising the consumption of healthy food choices. We also found an association between excess added sugar intake and high score for HEI-2015 component of sodium, that is considered as “consumed in moderation” (high score represents low consumption of the component). This finding suggested the potentially protective role of high added sugar intake in reducing the consumption of sodium, a known risk factor for hypertension and other chronic diseases.^{11,12,13}

Although previous studies have reported the association between excess added sugar intake and reduced diet quality,^{2,4,5} our study further investigated the relationship between added sugar and sodium, as two ingredients recommended to be “consumed in moderation” in the diet. Our findings revealed that the desired health benefits of low added sugar intake may be compensated by higher sodium intake among American adults, regardless of energy intake. Therefore, our study adds to an understanding of the potential impact of added sugar intake on diet quality given that high added sugar intake is typically linked to high fat and high sodium intake.⁵

We found that individuals were more likely to have a lower quality diet if they were male, younger, less educated, single or never-married, low-income, and were from bigger households. With regards to the association between added sugar intake and diet quality, our findings are largely consistent with previous observations that increased consumption of added sugar has been linked to an overall reduction in diet quality,² possibly by contributing to excess calories intake and potentially displacing nutrient-dense foods from the diet.³ A recent systematic review of 52 studies found that higher intake of added sugar was associated with poorer diet quality, after adjusting for total caloric intake.⁵

However, the impact of excess added sugar intake on diet quality, including specific changes in food group consumption, is still poorly defined. In this study, our findings examined the relationship between the consumption of different food groups, regardless of whether they are in “adequacy” or “moderation” categories. Our findings suggested that despite the known detrimental association of added sugar intake on diet quality, lower intakes of sodium and saturated fat were seen among excess added sugar consumers, indicating the potential complexity of evaluating the actual health impact of added sugar consumption levels. Furthermore, our findings support the importance of focusing on the health promoting effects of dietary patterns, instead of focusing on one ingredient or component of the diet, even though added sugar has gained lots of scientific and public attention recently.

In addition, our findings are consistent with previous observations that increased consumption of added sugar has been linked to higher energy intake and reduced intakes of certain nutrients. Based on NHANES 1999-2000, adults with highest intake of sugar-sweetened beverages (SSBs) had a higher intake of calories, carbohydrates, as well as a lower intake of fiber, orange juice, and low-fat milk.⁴ However, some researchers reported that the median estimated nutrient intake was lowest among those who consumed greater than 25% of total calories from added sugar,⁶ which was different from our findings. In this study, we did not detect significant differences of the intakes of total fat, MUFA, saturated fat, cholesterol, iron, riboflavin, vitamin B12, vitamin C, and vitamin D between higher and lower added sugar consumers, suggesting that excess added sugar may not affect diet quality by compromising all nutrient intakes.

Added sugar may affect diet quality by regulating appetite and eating behaviors.¹⁴ It was suggested that foods rich in added sugar may trigger brain activity by stimulating certain cells in the digestive system¹⁵ involving brain mechanisms that regulate glucose signaling.¹⁶ These effects of added sugar consumption on the nervous system may be drug-like (but at a significantly lower level) and may partially explain why many people report seeking sweet foods for comforting and mood-altering psychoactive effects.¹⁷ Therefore, these possible effects of added sugars in the diet may explain why a number of people have difficulty lowering their added sugar intake after being habitually exposed to sugar-laden foods and beverages.¹⁸ Interestingly, similar findings were reported in salt studies that, the distinct enjoyment of high salt foods in many people may result from conditioned learning in association with other flavor preferences, just like that of sweet foods.¹⁹ Even though it remains unclear whether salt mainly increases the reward properties of food or its physiological consequences, this mechanism may help explain our finding that individuals may consume increased salty flavored diet as a compensate while being able to enjoy foods and beverages low in added sugar.

Our study has important strengths, including a large and diverse sample of adult representatives of the US population, and the use of a validated measurement of added sugar intake as part of the dietary data collection and analysis. In addition, this study used the most recent version of Healthy Eating Index (HEI-2015) to measure diet quality and, to the best of our knowledge, is the first analysis paper of NHANES examining the association between added sugar intake and HEI-2015. Besides using the binary variable of added sugar intake above or below the recommended 10% cutoff, we examined

quintile of percent of dietary calories from added sugar in our study to avoid arbitrary categorizing low and high added sugar intake groups.

Our findings should be interpreted in the context of several study limitations. First, due to the cross-sectional nature of NHANES study design, we were unable to determine causality of the relationships between added sugar intake and diet quality, and energy and nutrient intakes. Second, we did not assess whether added dietary sugar intake in a liquid or solid form was more important in influencing the association between added sugar and diet quality. Third, information bias may be a concern since added sugar intake and other dietary information were self-reported using 24-hour dietary recall. However, all protocols are clearly specified and are administered systemically to all NHANES participants by trained staff during a structured in-person interview at the participants' homes. Therefore, the probability of non-differential misclassification of exposure occurring during the process of two-day dietary 24-hour dietary recall was highly unlikely. Additionally, participants were blinded to the hypothesis of our study as data was collected for general nutrition and health information and was for public use. It is believed that it was highly unlikely that interviewers would prompt selected participants to report added sugar intake differently than their counterparts.

9.6 Conclusion

In summary, we found that excess added sugar intake is linked to an overall reduction of diet quality and compromised intake of most nutrients among American adults 20 years or older. However, the association between high added sugar intake and lower sodium intake, regardless of energy intake, may imply future studies exploring the interactions between added sugar and salt in the diet are needed. Our study adds to a

better understanding of food group consumption and dietary components associated with added sugar intake. Further research is needed to determine whether changes in added sugar intake predict food group consumption and nutrient intakes in specific dimensions, and whether these findings can help us understand the relationship between added sugar intake and the overall dietary practices, to guide future intervention and policy efforts.

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CHAPTER 10

“EXCESS ADDED SUGAR INTAKE CONTRIBUTES TO LOW HDL- CHOLESTEROL AND INCREASED LEVELS OF TRIGLYCERIDES, BUT SHOWS NO EFFECT ON INFLAMMATION AMONG ADULTS 20 YEARS OR OLDER FROM NHANES 2007-2010”

10.1 Abstract

Chronic health conditions, including systemic inflammation, obesity, and metabolic syndrome, have presented a tremendous public health concern in the U.S. and globally. It is largely believed that excess intake of added sugar may play a role in the development of obesity and metabolic diseases. However, some researchers concluded that there is no convincing evidence that added sugar has a different effect on the development of chronic diseases such as obesity and diabetes, compared to any other source of calories. Therefore, the impact of added sugar consumption on health outcomes continues to be controversial.

We conducted a secondary data analysis among 3,233 adults aged ≥ 20 years from the cross-sectional National Health and Nutrition Examination Survey (NHANES) 2007-2010, to evaluate the associations between added sugar intake and health outcomes including systemic inflammation and metabolic syndrome. Added sugar intake was assessed based on the 24-hour dietary recall data, using Food and Nutrient Database for Dietary Studies 4.1 (FNDDS 4.1) and Food Patterns Equivalent Database (FPED) to convert foods and beverages to teaspoon equivalents of added sugar. Added sugar intake was further determined by the percent of total calories from added sugar in the diet,

presented as tertiles ($\leq 10\%$, 10-25%, and $>25\%$ of total calories from added sugar in the diet). With regards to assessment of health outcomes, anthropometrics including height, weight, and waist circumference were measured on each participant. Repeated blood pressure readings were also obtained by trained personnel during the physical examination. In addition, fasting whole blood samples were collected and serum high-sensitivity CRP was quantified as an indicator of inflammation. Concentrations of other serum biomarkers were also examined, including triglycerides, total cholesterol, HDL-cholesterol, LDL-cholesterol, glucose, and insulin. As a cluster of related health problems, the metabolic syndrome was defined based on the National Cholesterol Education Program Adult Treatment Panel (ATP) III definition, with at least three out of five criteria being met.

To account for NHANES' complex survey design, we incorporated the sampling weights to analyze 3,233 observations. After adjusting for age, gender, race/ethnicity, education, household income, energy intake, BMI, physical inactivity, use of medication, and current smoking, consuming more than 25% of calories from added sugar in the diet increased the likelihood of having low HDL-cholesterol by nearly 4 times compared to consuming $\leq 10\%$ of calories from added sugar, regardless of gender and weight status. In addition, consuming more than 25% of calories from added sugar in the diet was positively associated with serum triglycerides levels compared to consuming $\leq 10\%$ of calories from added sugar, regardless of gender. No relationship was observed between added sugar intake and hs-CRP levels. These findings indicated the detrimental role of high added sugar intake in affecting blood lipid profile and related adverse health outcomes. Our study adds to a better understanding of the health impacts of added sugar

intake among adults. Further research is needed to determine whether changes in added sugar intake predict inflammation and risks of metabolic syndrome in specific dimensions, as well as to examine the potential underlying mechanisms.

10.2 Introduction

Non-communicable chronic health conditions, including systemic inflammation, obesity, type 2 diabetes (T2DM), cardiovascular disease (CVD), dyslipidemia, and hypertension, have presented a growing public health problem in the US and globally.¹ Metabolic syndrome (MetS) is the constellation of these closely related anomalies and has been used to help identify individuals at high risk of T2DM and CVD.² Some epidemiologic studies have suggested that excess intake of added sugar may play a role in the development of obesity and metabolic diseases.³ However, other researchers concluded that there is no clear evidence that added sugar has a unique or detrimental effect on the development of chronic diseases such as obesity and diabetes, relative to any other source of calories.⁴ Therefore, the impact of added sugar consumption on chronic health outcomes continues to be controversial.

There have been inconsistent findings on the relationship between added sugar intake and hs-CRP as an inflammatory biomarker. Using data from NHANES 1999 to 2010, it was found that decreased sugar-sweetened beverages (SSBs) consumption significantly decreased hs-CRP, independent of demographic and lifestyle factors.⁵ A large cross-sectional study in England reported that sugar added to tea, coffee, and cereals were associated with CRP, but sugar from food sources such as cakes, squash drinks, dairy, egg dishes, and fruits and vegetables were not associated with CRP levels.⁶

In a prospective randomized controlled trial among 29 healthy young men, Aeberli et al. reported that fasting glucose and CRP level increased significantly after all interventions on SSBs consumption after six 3-week interventions.⁷ Another clinical controlled trial among 31 patients with type 1 diabetes revealed that sucrose intake increased CRP levels, whereas no association was found between total sugar in the diet and CRP.⁸

A number of studies have shown that consuming higher amounts of added sugar, especially SSBs, significantly increases risks of overweight/obesity,^{9,10} T2DM,^{11,12} dyslipidemias,^{13,14,15} hypertension,^{15,16} and metabolic syndrome.^{11,17} However, there have been different findings. A recent clinical controlled trial found that sucrose intake, along with a disciplined diet, did not affect anthropometric variables, body composition, as well as lipemic and glycemic control.⁸ Based on NHANES 1999-2006, Sun et al. found that fructose, as a common type of added sugar, was not associated with indicators of metabolic syndrome among participants 12-80 years old.¹⁸ A follow up study of Nurses' Health Study for 24-30 years also reported that replacing saturated fats with carbohydrates from refined starches or added sugar was not associated with heart disease risks.¹⁹ In a recent systematic review, V Ha et al. reported that no adverse effect was found of isocaloric substitution of fructose for other carbohydrates on blood pressure.²⁰ Another systematic review concluded that fructose intake was not associated with increased risk of hypertension.²¹

The present study assesses the relationship between added sugar intake and adverse health outcomes including inflammation, metabolic syndrome and related cardio-metabolic indicators, based on the 2007-2008 and 2009-2010 NHANES. The primary goal was to assess how added sugar intake was related to inflammation and the risk of

metabolic syndrome, determined by serum hs-CRP level and a series of metabolic disease indicators, among 3,233 adults aged ≥ 20 years. Examining the associations between added sugar intake and adverse health outcomes enables us to gain a better understanding of the health impact of added sugar and may guide future interventions in reducing added sugar consumption as a part of healthy dietary practice.

10.3 Methods

10.3.1 Study Design and Study Population

This cross-sectional study was based on data from adults aged ≥ 20 years from the 2007-2008 and 2009-2010 cycles of NHANES. NHANES is a large nationally representative population-based study of risk factors, dietary status and health conducted continuously in the United States. The National Center for Health Statistics Research Ethics Review Board (ERB) has reviewed and approved the NHANES protocol.²²

NHANES uses a multistage, stratified, and clustered sampling method to recruit participants who are representative of the U.S. population. All the counties in the U.S. are divided into 15 groups based on their characteristics such as metropolitan areas. One county is selected from each large group, and together they form the 15 counties in the NHANES surveys for each year. Within each county, smaller groups, comprised of a large number of households in each, are formed and 20-24 of these small groups will be selected. All of the households or apartments within those selected small groups are identified and a sample of about 30 households are selected within each group. One person in the selected households is approached by NHANES interviewers at home and is asked about information (age, race, and gender) on all persons in the household, and a

computer algorithm randomly selects some, all, or none of the household members. To produce reliable statistics, NHANES oversample persons 60 and older, African Americans, and Hispanics. Details of the NHANES probability sampling and data collection procedures are available at the NHANES website.²²

Due to markedly differences in food choices and subsequent added sugars intake among youths and adults, we limited our study population to adults aged 20 years and older. We excluded those younger than 20 years; those who are pregnant; those who had missing data on dietary intakes, or consumer behaviors, and those who had missing data on serum biomarkers. The remaining sample contained 3,233 observations.

10.3.2 Assessment of Added Sugar Intake

The NHANES 24-h dietary recall utilized a multi-pass method, where respondents reported the types and amounts of all food and beverages consumed in the preceding 24-hours, from midnight to midnight. Two dietary recalls were collected for most participants, with the first one completed in-person at the Mobile Examination Center with a trained interviewer, whereas the second was completed over the telephone some days later. To calculate the amount of added sugars intake, we used the original Food and Nutrient Database for Dietary Studies 4.1 (FNDDS 4.1) as a tool to help provide nutrient composition of the over 7,000 food and beverages collected in NHANES.²³ This database converts single ingredient foods, including orange juice, cooked rice, or skim milk, into nutrient composition. However, many of the foods such as pizza, fruit salad, and casserole are multi-ingredient foods consisting of ingredients from more than one food groups. Hence, we used another tool named the Food Patterns Equivalent Database (FPED) which was created by USDA, Agricultural Research Service (ARS), and Food

Surveys Research Group (FSRG). FPED disaggregate multi-ingredient foods to ingredients that can be assigned to a food pattern before computing the amount present in the food. The methodology used to develop the FPED has been described elsewhere.²⁴

FPED converts FNDDS foods to the respective number of teaspoon equivalents of added sugar. For example, cane sugar, honey, and all types of syrups are examples of added sugar in their pure form. Ingredients that are added sugar present in multi-ingredient foods such as cakes, cookies, and ice cream are also assigned to the added sugar component. FPED uses the sugar content of foods defined as added sugar to compute teaspoon equivalent of added sugar. One teaspoon equivalent of added sugar is defined as 4.2 grams of granulated sugar.²⁴ In our study, added sugar intake was further calculated as percent of calories from added sugar in the diet, and was presented in tertiles.

10.3.3 Assessment of Adverse Health Outcomes

During the physical examination, blood specimens were collected and processed. For serum hs-CRP measurement, blood samples were stored and shipped to University of Washington, Seattle, WA for analysis. CRP was measured by latex-enhanced nephelometry. Particle-enhanced assays performed on a Behring Nephelometer were also applied. These assays were based on the reaction between a soluble analyte and the corresponding antigen or antibody bound to polystyrene particles. For the quantification of CRP, particles consisting of polystyrene cores and a hydrophilic shell were used to link anti-CRP antibodies covalently. A dilute solution of test samples was mixed with

latex particles coated with mouse monoclonal anti-CRP antibodies. CRP present in the test sample forms an antigen antibody complex with the latex particles. An automatic blank subtraction was performed and CRP concentrations were computed by using a calibration curve.²²

Several anthropometric measurements and blood biomarkers will be used in assessing metabolic syndrome. In this study, metabolic syndrome was determined by the criteria developed by the National Cholesterol Education Program: Third Adult Treatment Panel (ATP III), with the presence of at least three of the following risk factors (NCEP, 2002): 1) Fasting plasma glucose $\geq 100\text{mg/dL}$ (5.6mmol/L); 2) Blood pressure $\geq 130/85\text{ mmHg}$; 3) Triglycerides $\geq 150\text{ mg/dL}$ (1.7 mmol/L); 4) HDL-cholesterol: Men $<40\text{ mg/dL}$ (1.03 mmol/L); women $<50\text{ mg/dL}$ (1.29 mmol/L); 5) Waist circumference: Men $>102\text{ cm}$ and women $>88\text{cm}$.

The waist circumference measurement was conducted among participants aged 2 years of age and older. Data were collected by trained health technicians, assisted by a recorder during the body measurement examination. Participant gathers his or her gown shirt above the waist, cross the arms, and place the hands on opposite shoulders. If necessary, pants and underclothing need to be lowered slightly below the waist. Measuring tape is extended around the participant's waist, in a horizontal plane at the level of the measurement mark (just above the uppermost lateral border of the right ilium of the pelvis). The measurement is taken to the nearest 0.1 cm at the end of the participant's normal expiration.

In order to obtain accurate measurement of blood pressure (BP), the BP examiners are certified for BP measurement through a training program from Shared Care Research and Education Consulting. After participant been resting quietly in a sitting position for 5 minutes and determining the maximum inflation level, three consecutive BP readings are obtained. If a BP measurement is interrupted or incomplete, a fourth attempt may be made. All BP determinations (systolic and diastolic) are taken in the mobile examination center (MEC).

Blood triglycerides, HDL, and LDL are measured for examinees that were examined in the morning session, who had fasted at least 8.5 hours or more but less than 24 hours. Blood specimens were processed, stored, and shipped to University of Minnesota, Minneapolis for analysis. 1) For triglycerides measurement, free glycerol is converted to glycerol-3-phosphate (G3P) by glycerol kinase. The hydrogen peroxide combines with 4-chlorophenol under the action of peroxidase to produce an oxidation product that does not react with the colorimetric component of reagent 2. After the initial reaction sequence is completed, the Mod P records a blank absorbance reading, then reagent 2 is added. The second reaction is driven when lipase is added in reagent 2 to convert triglycerides to glycerol, and 4-aminophenzone added to react with the hydrogen peroxide produced in the last reaction. The reaction is measured at 505 nm. 2) For HDL measurement, a magnesium/dextran sulfate solution is added to form water-soluble complexes with non-HDL cholesterol fractions. With addition of reagent 2, HDL-cholesterol esters are converted to HDL-cholesterol by PEG-cholesterol esterase. The HDL-cholesterol is acted upon by PEG-cholesterol oxidase, and the hydrogen peroxide produced from this reaction combines with 4-amino-antipyrine and

HSDA under the action of peroxidase to form a purple/blue pigment that is measured photometrically at 600 nm. 3) For LDL levels, LDL-cholesterol is calculated from measured values of total cholesterol, triglycerides, and HDL-cholesterol according to the Friedewald calculation:

$$[\text{LDL-cholesterol}] = [\text{total cholesterol}] - [\text{HDL-cholesterol}] - [\text{triglycerides}/5].$$

For plasma fasting glucose and insulin, blood specimens were collected in the morning examination sessions only. Blood samples were later processed, stored and shipped to Fairview Medical Center Laboratory at the University of Minnesota, Minneapolis, MN for analysis. Using an enzymatic method, glucose is converted to glucose-6-phosphate (G-6-P) by hexokinase in the presence of ATP. G-6-P dehydrogenase then converts the G-6-P to gluconate-6-P in the presence of NADP⁺. As the NADP⁺ is reduced to NADPH during this reaction, the resulting increase in absorbance at 340 nm is measured. This is an endpoint reaction that is specific for glucose. Referring to insulin measurements, the Merocodia Insulin ELISA was utilized. Insulin present in the sample binds to anti-insulin antibodies bound to the sample well, while the peroxidase-conjugated anti-insulin enzyme-labelled antibodies also bind to the insulin at the same time. After washing to remove unbound enzyme- labelled antibodies, a labelled substrate is added and binds to the conjugated antibodies. Acid is added to the sample well to stop the reaction and the colorimetric endpoint is read on a microplate spectrophotometer set to the appropriate light wavelength (CDC, 2010). Insulin resistance was determined by the homeostatic model assessment of insulin resistance (HOMA-IR), calculated using the formula as below.

Glucose in mass units (mg/dL)

$$\text{HOMA} - \text{IR} = \frac{\text{Glucose} \times \text{Insulin}}{405}$$

10.3.4 Assessment of Covariates and Confounders

We considered as possible covariates a selected set of demographic and anthropometric, and lifestyle factors available through data collection during the demographic section and physical activity sections of the NHANES questionnaire, as well as the examination section. Gender was self-reported and was used as male or female. Age was classified into four categories: 20-29 years, 30-44 years, 45-64 years, and 65 years or older. According to the National Center for Health Statistics (NCHS) standard definitions for ethnicities, subjects were categorized as non-Hispanic whites, non-Hispanic blacks, Mexican-Hispanics, other Hispanics, and other race. Educational attainment was measured as the highest completed grade of school for those above the age of 20 and was categorized into four levels: less than high school, high school or equivalent, some college, and college graduate or above. Household income was calculated as the ratio of family income to the federal poverty threshold and was categorized as <1.5 (low income), 1.5-3.5 (medium income), and >3.5 (high income).

Body mass index (BMI) was computed from height and weight measurements (kg/m^2) and was categorized into four standard categories: underweight ($\text{BMI} < 18.5 \text{ kg/m}^2$), normal weight ($18.5 \text{ kg/m}^2 \leq \text{BMI} < 25 \text{ kg/m}^2$), overweight ($25 \text{ kg/m}^2 \leq \text{BMI} < 30 \text{ kg/m}^2$), and obese ($\text{BMI} \geq 30 \text{ kg/m}^2$). Energy intake was categorized into tertile group, coded as “1-3” representing from the lowest to the highest daily caloric intake. Sedentary

lifestyle covariate was assessed by asking participants about how many minutes they conduct sedentary activity on a typical day, including sitting or reclining at work, at home, or at school, but excluding time spent sleeping. This covariate was categorized into tertiles. Current smoking and the use of medication in the past month were categorized as “0” and “1”, representing “no” and “yes”, respectively.

10.3.5 Data Analysis

The multistage, stratified, and clustered sampling method used for NHANES data collection was incorporated into all data analyses using the “svy” command with appropriate weighting in Stata 15.0 (StataCorp LP, College Station, TX). Detailed information on the procedures for taking into account NHANES survey sampling weights have been described elsewhere.

Descriptive analyses calculated mean values of hs-CRP, metabolic syndrome indicators including waist circumference, blood pressure, HDL-cholesterol, triglycerides and fasting glucose, as well as added sugar intake categories. Population subgroups were defined based on gender, age group (20-29 y, 30-44 y, 45-64 y, ≥ 65 y), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican-American, other Hispanic and other race), family income-to-poverty ratio (<1.5 , $1.5-3.5$, >3.5); and education ($<$ high school, high school graduate/equivalent, some college and college graduate). Survey-weighted tests were used to evaluate whether mean descriptive statistics were calculated for the overall sample using means and standard errors for continuous variables and frequency distributions for categorical variables. Natural logarithmic transformations were performed on hs-CRP, fasting glucose, triglycerides, HDL-cholesterol, LDL-cholesterol, and total cholesterol, to normalize the distribution, and their geometric means and 95%

confidence intervals are presented. Two-sample t tests, one-way ANOVA and Pearson's Chi square tests were carried out to assess crude differences in the outcome variables, by added sugar intake. Trend analyses were also conducted using Pearson's correlation tests.

To explore the associations between exposure and outcome variables, unadjusted linear regression models were first derived to evaluate crude relationships between exposure and individual outcome variables. For all covariates that have a p value less than 0.2 in the adjusted regression analyses, they were retained in the multiple linear regression models. In addition, known risk factors for dietary intakes from the literature, such as gender and body mass index (BMI) were retained in the models. The regression coefficient (β) and standard error (SE) will be presented with the corresponding p-value.

10.4 Results

The sociodemographic, anthropometric, inflammatory and cardio-metabolic characteristics of the 3,233 adults who comprise our final sample are shown in Table 9. The mean age of our sample was 47.4 years. There were 1,554 males (48.1%) and 1,679 females (51.9%). Majority of the population were non-Hispanic White (73.8%), married or living with a partner (65.7%), living in a small-medium size (2-4 persons) household (71.5%), had a high school or above degree (83.6%), and reported their household income equal to or above 150% of the federal poverty line (76.8%). Women were more likely to be older ($p=0.004$) or poorer ($p=0.006$) compared to men. However, there was no significant difference in racial/ethnic composition and educational attainment between men and women. With regards to anthropometric measurements, women were more

likely to be underweight or normal weight and have smaller waist circumference than men (both p-values<0.001). In addition, women had lower systolic and diastolic blood pressure, lower fasting glucose levels, and lower triglycerides levels versus men (all p-values<0.001), whereas men had lower hs-CRP and HDL-cholesterol levels than women (both p-values<0.001). According to the ATP III criteria, metabolic syndrome rate was 29.5% among men, and 30.3% among women. However, this difference was not statistically significant.

Table 9. Characteristics of demographic, anthropometric, CRP and cardio-metabolic marker measurements of adults 20 years or older from NHANES 2007-2010

Characteristics	Total (n=3,233) Mean ± SE	Men (n=1,554) Mean ± SE	Women (n=1,679) Mean ± SE	p-value
Age (years)	47.4 ± 0.49	46.5 ± 0.59	48.1 ± 0.51	0.004
Race/ethnicity, %				0.06
Non-Hispanic White	73.8	73.6	73.9	
Non-Hispanic Black	9.3	8.7	9.9	
Mexican American	7.7	8.4	7.1	
Other Hispanic	4.3	4.1	4.4	
Others	5.0	5.2	4.7	
Education, %				0.3
Less than high school	16.4	17.1	15.8	
High school or GED	22.7	22.2	23.2	
Some college	29.6	28.0	31.2	
College or above	31.1	32.5	29.8	
Household income, %				0.006
<150% poverty	23.2	20.9	25.4	
150-350% poverty	31.6	31.3	31.9	
>350% poverty	45.2	47.8	42.7	
Body mass index category, %				<0.001
Underweight (<18.5)	1.1	0.73	1.5	
Normal weight (18.5-24.9)	29.4	25.7	32.8	
Overweight (25-29.9)	35.1	39.8	30.8	
Obesity (30 or above)	34.4	33.8	34.9	
Waist circumference (cm)	98.3 ± 0.44	101.7 ± 0.62	95.2 ± 0.51	<0.001
Systolic BP (mmHg)	119.4 ± 0.42	121.4 ± 0.50	117.6 ± 0.47	<0.001
Diastolic BP (mmHg)	68.9 ± 0.40	70.9 ± 0.36	67.0 ± 0.48	<0.001
hs-CRP (mg/dL)	0.36 ± 0.01	0.30 ± 0.02	0.42 ± 0.02	<0.001
Fasting glucose (mg/dL)	104.2 ± 0.66	107.7 ± 1.1	100.9 ± 0.61	<0.001
HDL-cholesterol (mg/dL)	54.2 ± 0.41	48.7 ± 0.45	59.3 ± 0.51	<0.001
Triglycerides (mg/dL)	122.2 ± 1.5	128.7 ± 2.1	116.2 ± 2.2	<0.001
Metabolic Syndrome (ATPIII criteria), %	29.9	29.5	30.3	0.7

Due to the inherent gender-related differences in the normal range of many health indicators, Table 10 shows the mean values of different anthropometric, blood pressure, and blood cardio-metabolic biomarkers, by gender and added sugar intake. No significant difference was observed in mean values of BMI, waist circumference, systolic blood pressure, diastolic blood pressure, triglycerides, total cholesterol, LDL-cholesterol, and HOMA-IR among groups of men consuming $\leq 10\%$, 10-25%, or $>25\%$ of calories from added sugar in the diet. However, it was found that men consuming higher percent of added sugar had significantly higher levels of serum hs-CRP ($p=0.03$), lower levels of HDL-cholesterol ($p<0.001$), and lower fasting glucose ($p=0.02$), compared to men consuming lower percent of calories from added sugar. These findings were different for the women group, where no significant difference was observed in mean BMI, waist circumference, diastolic blood pressure, hs-CRP, triglycerides, total cholesterol, LDL-cholesterol, fasting glucose, and HOMA-IR across added sugar consumption categories. Women consuming higher percent of calories from added sugar in the diet had significantly lower systolic blood pressure ($p=0.001$) and lower HDL-cholesterol ($p<0.001$), versus women who consumed lower percent of calories from added sugar.

Table 10 Mean anthropometric and cardio-metabolic biomarker values by weighted added sugar intake among men and women, for adults 20 years or older from NHANES 2007-2010

Characteristics	Men (n=1,554) Mean (95%CI)				Women (n=1,679) Mean (95%CI)			
	Percent of calories from added sugar in the diet				Percent of calories from added sugar in the diet			
	≤10% (n=626)	10-25% (n=784)	>25% (n=144)	p-value	≤10% (n=646)	10-25% (n=872)	>25% (n=161)	p-value
BMI (kg/m²)	28.8 (28.2, 29.5)	28.5 (28.0, 29.1)	28.9 (27.7, 30.1)	0.6	28.4 (27.8, 28.9)	28.6 (28.1, 29.2)	28.1 (27.0, 29.2)	0.7
Waist circumference (cm)	102.7 (100.8, 104.5)	101.0 (99.4, 102.5)	101.3 (98.0, 104.7)	0.3	95.0 (93.6, 96.4)	95.4 (94.1, 96.8)	94.6 (92.1, 97.2)	0.8
Systolic BP (mmHg)	122.0 (120.5, 123.6)	121.1 (120.1, 122.3)	120.1 (117.9, 122.2)	0.2	118.3 (116.8, 119.8)	117.7 (116.5, 118.9)	114.1 (112.3, 115.9)	0.001
Diastolic BP (mmHg)	70.6 (69.4, 71.8)	71.3 (70.4, 72.1)	70.6 (68.3, 72.8)	0.6	66.7 (65.4, 68.0)	67.3 (66.2, 68.4)	66.7 (64.1, 69.3)	0.6
hs-CRP (mg/dL)	0.24 (0.20, 0.27)	0.31 (0.26, 0.37)	0.55 (0.20, 0.89)	0.03	0.41 (0.36, 0.46)	0.43 (0.39, 0.48)	0.37 (0.29, 0.46)	0.5
Triglycerides (mg/dL)	127.0 (119.6, 134.3)	127.6 (121.3, 133.8)	142.3 (127.2, 157.5)	0.2	115.6 (108.3, 122.8)	115.9 (110.6, 121.2)	120.4 (107.9, 132.9)	0.3
Total cholesterol (mg/dL)	192.8 (190.0, 196.7)	190.0 (186.6, 193.4)	194.2 (185.5, 202.8)	0.3	199.1 (195.4, 202.7)	200.0 (197.5, 202.5)	194.0 (187.2, 200.8)	0.2
HDL-cholesterol (mg/dL)	51.1 (49.5, 52.6)	47.4 (46.2, 48.6)	45.6 (42.5, 48.7)	<0.001	61.2 (59.5, 63.1)	59.1 (57.9, 60.3)	52.7 (50.5, 55.0)	<0.001
LDL-cholesterol (mg/dL)	116.4 (112.7, 120.1)	117.1 (114.0, 120.3)	120.1 (112.8, 127.4)	0.7	114.7 (111.7, 117.8)	117.7 (115.6, 119.9)	117.2 (110.9, 123.6)	0.2
Fasting glucose (mg/dL)	111.4 (107.3, 115.4)	105.5 (103.1, 108.0)	103.5 (99.9, 107.2)	0.02	102.7 (100.5, 104.8)	99.9 (98.4, 101.4)	99.2 (95.6, 102.9)	0.1
HOMA-IR	3.6 (3.2, 4.1)	3.7 (3.2, 4.2)	4.2 (3.2, 5.2)	0.6	3.0 (2.8, 3.3)	3.2 (2.9, 3.5)	3.5 (2.6, 4.4)	0.5

The crude and adjusted associations between values of anthropometric and cardio-metabolic markers and added sugar intake categories by gender are presented in table 11. The analysis revealed that, after adjusting for age, race/ethnicity, education, household income, energy intake, BMI, physical inactivity, current smoking and use of medication, consuming more than 25% of calories from added sugar in the diet was significantly associated with lower log-transformed HDL-cholesterol, regardless of gender ($\beta=-0.16$ among men, $p=0.003$; $\beta=-0.18$ among women, $p<0.001$) (p-values not shown in the table). Similar finding was seen in serum triglycerides, that consuming higher than 25% of calories from added sugar was related to higher log-transformed serum triglycerides levels, regardless of gender ($\beta=0.19$ among men, $p=0.006$; $\beta=0.17$ among women, $p=0.007$) (p-values not shown in the table).

Table 11 also illustrates that increasing added sugar intake from $\leq 10\%$ to 10-25% was related to decreased log-transformed levels of fasting glucose ($\beta=-0.04$, $p=0.008$) (p-value not shown in the table) among men, but not in women. It was also observed that among men only, consuming higher than 25% of calories from added sugar in the diet was positively associated with hs-CRP levels in unadjusted model, but such association was attenuated after adjusting for demographic variables, further down to a non-significant association after controlling for other confounders.

Table 11 Linear regression of associations between anthropometric, inflammatory, and cardio-metabolic measurements and weighted added sugar intake among men and women, adults 20 years or older from NHANES 2007-2010

Percent of calories from added sugar	Waist circumference			Log-transformed HDL			Log-transformed triglycerides			Log-transformed fasting glucose			BP (systolic, diastolic)			Log-transformed hs-CRP		
	Raw	Model 1	Model 2	Raw	Model 1	Model 2	Raw	Model 1	Model 2	Raw	Model 1	Model 2	Raw	Model 1	Model 2	Raw	Model 1	Model 2
	β	β	β	β	β	β	β	β	β	β	β	β	β	β	β	β	β	β
Men																		
$\leq 10\%$	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
10-25%	-1.7	-1.6	-0.74	-0.07**	-0.07**	-0.08**	0.01	0.01	-0.012	-0.04*	-0.03*	-0.04*	S: -0.88 D: 0.65	S: -0.99 D: 0.38	S: -1.59 D: 0.05	0.04	0.03	0.06
>25%	-1.3	0.26	-1.33	-0.12**	-0.11*	-0.16*	0.14*	0.16**	0.19*	-0.05*	-0.03	-0.03	S: -1.95 D: -0.06	S: -1.1 D: -0.26	S: -0.97 D: 0.51	0.12*	0.12*	0.13
Women																		
$\leq 10\%$	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
10-25%	0.44	0.27	-0.12	-0.04	-0.03	-0.06*	0.004	0.02	0.07	-0.02	-0.02	-0.01	S: -0.65 D: 0.61	S: -0.12 D: 0.56	S: -1.43 D: 1.57	0.01	0.002	-0.02
>25%	-0.37	-1.36	-1.03	-0.15**	-0.11**	-0.18**	0.04	0.07	0.17*	-0.03*	-0.02	-0.03	S: -4.24** D: 0.03	S: -2.4* D: -0.55	S: -2.97 D: -0.30	-0.02	-0.05	-0.03

* p-value<0.05

** p-value<0.001

1. Model 1 was adjusted for age, race/ethnicity, education, and household income. Sample size for model 1 was 3,233.

2. Model 2 was adjusted for model 1 variables, BMI, kcal, physical inactivity, current smoking and use of medication. Sample size for model 2 was 1,483.

Table 12 Linear regression of associations between metabolic syndrome and related abnormalities and weighted added sugar intake among men and women, adults 20 years or older from NHANES 2007-2010

Percent of calories from added sugar	Metabolic Syndrome			Abdominal Obesity			Hypothalipoproteinemia			Hypertriglyceridemia			Hyperglycemia			Hypertension		
	Raw	Model 1	Model 2	Raw	Model 1	Model 2	Raw	Model 1	Model 2	Raw	Model 1	Model 2	Raw	Model 1	Model 2	Raw	Model 1	Model 2
	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR
Men																		
≤10% (ref)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10-25%	1	0.98	1.15	0.91	0.89	1.54	1.64*	1.59*	1.38	1.05	1.04	1.04	0.86	0.93	1.08	1.02	1.02	0.95
>25%	0.91	0.97	1.45	0.78	0.87	0.90	3.03**	2.80*	3.68*	1.16	1.19	1.32	1.11	1.42	1.78	0.85	0.98	0.85
Women																		
≤10% (ref)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10-25%	1.02	1.07	0.99	0.97	0.97	0.74	1.16	1.11	1.46	0.90	0.95	1	0.89	0.95	0.95	1	1.11	1.53 ³
>25%	1.11	1.15	1.43	0.87	0.84	1.23	2.56**	1.95*	3.88**	1.06	1.17	1	0.78	0.88	0.82	0.46*	0.57	0.89 ³

* p-value<0.05

** p-value<0.001

1. Model 1 was adjusted for age, race/ethnicity, education, and household income. Sample size for model 2 was 3,233.

2. Model 2 was adjusted for model 1 variables, BMI, kcal, physical inactivity, current smoking and use of medication. Sample size for model 2 was 1,483.

3. Maximum likelihood estimation was used in logistic regression

The crude and adjusted associations between metabolic syndrome and related abnormalities and added sugar intake categories by gender are presented in table 12. After adjusting for age, race/ethnicity, education, household income, energy intake, BMI, physical inactivity, current smoking and use of medication, consuming more than 25% of calories from added sugar in the diet increased the likelihood of low HDL-cholesterol by nearly 4 folds for both gender (OR=3.68 among men, $p=0.01$; OR=3.88 among women, $p<0.001$), compared to those who consumed $\leq 10\%$ of calories from added sugar. Excess consumption of added sugar was not significantly associated with the risk of having metabolic syndrome, abdominal obesity, hypertriglyceridemia, hyperglycemia, and hypertension for both gender, after controlling for confounders.

10.5 Discussion

In this large representative sample of American adults ≥ 20 years, we found that after adjusting for confounders, consuming more than 25% of calories from added sugar in the diet increased the likelihood of having low HDL-cholesterol by nearly 4 times compared to consuming $\leq 10\%$ of calories from added sugar, regardless of gender and weight status. In addition, consuming more than 25% of calories from added sugar in the diet was positively associated with serum triglycerides levels compared to consuming $\leq 10\%$ of calories from added sugar, regardless of gender. These findings indicated the detrimental role of high added sugar intake in affecting blood lipid profile and related adverse health outcomes.

Our findings are largely consistent with previous literature^{25,26,27,28,29} that individuals at higher risk of consuming excessive added sugar were younger, less educated, single or never-married, and from the low-income households (data shown elsewhere). With regards to the association between high added sugar intake and low HDL-cholesterol, our findings are consistent with previous large population-based studies that increased consumption of added sugar in the diet was linked to decreased levels of HDL-cholesterol among American adolescents^{14,30} and Korean adults³¹. Furthermore, the positive relationship between added sugar intake and levels of triglycerides was consistent with previous studies. A recent non-randomized double-blinded intervention study among adult participants reported that added sugar intake significantly increased postprandial triglycerides.³² A recent study among children also found that, intake of SSBs was positively associated with triglycerides concentrations, and changes in SSBs consumption were inversely associated with HDL-cholesterol concentration changes over 12 months.³³

Despite that a number of studies have shown that consuming higher amounts of added sugar, especially SSBs, significantly increases risks of metabolic syndrome,^{11,17} overweight/obesity,^{9,10} dyslipidemias,^{13,14,15} and hypertension.^{15,16} Our study failed to report significant associations between high added sugar intake and metabolic syndrome as well as related abnormalities including abdominal obesity, hypertriglyceridemia, hyperglycemia, and hypertension, among both men and women. However, these findings were similar to results from selected previous studies. A recent clinical controlled trial found that sucrose intake, along with a disciplined diet, did not affect anthropometric variables, body composition, as well as lipemic and glycemic control.⁸ Based on

NHANES 1999-2006, Sun et al. found that fructose, as a common type of added sugar, was not associated with indicators of metabolic syndrome among participants 12-80 years old.¹⁸ A follow up study of Nurses' Health Study for 24-30 years also reported that replacing saturated fats with carbohydrates from refined starches or added sugar was not associated with heart disease risks.¹⁹ In a recent systematic review, V Ha et al. reported that no adverse effect was found of isocaloric substitution of fructose for other carbohydrates on blood pressure.²⁰ Another systematic review concluded that fructose intake was not associated with increased risk of hypertension.²¹

It is noticeable that, we also failed to detect an association between high added sugar intake and levels of hs-CRP in this study, which was consistent with some previous reports. There have been inconsistent findings on the relationship between added sugar intake and CRP level as an inflammatory biomarker. Using data from NHANES 1999 to 2010, it was found that decreased sugar-sweetened beverages (SSBs) consumption significantly decreased CRP, independent of demographic and lifestyle factors.⁵ A large cross-sectional study in England reported that sugar added to tea, coffee, and cereals were associated with CRP, but sugar from food sources such as cakes, squash drinks, dairy, egg dishes, and fruits and vegetables were not associated with CRP levels.⁶ In a prospective randomized controlled trial among 29 healthy young men, Aeberli et al. reported that fasting glucose and CRP level increased significantly after all interventions on SSBs consumption after six 3-week interventions.⁷ Another clinical controlled trial among 31 patients with type 1 diabetes revealed that sucrose intake increased CRP levels, whereas no association was found between total sugar in the diet and CRP.⁸

In this study, we did not see any association between added sugar intake and insulin resistance, determined by HOMA-IR. There have been conflicting research findings about the relation between added sugar intake and insulin resistance.^{34,35,36} Based on a large cross-sectional study in Spain, the consumption of SSBs was associated with a higher HOMA-IR in men and in non-overweight women.³⁶ An adolescent study in Taiwan revealed that fructose-rich SSB intake was associated with elevated levels of insulin resistance.³⁷ However, a recent randomized prospective study reported that added sugar consumed at the median American intake level does not produce changes in measures of insulin sensitivity or glucose tolerance, suggesting that no sugar has more deleterious effects than others.³⁴

Our study has important strengths. To the best of our knowledge, this is the first analysis paper of NHANES 2007-2008 and 2009-2010 cycles examining the associations between added sugar intake and inflammation and metabolic syndrome risks among adults. Other strengths include a large and diverse sample of adult representatives of the US population, and the use of a validated measurement of added sugar intake as part of the dietary data collection and analysis. In addition, this study used a number of objective measurements such as anthropometrics, blood pressure, and blood biomarkers via standardized protocol. In order to avoid potential arbitrary by using the binary variable of added sugar intake above or below the recommended 10% cutoff, we categorized percent of calories from added sugar in our study. Furthermore, besides those generally controlled variables such as sociodemographic characters, BMI, and energy intake, well-documented risk factors of inflammation and metabolic syndrome including sedentary lifestyle, current smoking were included in the models of regression analyses. Recent use

of medication was also considered in our study to avoid potential masking of symptoms due to related prescriptions.

Our findings should be interpreted in the context of several study limitations. First, due to the cross-sectional nature of NHANES study design, we were unable to determine causality of the relationships between added sugar intake and health outcome indicators. Second, we did not assess whether added sugar intake in a liquid or solid form was more important in influencing the association between added sugar and inflammation as well as metabolic syndrome risks. Third, information bias may be a concern since added sugar intake and other dietary information were self-reported using 24-hour dietary recall. However, all protocols are clearly specified and are administered systemically to all NHANES participants by trained staff during a structured in-person interview at the participants' homes. Therefore, the probability of non-differential misclassification of exposure occurring during the process of two-day dietary 24-hour dietary recall was highly unlikely. Additionally, participants were blinded to the hypothesis of our study as data was collected for general nutrition and health information and was for public use. It is believed that it was highly unlikely that interviewers would prompt selected participants to report added sugar intake differently than their counterparts.

10.6 Conclusion

In summary, we found that excess added sugar intake is linked to increased risk of low HDL-cholesterol and higher levels of serum triglycerides, regardless of gender and weight status, after adjusting for covariates. These findings indicated the detrimental role of high added sugar intake in affecting blood lipid profile and related adverse health

outcomes. Our study adds to a better understanding of the health impacts of added sugar intake among adults. Further research is needed to determine whether changes in added sugar intake predict inflammation and risks of metabolic syndrome in specific dimensions, as well as to examine the potential underlying mechanisms.

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CHAPTER 11

CONCLUSION AND SIGNIFICANCE

Given the prevalence of added sugar overconsumption in the US, the main aim of this dissertation was to identify food-related consumer behaviors related to added sugar intake, as well as to examine the impact of excess added sugar intake on diet quality and cardio-metabolic health status. Our work reveals that stocking up soft drink was a risky behavior for high added sugar intake, whereas home cooking and food label use were protective behaviors against excess added sugar intake. Despite the typical perception of grocery stores as healthy food resources, frequency of grocery shopping was not associated with added sugar intake. We also found that diet quality was compromised by excess added sugar intake, manifested as lower consumption of healthy food components and increased intake of “consumed in moderation” food components. However, sodium intake was negatively associated with added sugar intake, even after adjusting for energy intake. Furthermore, we found that those who consumed highest amounts of added sugar had nearly 4-fold risk of having low HDL-cholesterol compared to the lowest added sugar intake group, across gender and weight status categories. Similar finding was seen between added sugar intake and levels of serum triglycerides as well.

These findings altogether indicate that how consumer behaviors during the stages of purchasing, storing, and food preparation, affect added sugar intake among adults. Overconsumption of added sugar may play a complicated role in affecting diet quality, and in the risks of developing cardio-metabolic abnormalities. This research expands our understanding of risk factors related to excess added sugar intake, as well as potential harms. Additionally, we provide evidences in support of future intervention and policy

changes in terms of reducing added sugar intake, to aid in efforts to promote healthy eating and overall health among adults.

CHAPTER 12

FUTURE DIRECTIONS

This dissertation work has contributed to the field of behavior and nutrition research by investigating how food-related behaviors related to added sugar intake, as well as the impact of excess added sugar intake on diet quality and cardio-metabolic health. Our findings, despite being limited by the cross-sectional nature of the NHANES study design, provide scientific justification for future prospective studies and intervention trials where the directionality of the associations between food-related consumer behaviors, added sugar consumption, diet quality, as well as cardio-metabolic health, can be examined over time to determine their contribution to each other. In addition, it should be noted that future studies may lead to the evaluation of the addictive and compensational roles of sodium and added sugar in the diet.

Furthermore, our findings emphasize the need for studies on grocery store shopping and added sugar intake in order to determine whether increased access to supposed-to-be-healthy food outlets would benefit to alleviate the epidemic of overconsumption of added sugar in the US, with policy changes and proper interventions. Future studies may also assess how added sugar intake was related to dietary inflammatory index and further to overall health status among adults. Although we did not classify added sugar in the diet as from liquid or solid food sources, future researchers may be able to test whether various sources of added sugar lead to differentiated findings in terms of diet quality and health.

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