DIETARY ASSOCIATIONS THAT MAY REDUCE METABOLIC SYNDROME RISK IN MEXICAN YOUNG ADULTS

BY

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THESIS

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ABSTRACT

The obesity epidemic has spread globally from the United States to other industrialized nations, one of which is Mexico. As of 2006, 72% of Mexican adults aged 20 years and older were overweight or obese (Barquera, Campos-Nonato et al., 2009), a statistic that surpasses the prevalence of these conditions in the United States. The Mexican young adult population (20-29 years of age) is also affected, with 55.8% of individuals who are overweight or obese – the equivalent of about 5.9 million people (Barquera, Campos-Nonato et al., 2009).

Obesity is related to the development of other conditions, including, but not limited to: abdominal obesity, dyslipidemia, elevated blood pressure, and type 2 diabetes (T2D). These conditions collectively form a disease known as metabolic syndrome (MetS) (Reaven, 1988). Results from a national survey in Mexico conducted in 2006 indicated that 36% of Mexican individuals aged 20 to 39 years had MetS (Rojas et al., 2010). The high occurrence of this cluster of diseases in such a relatively young population indicates a need for effective prevention and intervention strategies. In order to do this, researchers must investigate the root cause of the environmental, social, and genetic risk factors of obesity and obesity-related diseases, particularly in the Mexican population. One risk factor of great importance is the diet.

Viewing the development of Mexico from a historical standpoint, one can begin to examine the evolution of the traditional Mexican diet. Various pre-Columbian indigenous groups – the Olmec, Toltec, Aztec, Maya, Zapotec, and Mixtec – provided the foundation for Mexico and the Mexican diet (Ruiz, 1993). Agriculture allowed them to cultivate corn, beans, and squash. After Hernán Cortés and his fellow conquistadors arrived in Mexico and brought many varieties of fruits, grains, vegetables, and meat, the two eating styles merged to create traditional Mexican cuisine. Dietary pattern analyses show a Westernized dietary pattern characterized by

high refined cereal, pastry, corn tortilla, and soda intake and low whole grain cereal, seafood, and dairy consumption emerging from the traditional dietary pattern (Denova-Gutierrez et al., 2011; Flores et al., 2010). This Westernized dietary pattern is associated with greater risk for obesity and metabolic syndrome (MetS). The transition from the traditional dietary pattern to the Westernized dietary pattern resulted in: (1) a reduction in dairy consumption; (2) an increase in refined sugar intake; (3) a decrease in fruit and vegetable intake; and (4) an increase in saturated fatty food consumption. The aims of the two studies presented in this thesis address the decreased dairy/increased refined sugar consumption trend and an ancient medical claim related to fruit and vegetable consumption.

The rise in the prevalence of MetS has been observed in conjunction with a decrease in dairy intake and an increase in sugar-sweetened beverage consumption (SSB) (Barquera et al., 2008). For the first cross-sectional study presented here, we hypothesized that individuals who were not meeting daily dairy recommendations would be at greater risk for MetS. The study participants (n = 339 Mexicans aged18 to 25 years) in this study were selected from a larger cohort study and had complete data on a validated Willett food frequency questionnaire adapted for the Mexican population, as well as the most complete data from the health clinic assessment that is required for admission to the university. MetS was diagnosed according to the International Diabetes Federation/American Heart Association harmonized criteria (Alberti et al, 2009). We included milk-based dairy products (whole milk, various cheeses, yogurt, and ice cream) only in addition to various SSB. Overall prevalence of MetS was 10.6%. We also determined that 77% of individuals were not meeting the recommended three daily servings of dairy per day. When controlling for age, sex, family history of cardiovascular disease (CVD) and T2D, and physical activity, we observed that individuals who failed to meet dairy recommendations may be at 2.9 times greater risk for MetS (95% CI 1.0-8.3, $p = 0.05$), but this must be further investigated. Our results did not indicate that SSB were displacing dairy in the diet and perhaps the study design was not ideal for detecting this relationship; however, our results support the importance of meeting daily dairy recommendations for the prevention of MetS in Mexican young adults.

When we assessed components of MetS in our subset of individuals, we determined that the prevalence of low high-density lipoprotein cholesterol (HDL-C) was 51.6%, which is about 10% lower than the prevalence previously reported in Mexican young adults aged 20 to 29 years. Nevertheless, it is important to investigate potential prevention and intervention strategies to raise HDL-C levels because this condition occurs in more than half of the population. For this second cross-sectional study, we used the same subset of 339 individuals and similar dietary and data analysis methodology to investigate the claim that consumption of papaya fruit can lower risk for dyslipidemias. Hypertriglyceridemia, low HDL-C, high low density lipoprotein cholesterol (LDL-C) and hypercholesterolemia were diagnosed based upon International Diabetes Federation and the National Cholesterol Education Program Adult Treatment Panel III criteria. We observed no differences in blood lipid profiles between the two groups; however, females who consumed < 3 servings of papaya per week may be at 1.5 times greater risk (95% CI 0.99-2.32, $p = 0.05$) of having low HDL-C after adjustment for age and family history of CVD and T2D compared to those who consumed fewer than 3 servings; however, because 1.0 is included in the confidence interval, we cannot make a definite conclusion. These findings were not observed in males and we did not observe risk for other at-risk blood lipid measures. However, prevalence of low HDL-C, hypertriglyceridemia, high LDL-C, and hypercholesterolemia was higher in those consuming < 3 weekly servings of papaya compared to those who consumed less. Our preliminary results suggest that consumption of at least 3 servings of papaya per week may help prevent dyslipidemias in Mexican college age individuals and that higher papaya intake may be a marker for an overall healthier dietary pattern, but further analyses must be done to confirm our initial observations.

Overall, these two studies conclude that meeting daily dairy recommendations may reduce individual risk for MetS and that a higher fruit and vegetable intake, indicated by more frequent papaya consumption, may reduce risk for certain dyslipidemias. Further research needs to be conducted so that these findings can be appropriately incorporated into prevention and intervention strategies for Mexican young adults.

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CHAPTER 1: INTRODUCTION

OBESITY

In order to prevent the continuing increase in the rates of overweight and obesity, particularly in the United States, it is important to consider the current and future characteristics of the people. The current trend in the U.S. is the rapid increase of the country's Latino population, which is projected to nearly triple to 132.8 million individuals, the majority of whom are from Mexico, during the 2008-2050 period (U.S. Census, 2008). The prevalence of overweight and obesity is also high in Mexico. Analysis of the Mexican National Health and Nutrition Survey 2006 (ENSANUT, 2006) data showed that the overall prevalence of overweight and obesity in children and adolescents aged two through 18 years was 26.3%. When analyzed by age categories, the prevalence of overweight and obesity was highest in the older age groups. While 16.7% of 2-4 year olds and 26.2% of 5-11 year olds were overweight and obese, a total of 30.9% of 12-18 year olds were overweight and obese (Bonvecchio et al., 2009). In Mexican college students aged 15 to 20 years, the prevalence of overweight and obesity has also increased over time. From 1994 to 2008, the prevalence of overweight doubled from 12.1% to 26.8%. Over the same time period, the prevalence of obesity rose from 13.2% to 37.3%—a three-fold increase in only 14 years (Garcia-Alcala et al., 2010). Another study of college students less than 40 years of age reported a total of 23.3% of Hispanic individuals classified as overweight (Koutoubi & Huffman, 2005). Although various countries have country-specific cutoff points for BMI status, the studies presented above used the Centers for Disease Control and Prevention (CDC) BMI-for-age growth charts for evaluation of subjects ≤ 18 years of age. For subjects aged ≥ 19 years, the World Health Organization cutoff points for BMI were used in the previously mentioned studies and will also be used for the studies presented in this thesis. With the prevalence of overweight and obesity at such high numbers, there is a need to assess overall metabolic disease risk in these individuals.

METABOLIC SYNDROME

The high prevalence of obesity and abdominal obesity among individuals of all ages has increased the interest for other obesity-related diseases, including MetS, a clustering of the following disease conditions: abdominal obesity, dyslipidemia, elevated blood pressure (EBP), and type 2 diabetes (T2D) (Gustafson et al., 2009). The MetS diagnosis allows physicians to try and identify subjects with MetS so that these individuals can be targeted with lifestyle and other treatment strategies to prevent or delay the onset of other conditions – namely T2D and cardiovascular disease (CVD) – that are the leading causes of death in Mexico (Sadikot & Hermans, 2010).

However, some researchers argue that MetS may only be useful as an educational concept and that it should simply be considered a premorbid condition with limited practical utility as a diagnostic or management tool, with one major critique being the fact that MetS lacks an agreed upon and clear, single unifying pathophysiological mechanism underlying the clustering of risk factors (Cameron, 2010; Sadikot & Hermans, 2010; Simmons et al., 2010). Some individuals argue that it is simple to treat the individual components of MetS, that treating the whole is unnecessary (Kahn, 2007; Simmons et al., 2010). However, with MetS, the whole may be greater than the sum of its parts; in other words, the risk factors do not explain or account for all of the risk for disease (Kannel & Larson, 1993). Some MetS risk factors are not typically detected clinically, including insulin resistance, proinflammatory states, and endothelial dysfunction; therefore, treatment of the whole may also improve other risk factors otherwise not detected or measured in the clinic (Sadikot & Hermans, 2010).

A unified definition for MetS may not be feasible because the risk for MetS-related diseases is different across various population groups (e.g. the United States compared to certain countries in Asia) (Patel et al., 2006). Furthermore, because MetS is defined by several disorders, there is not a single pathophysiological mechanism that underlies the condition and one can argue that we also do not completely understand all mechanisms underlying T2D or hypertension (HTN), yet these are not considered premorbid (Sadikot & Hermans, 2010). One author states, "an essential characteristic of scientific thought is the precision of the language used and the giving of a specific and unambiguous meaning to the words employed in scientific writing and speech" (Federspil, Nisoli, & Vettor, 2006). When evaluating multifactorial diseases, communicating with precision is often difficult, as the diseases themselves are complex and perhaps not fully understood. The clinical utility of MetS lies in its ability to readily identify individuals who are at a high risk for both T2D and CVD. A MetS diagnosis can also alert the treating physician that the presence of any one risk factor should make him/her look for the presence of other risk factors as well. While there is evidence for and against the use of this diagnosis, MetS can be used as a tool to make treatment and prevention available easily and *early*, especially when such risk factors are observed in children and young adults (Sadikot & Hermans, 2010).

In 2009, the International Diabetes Federation (IDF) and American Heart Association (AHA) released an updated consensus statement outlining the definition of MetS. For individuals aged 16 years and up, MetS is defined as presenting with three or more of the following: elevated WC based on population- and country-specific definitions (cutoffs for Latinos: males, ≥ 90 cm; females, ≥ 80 cm); elevated triglycerides (TG) or drug treatment for elevated TG (cutoff: ≥ 150 mg/dL); reduced high-density lipoprotein cholesterol (HDL-C) or drug treatment for low HDL-C (cutoff: for males, < 40 mg/dL; for females, < 50 mg/dL); elevated blood pressure (EBP) or antihypertensive drug treatment for a patient with a history of HTN (cutoffs: systolic, ≥ 130 mmHg and/or diastolic ≥ 85 mmHg); elevated fasting glucose or drug treatment for elevated glucose (cutoff: ≥ 100 mg/dL) (Alberti et al., 2009). This clustering of conditions can be credited to obesity, which, in children, has been associated with EBP (Flores-Huerta, Klunder-Klunder, de la Cruz, & Santos, 2009), abnormal glucose metabolism, insulin resistance (Krekoukia et al., 2007), reduced HDL-C, elevated triglycerides, compromised vascular function, and inflammation (Alberti et al., 2009). This IDF/AHA definition was chosen for the analyses presented in this thesis due to its ability to detect at-risk individuals sooner than other definitions allow.

Because other definitions of MetS exist, including those of the World Health Organization, the American Association of Clinical Endocrinologists (AACE), the AHA/National Heart, Lung, and Blood Institute (NHLBI), the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), and the IDF, the prevalence of MetS in individuals varies from study to study. (Please see Table 1 for a summary of the following MetS definitions.) The World Health Organization definition for MetS is diagnosis of glucose intolerance, insulin resistance, and/or T2D with two or more of the following: (1) impaired glucose regulation or diabetes; (2) insulin resistance; (3) raised arterial pressure of ≥ 160/90 mmHg; (4) raised plasma TG ≥ 150 mg/dL and/or low HDL-C < 35 mg/dL in males and < 39 mg/dL in females; (5) central obesity defined by waist-to-hip ratio > 0.90 for males and > 0.80 for females and/or BMI > 30 kg/m^2; and (6) microalbuminuria, urinary albumin excretion rate ≥ 20 mcg/min or albumin:creatinine ratio ≥ 20 mg/g (Alberti & Zimmet, 1998). The AACE definition of MetS depends on clinical judgment based upon the following criteria: (1) BMI ≥ 25

kg/m^2; (2) elevated TG ≥ 150 mg/dL; (3) low HDL-C < 40 mg/dL in males and < 50 mg/dL in females; (4) EBP ≥ 130/85 mmHg; (5) 2-hour postglucose challenge > 140 mg/dL; (6) fasting glucose between 110 and 126 mg/dL; and (7) other risk factors, such as family history of T2D, CVD, or HTN; polycystic ovary syndrome; sedentary lifestyle; advancing age; ethnic groups of high predisposition for T2D or CVD (Einhorn, et al., 2003). The AHA/NHLBI criteria for diagnosing MetS (individual must present with three or more of the five criteria) include: (1) elevated WC ≥ 102 cm (males) and ≥ 88 cm (females); (2) elevated TG ≥ 150 mg/dL or drug treatment for elevated TG; (3) reduced HDL-C < 40 mg/dL (males) and < 50 mg/dL (females) or drug treatment for reduced HDL-C; (4) EBP diagnosed as SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or antihypertensive drug treatment; and (5) elevated fasting glucose ≥ 100 mg/dL or treatment for elevated glucose (Grundy, et al., 2005). The NCEP ATP III criteria for diagnosing MetS include a diagnosis of three or more of the following factors: (1) abdominal obesity, diagnosed by WC ≥ 102 cm (males) and ≥ 88 cm (females); (2) TG ≥ 150 mg/dL; (3) HDL-C < 40 mg/dL (males) and < 50 mg/dL (females); (4) blood pressure ≥ 130/≥ 85 mmHg; and (5) fasting glucose ≥ 110 mg/dL (Cleeman, 2001). The IDF definition for the diagnosis of MetS includes central obesity (defined by WC ≥ 94 cm in Europid males and ≥ 80 cm for Europid females; however, the physician must apply appropriate ethnic specific values for WC) and two or more of the following risk factors: (1) raised TG level ≥ 150 mg/dL or specific treatment for raised TG; (2) reduced HDL-C < 40 mg/dL (males) and < 50 mg/dL (females) or specific treatment for reduced HDL-C; (3) raised blood pressure of SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or treatment for previously diagnosed hypertension; and (4) raised fasting plasma glucose ≥ 100 mg/dL or previously diagnosed T2D (International Diabetes Federation, 2006).

Using an adapted definition based upon NCEP ATP III criteria, Cook et al. found the overall prevalence of MetS in adolescents aged 12 to 19 years from the Third National Health and Nutrition Examination Survey (1988-1994) to be 4.2% (Cook, et al., 2003). Ford et al. analyzed a sample of 2,014 participants aged 12 to 17 years from them National Health and Nutrition Survey 1999-2004 and, using the IDF definition from 2007, found the prevalence to be 4.5% (Ford, et al., 2008). These two studies present a prevalence that is toward the lower end of the range than those frequencies reported by other groups. When examining more specific, targeted populations, some analyses reveal more surprising numbers. The overall prevalence of MetS in a subset of 113 participants aged 8 to 13 years (at baseline) from the University of Southern California Study of Latino Adolescents at Risk for Diabetes Project was 22% (Ventura et al., 2008). In a study sample representative of adolescents in the U.S. population, the estimated prevalence of MetS was 8.6%, which extrapolates to almost 2.5 million adolescents in the general population (Johnson et al., 2009). Out of these individuals, the prevalence of MetS was highest in Hispanic males and females, with a total of 11.2% meeting three or more criteria (Johnson et al., 2009). Results from ENSANUT 2006 in Mexico indicated that 49.8% of Mexican adults aged 20 years and older had MetS. For individuals aged 20 to 39 years in the survey, the prevalence of MetS was 36.0% (Rojas et al., 2010). When compared to U.S. young adults of similar age, Mexican young adults have higher rates of MetS (compared to 20% and 16% in U.S. males and females below age 40, respectively) (Ervin, 2009).

Because MetS is comprised of five risk factors, it is important to examine the trends of those conditions in order to better understand the course of MetS development in these individuals.

Abdominal Obesity

As early as the 1950s, it has been shown that abdominal obesity, characterized by excess fat in the abdominal area, is closely associated with metabolic conditions (Vague, 1956). Abdominal obesity is typically clinically measured by waist circumference (WC), but may also be assessed using waist-to-hip ratio and abdominal visceral adipose tissue, which may also aid in detecting cardiovascular risk (Barreira et al, 2012). Specifically, abdominal obesity is tightly coupled to the development of cardiovascular disease and non-insulin dependent diabetes mellitus, as well as to the established risk factors of insulin resistance, hyperinsulinemia, dyslipidemia, and hypertension (Bjorntorp, 1992; Phillips & Prins, 2008). A study of Canadian men aged 18 to 42 years with body mass indices between 16 and 38 kg/m^2 showed that higher levels of obesity were associated with higher amounts of deep abdominal tissue, therefore leading to greater risk for diabetes, dyslipoproteinemia, hypertension, and cardiovascular disease. Overall, the results of the previously mentioned study indicated that WC was a significant correlate of total and deep abdominal tissue deposition, suggesting that the WC measurement may provide information on the risk of cardiovascular disease and diabetes (Despres, Prudhomme, Pouliot, Tremblay, & Bouchard, 1991). Waist circumference has also proven a significant marker of total and abdominal fat, independent of BMI percentiles, in younger individuals. Moreover, WC is a strong independent predictor of insulin resistance, elevated fasting insulin, and proinsulin levels, all of which are associated with increased metabolic risk (Lee, Bacha, Gungor, & Arslanian, 2006). Furthermore, results from a recent longitudinal study indicate that abdominal obesity is the single most important predictor of metabolic syndrome (MetS) in young adults (Kelly et al., 2011).

Concurrent with obesity rates, the prevalence of abdominal obesity has also increased. From 1988 to 2004, the prevalence of abdominal obesity in Mexican American boys and girls aged 18 to 19 years increased from 12.5% to 18.7% and 10.6% to 24.6%, respectively (Li, Ford, Mokdad, & Cook, 2006). At age 20 to 39 years, the prevalence of abdominal obesity in Mexican and Mexican American women was 45% (Vella, Zubia, Ontiveros, & Cruz, 2009). In the national report of the Mexican population aged 20 to 29 years, the actual mean value for WC is reported to be under the at-risk cutoff of 90 cm for males and over the at-risk cutoff of 80 cm for females. The frequency of abdominal obesity is not provided (Barquera, Campos-Nonato et al., 2009).

Elevated Blood Pressure

Elevated blood pressure (EBP), less than defined HTN, is a component of MetS that was established to identify those at risk for HTN. Elevated blood pressure is defined as having systolic blood pressure (SBP) ≥ 135 mmHg and/or diastolic blood pressure (DBP) ≥ 85 mmHg (Alberti et al., 2009). The prevalence of EBP and HTN has increased over time in conjunction with the rising rates if obesity. In 1993, the prevalence of HTN in Mexican adults aged 20 years and older was 23.8% (Castro, Gomez-Dantes, Negrete-Sanchez, & Tapia-Conyer, 1996), a number that increased to 30.7% in 2007 (Barquera et al., 2010). In 2006, the prevalence of HTN was 43.2%, over half of which were newly diagnosed cases. Specifically in Mexican young adults aged 20 to 29 years, the prevalence of HTN was 23.0%, which is similar to the reported prevalence of 24.1% in U.S. young adult males and higher than the prevalence of 6.8% in U.S. young adult females (Barquera et al., 2010; Ervin, 2009). These rates are of great concern due to the mortality risk associated with EBP and HTN. The second most frequent cause of mortality in Mexican adults is cardiovascular disease (CVD) (Meaney et al., 2007). With the rising prevalence of EBP and HTN in Mexican young adults, we must consider the possibility that the mortality risk may be greater earlier in life for those affected.

Type 2 Diabetes, Insulin Resistance, or Glucose Intolerance

The current leading cause of death in Mexican adults is T2D, whose prevalence has also increased over time in the Mexican population (Barquera, Tovar-Guzman, Campos-Nonato, Gonzalez-Villalpando, & Rivera-Dommarco, 2003). For MetS, elevated fasting glucose above 100 mg/dL or previously diagnosed impaired fasting glucose indicates presence of this risk factor. The mortality associated with this condition increased from a rate of 48/100,000 inhabitants in 1980 to 73/100,000 inhabitants in the year 2000 (Villalpando, Shamah-Levy, Rojas, & Aguilar-Salinas, 2010). In 1993, the prevalence of T2D in Mexican adults aged 20 years and older was 6.7% (Villalpando, Shamah-Levy, Rojas, & Aguilar-Salinas, 2010). Seven years later, in 2000, the prevalence had increased to 7.5% (Olaiz-Fernandez, Rojas, Aguilar-Salinas, Rauda, & Villalpando, 2007). By the most recent assessment in 2006, the prevalence of T2D in Mexican adults had increased to 14.4%, half of which were newly diagnosed cases (Villalpando, Shamah-Levy, Rojas, & Aguilar-Salinas, 2010). The higher prevalence of T2D observed in 2006 is associated with onset at an earlier age (Garcia-Garcia, Aguilar-Salinas, Tusie-Luna, & Rull-Rodrigo, 2002). The prevalence of T2D diagnosed before 40 years of age increased from 1.8% in 1993 to 5.8% in 2006 (Villalpando, Shamah-Levy, Rojas, & Aguilar-Salinas, 2010). In U.S. young adults aged 20 to 39 years, the prevalence of high fasting glucose or glucose controlling medication use was 28.8% in males and 13.4% in females (Ervin, 2009).

Hypertriglyceridemia

Hypertriglyceridemia, defined as having fasting serum TG levels ≥ 150 mmHg, is among the most common cardiovascular risk factors among Mexican adults (Barquera et al., 2007). An interaction of genetic and environmental factors, including dietary trends, such as increased sugary beverage consumption and decreased fruit and vegetable intake, gives insight into the reason behind the large percentage of the Mexican population affected by lipid disorders (Aguilar-Salinas et al., 2010). Results from ENSANUT 2006 showed that 31.9% of Mexican adults aged 20 years and older had hypertriglyceridemia. Among young adults aged 20 to 29 years, the prevalence of hypertriglyceridemia was 22.3% (Aguilar-Salinas et al., 2010). This rate is lower than the risk observed in U.S. young adult males, 29.6%, and slightly higher than the reported prevalence of 17.8% in U.S. young adult females. However, it is important to note that in the U.S. population that was analyzed, the prevalence was highest among Latinos (Ervin, 2009).

Low High-Density Lipoprotein Cholesterol

Perhaps more alarming than the prevalence of hypertriglyceridemia in the Mexican young adult population is the overall prevalence of low HDL-C. From the same ENSANUT 2006 analysis, it was determined that low HDL-C occurred in 60.5% of the Mexican adult population aged 20 years and older, which translates to about 20.5 million individuals with this condition. The prevalence of low HDL-C in Mexican young adults aged 20 to 29 years was 61.9%, slightly higher than the overall prevalence in the total adult population (Aguilar-Salinas et al., 2010). The prevalence observed in the Mexican population is almost double that of the United States, which, in adult males and females, is 35% and 39%, respectively (Singh, Sharma, Kumar, & Deedwania, 2010). In U.S. younger adults aged 20 to 39 years, the prevalence of low HDL-C is 21.4% and 29.4% in males and females, respectively (Ervin, 2009).

EATING HABITS AND HEALTH: DIETARY PATTERNS THAT PREDISPOSE TO METABOLIC SYNDROME AND ITS COMPONENTS

The development of obesity and obesity-related diseases, including the components of MetS, can be attributed to social, environmental, and genetic factors. Such complex etiology makes the development of prevention and intervention strategies quite complicated and difficult, therefore posing quite a challenge to researchers who strive to make these advances.

Concurrent with the obesity epidemic, related research has investigated various dietary patterns in different populations that may predispose individuals to obesity and obesity-related diseases. Analysis of 737 non-overweight women in the Framingham Offspring/Spouse cohort study revealed five dietary patterns at the time of baseline measurement: (1) Heart Healthy, characterized by consumption of more servings of fruits, vegetables, low-fat milk, and other low-fat and fiber-rich foods (including whole grains, fish, low-fat cheeses, lean poultry, and legumes) and fewer servings of diet beverages and firm vegetable fats than the other dietary patterns; (2) High Fat, characterized by consumption of higher amounts of animal and vegetable fats, sweets and desserts, and meats and mixed dishes; (3) Empty Calorie, similar to the High Fat pattern, except for a greater contribution of sugar-sweetened beverages; (4) Light Eating, characterized by a more moderate eating pattern and a greater contribution of beer and poultry with skin; and (5) Wine and Moderate Eating, characterized by a moderate eating pattern and greater consumption of wine. In terms of dietary quality, the Heart Healthy pattern had a more favorable nutrient intake, with a lower total fat, saturated fat, and cholesterol content, but a higher carbohydrate and fiber content than the other dietary patterns. Despite lower energy intake, the Light Eating pattern had a higher total fat and saturated fat content, but still not as high as the High Fat pattern, which was lower in fiber and micronutrient density. After analysis for health effects of these dietary patterns over a period of 12 years, it was observed that 29% of the original cohort of women became overweight. Although the Light Eating pattern had the highest percentage of women with fluctuating weight, the prevalence of overweight was highest in the

Empty Calorie pattern and lowest in the Wine and Moderate Eating pattern (Quatromoni, Copenhafer, D'Agostino, & Millen, 2002).

On the other hand, analysis of 1,666 men in the Framingham Offspring/Spouse cohort study revealed five slightly different dietary patterns: (1) Transition to Heart Healthy, characterized by higher intake of fruits, vegetables, shellfish, vegetarian foods, whole grains, oils, lower-fat foods, organ meats, fish, and soup and lower intake of refined grains and desserts; (2) Higher Starch, characterized by higher contribution of leaner protein foods, caffeinated low-energy beverages, firm vegetable fats, refined grains, and desserts; (3) Average Male, which was higher in unsweetened beverages and lower in leaner protein foods (including dairy), but moderate in other food groups; (4) Lower Variety, characterized by the lowest contribution of most food groups, including high-fat animal proteins, whole milk, animal and vegetable fats, sweets, fruits, vegetables, whole grains, and oils; and (5) Empty Calorie, with the highest levels of refined grains, desserts, high-fat animal proteins, whole milk, eggs, animal fats, sweets, and daily snacks and the lowest level of low- and nonfat dairy. It was observed that chronic disease risk factor levels were high in all male dietary pattern subgroups at baseline and follow-up, which was expected; however, men in the Transition to Heart Healthy subgroup had lower total and low-density lipoprotein cholesterol levels and rates of overweight than the other groups (although, mean glucose levels and diabetes rates were slightly higher) (Millen et al., 2005).

Assessment of dietary patterns in various Korean populations has revealed similar findings, despite differences in food types. In a Korean population of 1,118 subjects aged 30 to 70 years old, three dietary patterns were identified: (1) Vegetable-Seafood, which was higher in vegetables, shellfish, seaweeds, soy foods, fish, and fruits; (2) Meat-Fat, which was high in red meat, oil, poultry, noodles, and processed meats; and (3) Snack, characterized by bread, cakes, pizza, crackers, cookies, and fruit products. Of the three dietary patterns, the Meat-Fat pattern was associated with obesity, while the other two patterns were not. In a separate analysis of 4,984 Korean women aged 30 to 79 years old, three dietary patterns were identified: (1) Western, characterized by fast foods, animal fat-rich foods, fried foods, grilled meat and seafoods, and sweet foods; (2) Healthy, characterized by green-yellow vegetables, healthy-protein foods, seaweeds, and bonefish; and (3) Traditional, with higher contribution of salted vegetables and seafoods, cereals, and light-colored vegetables. The Healthy pattern was associated with reduced risk for MetS, while the other two patterns showed no association with MetS overall (Cho, Shin, & Kim, 2011). Results from the Korean National Health and Nutrition Examination Survey revealed four dietary patterns in a group of 9,850 Korean adults aged 19 years and older. The four patterns, named based upon the major contributing foods, were: (1) White Rice and Kimchi; (2) Meat and Alcohol; (3) High Fat, Sweets, and Coffee; and (4) Grains, Vegetables, and Fish. The White Rice and Kimchi and High Fat, Sweets, and Coffee patterns were not associated with negative health outcomes; however, the Meat and Alcohol pattern was associated with increased risk for hypertriglyceridemia and EBP. Conversely, the Grains, Vegetables, and Fish pattern was associated with reduced risk for hypertriglyceridemia and MetS (Kim & Jo, 2011). In a group of 284 seven- to eight-year-old Korean children, three major dietary patterns were isolated: (1) Korean, characterized by higher contribution of seasonings, vegetables, white rice, and kimchi; (2) Modified Western, characterized by higher consumption of kimchi, all beverages, and potatoes; and (3) Western, characterized by higher intake of noodles, ramen, cookies, crackers, chips, sugar, sweets, pizza, and hamburgers. Although these dietary patterns were similar to those found in other studies, there was no significant difference in health factors (BMI, percent body fat, SBP, DBP, TG, leptin, and insulin) between the Korean and Western dietary patterns (Choi et al., 2011).

Similar trends in dietary patterns are observed in other populations across Asia, Europe, and the United States. In a group of 425 Iranian subjects aged 35 to 55 years old, five major dietary patterns were identified: (1) Western, which was high in sweets, butter, soda, mayonnaise, sugar, cookies, tail of lamb, hydrogenated fat, and eggs; (2) Prudent, characterized by a high contribution of fish, peas, honey, nuts, juice, dry fruits, non-hydrogenated vegetable oil, liver and organ meats, and coconuts and a low contribution of hydrogenated fat and non-leafy vegetables; (3) Vegetarian, characterized by high intake of potatoes, legumes, vitamin C-rish fruits, rice, green leafy vegetables, and fruits rich in vitamin A; (4) High-Fat Dairy, with a high contribution of high-fat yogurt and high-fat milk and a low contribution of peas, bread, and low-fat yogurt; and (5) Chicken and Plant, characterized by high intake of chicken, vitamin A-rich fruits, green leafy vegetables, and mayonnaise and a low intake of beef, liver, and organ meats. Of the five patterns, only two were associated with MetS and/or features of MetS. The Vegetarian pattern was associated with increased odds of abnormal plasma glucose, while the Western pattern was associated with greater odds of increased serum TG, high blood pressure, and MetS overall (Amini, Esmaillzadeh, Shafaeizadeh, Behrooz, & Zare, 2010).

In the Health Effects of Arsenic Study conducted in Bangladesh, analysis of the 11,116 subjects between the ages 18 and 75 years revealed three dietary patterns: (1) Balanced, characterized by higher contribution of steamed rice, red meat, fish, fruit, and vegetables; (2) Animal Protein, with greater intake of eggs, milk, red meat, poultry, bread, and vegetables; and (3) Gourd, not Vegetables, characterized by intake of a variety of gourds, radishes, pumpkin, sweet potato, and spinach. It was shown that adherence to the Animal Protein pattern was associated with higher risk of death from heart disease and disease of the circulatory system (Chen et al., 2012).

The European Prospective Investigation into Cancer and Nutrition (EPIC)-Cohort Study examined dietary patterns and risk for coronary heart disease (CHD) in 40,757 Spanish adults aged 29 to 69 years old. Two major dietary patterns were identified: (1) a Westernized pattern (characterized by frequent consumption of refined grains, fried potatoes, potatoes, unprocessed red meat, wine, eggs, legumes, and processed red meat and low intake of fat-free dairy and whole grains) and (2) an Evolved Mediterranean pattern (characterized by frequent consumption of vegetables, olive oil, non-oily fish, fruits, and whole grains and low consumption of whole fat dairy and vegetable oils other than olive oil). Contrary to the authors' hypothesis, there was no association between the Westernized dietary pattern and risk for CHD; however, the Evolved Mediterranean diet was associated with lower risk of CHD, an outcome that would be expected (Guallar-Castillon et al., 2012). Another European study that was conducted in Portuguese adults (820 non-fatal acute myocardial infarction cases and 2,196 controls) investigated the relationship between dietary patterns cardiovascular risk factors in males and females. Four dietary patterns were identified both in females and males. In females, the dietary patterns were: (1) Healthy, with the highest contribution of vegetables, fruit, and dairy and the lowest contribution of red meat, fast foods, and soft drinks; (2) Low Fruit and Vegetable, with the lowest overall intake of all patterns, particularly fruits and vegetables; (3) Red Meat and Alcohol, characterized by the highest intake of red meat and alcohol and the lowest consumption of dairy products and vegetable soup; and (4) In Transition to Fast Food, characterized by the highest intake of white meat, sweets, and fast foods and the second highest intake of red meat, vegetables, and dairy products. The patterns identified in men were somewhat different: (1) Healthy, characterized by the highest consumption of vegetable soup, fruits, dairy products, and cereals and the lowest consumption of red meat, fast foods, and alcoholic beverages; (2) Fish, characterized by the highest intake of fish and vegetables; (3) Red Meat and Alcohol, with the highest intake of red meat, alcohol, and fast foods and the lowest intake of fruits, vegetable soup, dairy products, and cereals; and (4) Intermediate Intake, characterized by intermediate consumption of most groups, except white meat. Overall, the Red Meat and Alcohol dietary pattern, present in both males and females, was associated with higher BMI, WC (females only), risk of acute myocardial infarction, SBP and DBP (males only), and total cholesterol to HDL-C ratio (females only) (Oliveira et al., 2011).

When examining dietary patterns in Puerto Rican adults living in Boston, it was determined that of three dietary patterns (Meat and French Fries, Traditional, and Sweets), only the Meat and French Fries pattern was associated with higher WC, SBP, and DBP (Mattei, Noel, & Tucker, 2011). Collectively, most studies show an inverse association of healthful dietary patterns with all-cause mortality and CVD risk (Kant, 2004). This risk is also observed in dietary pattern analyses in Mexican populations.

Mexican Dietary Patterns Related to Metabolic Syndrome and Its Risk Factors

Dietary patterns. The traditional Mexican diet appears to be higher in nutritional quality, yet 72% of Mexican young adults are overweight or obese (Barquera, Campos-Nonato et al., 2009). Since the Spanish conquest of Mexico, various dietary trends and patterns have emerged, some of which have been shown to have a negative effect on health, as is observed in other populations as described previously. Using cluster analysis, a report from the ENSANUT 2006 identified three dietary patterns in 15,890 Mexican adults aged 20-59 years: refined foods and sweets (RS), traditional (T), and diverse (D). The RS pattern had the highest contribution to total energy intake from alcohol, soft drinks, white bread, fast food, sweets and candies, and salty snacks. Overall, the T pattern showed low dietary diversity, with maize and maize-based foods comprising ~50% of total energy intake. With the exception of beans and legumes, this pattern had the lowest contribution of other food groups, but was higher in fiber and calcium than the other patterns. The main contributors to the total energy of the T pattern, corn and beans, represent the main foods consumed by the previously mentioned pre-Columbian civilizations, which is not surprising considering that almost 60% of those consuming this pattern were indigenous and predominantly resided in rural areas of Mexico. Individuals consuming the T pattern also had lower BMI and engaged in more physical activity than did individuals in the other two consumption patterns. On the other hand, the D pattern had the lowest contribution of maize and the highest proportion of whole-fat dairy, rice and pasta, meat, poultry, eggs, saturated fat, fruits, and vegetables. Individuals consuming this pattern had the highest vitamin A and C intakes. The RS and D patterns, which are essentially a diversion from the T pattern, are associated with greater risk of overweight and obesity than the T pattern. Specifically, those who consumed the RS or D patterns had 14% or 17% greater risk of being overweight compared to individuals who consumed the T dietary pattern. The risk of being obese was 20% greater in individuals who consumed either the RS or D dietary pattern compared to those who consumed the T pattern. The effect of the RS dietary pattern on obesity increased with age, making characteristics of this dietary pattern a target for intervention efforts (Flores et al., 2010).

Further investigation of dietary patterns that are associated with obesity and related diseases in the urban Mexican population has extrapolated a Westernized dietary pattern. Among the 6,070 adults aged 20 to 70 years participating in the Health Workers Cohort Study of Mexico, Denova-Gutierrez and colleagues isolated three major dietary patterns using factor analysis of a 116-item food frequency questionnaire: (1) the prudent dietary pattern, which was high in fruits, vegetables, and legumes and low in pastries, refined cereals, and cookies; (2) the Westernized dietary pattern, characterized by high refined cereal, pastry, corn tortilla, and soda intake and low whole grain cereal, seafood, and dairy consumption; and (3) the high-animal protein/-fat dietary pattern, which was high in processed meat, red meat, poultry, butter, and eggs and low in fresh fruits and pastries. Participants in the top quintile of the prudent pattern were older, smoked less, and were more physically active compared to those in the lowest quintile. Participants in the upper quintile of the Westernized pattern were less likely to exercise and had a higher prevalence of general and central obesity and a high proportion of body fat. Participants in the upper quintile of the high-animal protein/-fat pattern were younger, less physically active, and more likely to be obese and abdominally obese. Nutritionally, the upper quintile of the prudent dietary pattern was associated with lower intakes of energy and higher intakes of fiber. Conversely, those in the upper quintile of the Westernized dietary pattern consumed more energy and less fiber. Similar to the prudent dietary pattern, individuals in the upper quintile of the high-animal protein/-fat pattern also had a lower energy intake. After analysis for association with different measures of obesity and adiposity, it was determined that the prudent pattern was inversely related with high-body fat proportion, whereas the Westernized pattern was positively associated with obesity, abdominal obesity, and high-body fat proportion, all independent of total energy and other lifestyle factors. In detail, participants in the upper quintile of the Westernized dietary pattern had 46% greater odds of obesity, 64% greater odds of abdominal obesity, and 17% greater odds of high-body fat proportion than those in the lower quintile of this dietary pattern. The results from this cross-sectional study suggest that a diet characterized by high consumption of soft drinks, refined grains, corn tortillas, and pastries and low consumption of dairy products, whole grains, and seafood is associated with higher odds of developing obesity, abdominal obesity, and high-body fat proportion in Mexican adults (Denova-Gutierrez et al., 2011).

Because of the association of obesity and abdominal obesity to metabolic disease risk, it is important to more closely examine the relationship between dietary patterns and obesity-related diseases, particularly those that constitute MetS. Using 5,240 participants aged 20 to 70 years from same Health Workers Cohort Study of Mexico, the three dietary patterns (prudent, Westernized, and high-animal protein/-fat) were analyzed with individual MetS risk factors and with MetS as a whole. The Westernized dietary pattern was associated with higher prevalence of high fasting glucose, high serum TG, low serum HDL-C, abdominal obesity, and high blood pressure. Further, participants in the highest tertile of Western dietary pattern scores had 71% greater odds of having high fasting glucose, 37% greater odds of having low HDL-C, and 43% greater odds of having central obesity than those in the lowest tertile. Analyses also revealed that the Westernized and high-animal protein/-fat dietary patterns were associated with greater odds of having MetS, while the prudent dietary pattern was not (Denova-Gutierrez et al., 2010).

When the Mexican diet overall was evaluated in terms of macronutrients, nationally, individuals were consuming fat, carbohydrates, and protein at an acceptable range (Barquera et al., 2009). In 2006, Mexican individuals aged 20 to 29 years consumed more total fat and saturated fat than older individuals, putting almost 15% of these young adults at risk for excessive fat intake. Results from this ENSANUT 2006 report on energy and nutrient consumption indicate that much of the Mexican population may be experiencing a nutrition transition, whereby total energy intake increases as a result of increased carbohydrate and fat consumption (Barquera et al., 2009).

However, the analytical methods of dietary patterns do have limitations. Score-based methods that dichotomize components (e.g. the participants either met or did not meet certain criteria) consider intake variability, but they do not consider intake amounts at the extremes; they do not take into account the full range of foods consumed. Score-based methods also have the additional limitations: (1) they are dependent on the selected dietary guidelines, which are typically not specific to one type of disease; (2) subjectivity of the researchers is introduced in the selection of foods to include in the analyses, the interpretation of the guidelines, and construction of the measurement scores; and (3) the summation of equally weighted dietary component scores implies that each component is equally important and additively related to health, which is usually not true of diet-disease relationships (Kant, 2004; Moeller et al., 2007). Data-driven dietary pattern analytical methods also have limitations. Such methods, including factor analysis and cluster analysis, allow for meaningful and interpretable results; however, there is limited data on the validity and reproducibility of these methods (Moeller et al., 2007). Furthermore, subjectivity is introduced at various time points in the analysis: at the grouping of dietary patterns, the treatment of the input variables (i.e. variable measurements as percent of intake, grams, or number of servings), analytic options and choices, and selecting a final pattern solution based upon the previous choices made (Kant, 2004; Moeller et al., 2007).

Focusing the analysis on a single nutrient or food also has its limitations and advantages. By centering the analysis around a single nutrient or food, there is a chance of confounding by the effect of the dietary patterns. On the other hand, this narrow focus lessens the possibility of the occurrence of statistically significant associations by chance that may occur in analyses of a large number of nutrients or food groups (Moeller et al., 2007). While the analysis of dietary patterns gives good insight into various health outcomes that are associated with certain eating behaviors, it does not provide a clear, feasible means for dietary modification. When striving to alter one's diet and overall lifestyle, it is important to remember that small, gradual changes should be made; it is not feasible to expect a person to automatically shift from one dietary consumption pattern to another in a very short time. For optimal results, setting easy-to-achieve short-term goals, such as increasing the servings of dairy consumed each day or decreasing the amount of SSB consumed each day, is essential (Foreyt, 2005). For this reason, the analyses presented in this thesis focus on the easy-to-achieve dietary modifications, the results of which can potentially be easily translated to the study population.

Taken with the analyses of dietary patterns in Mexico, it appears that current dietary trends are characterized by: (1) a reduction in dairy consumption; (2) an increase in refined sugar intake; (3) a decrease in fruit and vegetable intake; and (4) an increase in saturated fatty food consumption, which is explained above.

Dairy consumption. Dairy products are often a target for health-related research because they contain a number of constituents, including minerals, proteins, peptides, medium-chain triglycerides, lactose, and organic acids, that may directly or indirectly beneficially affect insulin sensitivity, body weight blood pressure, and lipid levels (Steijns, 2008).

When examining studies related to dairy intake and health, some results are conflicting, which makes it difficult to determine whether this dietary characteristic has a negative or positive impact on obesity and obesity-related diseases. Of the 1,266 adults in the Bogalusa Survey from 1995 to 1996, only 12% consumed the recommended three daily servings of dairy. However, in those who consumed higher amounts of dairy, they also had higher intakes of calcium, magnesium, potassium, zinc, sodium, folate, thiamin, riboflavin, and vitamins B_6, B_{12}, A, D, and E, resulting in a more favorable dietary profile (Ranganathan, Nicklas, Yang, & Berenson, 2005). In a group of 76 U.S. college students who completed seven day food records at both the beginning and end of the school year, subjects who consumed a higher amount of low-fat dairy products had better diet quality, gained less body weight, and had reductions in WC, percent truncal fat (fat in the trunk, or abdomen region), and percent total body fat compared to those with lower dairy intake (Poddar et al., 2009). A study of 22,570 women and 20,126 men aged 50 to 64 years from the Danish Diet, Cancer, and Health Study found that WC was inversely related to high-fat dairy intake in females, but not in males (Halkjær, Tjønneland, Overvad, & Sørensen, 2009). Another analysis of 248 volunteers from the Quebec Family Study also found somewhat mixed results. Skimmed and partly skimmed milk intake was associated with lower WC, while higher intake of low-fat yogurt was associated with increased risk for increased WC (Drapeau, et al., 2004). Recently, frequent dairy intake has also been shown to improve cognitive function, which is greatly affected by one's nutritional status (Crichton, Murphy, Howe, Buckley, & Bryan, 2012; Crichton, Elias, Dore, & Robbins, 2012). Overall, as supported by many studies, higher dairy intake has been related to decreased odds of impaired fasting glucose, hypertriglyceridemia, and MetS (Hong et al., 2012; Kelishadi et al., 2008; Mennen et al., 2000); although some studies have shown that dairy consumption has no effect and/or a negative effect on health (Louie, Flood, Hector, Rangan, & Gill, 2011).

Using data from the Health Professionals Follow-up Study, a prospective cohort of men aged 40 to 75 years, Rajpathak et al. observed no association between weight change and total, dietary, dairy, or supplemental calcium intake. Furthermore, men who had the largest increase in dairy intake over time gained more weight than men who decreased their dairy intake over the time of the study (Rajpathak, Rimm, Rosner, Willet, & Hu, 2006). Of 2,064 men and women aged 50 to 75 years who participated in the Hoorn Study, high dairy consumption was not associated with lower weight or more favorable levels of components of MetS, although there was a modest association with lower blood pressure (Snijder, et al., 2007). In a group of 1,306 young adults aged 19 to 38 years who participated in the 1995-1996 Bogalusa Heart Study young adult survey, no significant association between dairy product consumption and BMI or WC was observed (Brooks, et al., 2006). A lack of association between dairy and obesity and obesity-related conditions has also been observed in younger groups. Newby, et al. investigated the relationship between consumption of various beverages and weight changes in a group of 1,345 preschool children aged 2 to 5 years who were participants in the North Dakota Special Supplemental Nutrition Program for Women, Infants, and Children (WIC). Results of this study showed that weight change was not significantly related to milk intake (Newby, et al., 2004). In a cohort of 268 children from western Sydney, Australia, milk intake was not associated with excess weight gain in early adolescence (Tam, et al., 2006). Analysis of a subset of 196 non-obese premenarchal girls aged eight to 12 years from the MIT Growth and Development Study showed no relationship between BMI z-score or percent body fat and dairy consumption (Phillips, et al., 2003). Additionally, a study of 1,210 African American and 1,161 Caucasian girls who participated in the NHLBI Growth and Health Study concluded that there was no association between dairy and BMI; however, increased soda consumption predicted the greatest increase in BMI over time (Striegel-Moore, et al., 2006). (A comprehensive list of related studies and their findings can be located in Appendix C.)

Refined sugar consumption. Because individuals who consume fewer servings of dairy tend to have increased refined sugar intake, which potentially contributes to adverse health outcomes, SSB are also a target for health-related research (Ranganathan, Nicklas, Yang, & Berenson, 2005). On occasion, studies may show that obesity risk is not associated with SSB consumption patterns (Sun & Empie, 2007); however, meta-analyses have concluded that SSB consumption is related to long-term weight gain, obesity, T2D, and CVD risk (Hu & Malik, 2010; Malik, Popkin, Bray, Després, & Hu, 2010; Malik et al., 2010). In a study of 1,944 children in Canada, after measuring the frequency of SSB consumption between meals, results showed that more frequent SSB consumption in between major meals more than doubled the odds of being overweight (Dubois, Farmer, Girard, & Peterson, 2007). Analysis of 4,867 adolescents aged 12 to 18 years who participated in NHANES 1999-2004 showed that higher SSB consumption is associated with higher serum uric acid levels and SBP, which may lead to downstream adverse health outcomes (Nguyen, Choi, Lustig, & Hsu, 2009). Indeed, in older populations, similar relationships are observed. In a cohort of 791 non-Hispanic white men and women aged 18 to 70 years old, increased frequency of SSB consumption was associated increased WC and increased visceral abdominal adipose tissue (Odegaard, Choh, Czerwinski, Towne, & Demerath, 2012). A meta-analysis based on 310,819 particpants, of which 15,043 were T2D cases, individuals in the highest SSB intake category had a 26% greater risk of developing T2D compared to those in the lowest SSB intake category (Malik et al., 2010). Another meta-analysis (conducted by the same group) of 19,431 participants, of which 5,803 were cases of MetS, individuals in the highest category of SSB intake had a greater risk of CVD of nearly 20% compared to individuals in the lowest category of intake (Malik et al., 2010). Additionally, high added sugar consumption (which occurs most commonly in the form of SSB) is associated with CVD risk factors, both independently and through the development of obesity (Kavey, 2010). Diet modification can be accomplished and is related to cardiovascular benefits. Given that college age and young adult populations are concerned about SSB intake, reducing

SSB consumption should be a critical dietary approach to reducing CVD risk into adulthood (Huffman & West, 2007; Kavey, 2010).

Fruit and vegetable intake. Fruit and vegetable intake also impacts CVD risk, as well as risk for other MetS risk factors. A systematic review of studies evaluating the relationship between fruit and vegetable intake and adiposity showed that increased fruit and vegetable intake contributed to reduced adiposity among overweight and obese adults, but no association was observed among children. The longitudinal studies included in the review concluded that in studies among overweight adults, increased fruit and vegetable intake was associated with slower weight gain. This inverse relationship was observed in some children studies; therefore, a conclusive relationship is unclear (Ledoux, Hingle, & Baranowski, 2011). A relationship between fruit and vegetable intake and CVD has been established. Analysis of 400,000 U.S. adults in the 2007 Behavior Risk Factors Surveillance System found that only 24.6% of adults consumed ≥ 5 servings of fruit and vegetables per day. Additionally, individuals who were overweight and obese consumed significantly less fruits and vegetables than their normal weight counterparts (Heo et al., 2011). In 15,792 45 to 64 year-old participants of the Atherosclerosis Risk in Communities study, Steffen et al. observed that higher consumption of fruit and vegetables reduced risk for overall mortality. Furthermore, there was an inverse association between fruit and vegetable intake and coronary artery disease in African Americans, but not in Caucasians (Steffen et al., 2003). Among the 38,876 female health professionals in the Women's Health Study, increased fruit and vegetable intake was protective against CVD and was also associated with lower risk of myocardial infarction (Liu et al., 2000). Studies indicate that fruit and vegetable intake may be protective against other MetS risk factors as well. In a study of 417 male T2D patients aged 65 years and older in the Japanese Elderly Diabetes Intervention Trial, higher total vegetable intake was associated with decreased glycated hemoglobin A1c (HbA1c), TG, and WC. Higher green vegetable intake was associated with lower BMI, HbA1c, TG, and WC, eluding to a protective relationship between vegetable intake and T2D (Takahashi et al., 2012). A comprehensive review concluded that increased fruit and vegetable intake reduces the risk for hypertension, CHD, and stroke, but it is also possible that greater fruit and vegetable intake may prevent weight and consequent conditions, such as T2D (Boeing et al., 2012). Due to the protective role of fruit and vegetables, this is a common behavioral target for weight reduction strategies, which are successful in individuals who increase their daily intake of fruit and vegetables (Epstein et al., 2001; Akers et al., 2012).

Because dairy and SSB consumption levels are often associated with such great disease risk, we chose to investigate this relationship in our study cohort. Chapter 2 of this thesis aims to address dairy and SSB intake in our study population, while Chapter 3 describes the results of our investigation on an ancient medicinal claim related to fruit and vegetable intake using the same cohort of individuals.

RELEVANCE

Given the prevalence rates of obesity and MetS risk factors in Mexican young adults, it is important to examine this group more closely. Current literature either focuses primarily on U.S. individuals less than 18 years old, or includes individuals who are 18 to 25 years old in the same study group as individuals who are as old as 90 years, which makes it difficult to generalize disease risk specifically to the young adult population, particularly when the few studies that include these individuals as a distinct category report such high prevalence of obesity and obesity-related diseases. Disparities not only in the assessment of MetS-related conditions, but also in the development of prevention and intervention strategies in the Mexican young adult population, create a need for more in-depth research studies that focus on potential effective dietary and lifestyle modifications. Because such research specific to this group is lacking, it is essential to study Mexican college-age young adults of 18 to 25 years of age to establish effective and feasible prevention and intervention plans both in Mexico and the United States, as it is possible that these individuals will migrate to the United States if current population projections hold true. Therefore, the hypotheses are the following: (1) Individuals who are not meeting dairy recommendations are at greater risk for MetS; and (2) Individuals who consumed fewer servings of papaya fruit have higher risk for low HDL-C and other dyslipidemias.

Table 1. Metabolic syndrome definitions according to various associations.

Metabolic Syndrome Definitions				
WHO	AACE	AHA/NHLBI	NCEP ATP III	IDF
Two or more of the following:	Clinical judgment based upon the following:	Three or more of the following:	Three or more of the following:	Central obesity (see below) and two or more of the remaining:
Impaired glucose regulation or type 2 diabetes	2-hour postglucose challenge > 140 mg/dL	Elevated fasting glucose ≥ 100 mg/dL or treatment for elevated glucose	Fasting glucose ≥ 110 mg/dL	Raised fasting plasma glucose ≥ 100 mg/dL or previously diagnosed T2D
Insulin resistance	Fasting glucose between 110 and 126 mg/dL			
Raised arterial pressure ≥ 160/90 mmHg	EBP ≥ 130/85 mmHg	EBP diagnosed as SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or antihypertensive drug treatment	Blood pressure ≥ 130/≥ 85 mmHg	Raised blood pressure of SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or treatment for previously diagnosed hypertension
Raised plasma TG ≥ 150 mg/dL and/or low HDL-C < 35 mg/dL in males and < 39 mg/dL in females	Elevated TG ≥ 150 mg/dL	Elevated TG ≥ 150 mg/dL or drug treatment for elevated TG	TG ≥ 150 mg/dL	Raised TG level ≥ 150 mg/dL or specific treatment for raised TG

Table 1 (cont.)

Central obesity defined by waist-to-hip ratio > 0.90 for males and > 0.80 for females and/or BMI > 30 kg/m^2	BMI ≥ 25 kg/m^2	Elevated WC ≥ 102 cm (males) and ≥ 88 cm (females)	Abdominal obesity, diagnosed by WC ≥ 102 cm (males) and ≥ 88 cm (females)	Central obesity (defined by WC ≥ 94 cm in Europid males and ≥ 80 cm for Europid females; however, the physician must apply appropriate ethnic specific values for WC)
Microalbuminuria, urinary albumin excretion rate ≥ 20 mcg/min or albumin:creatinine ratio ≥ 20 mg/g	Low HDL-C < 40 mg/dL in males and < 50 mg/dL in females	Reduced HDL-C < 40 mg/dL (males) and < 50 mg/dL (females) or drug treatment for reduced HDL-C	HDL-C < 40 mg/dL (males) and < 50 mg/dL (females)	Reduced HDL-C < 40 mg/dL (males) and < 50 mg/dL (females) or specific treatment for reduced HDL-C
	Other risk factors, such as family history of T2D, CVD, or hypertension; polycystic ovary syndrome; sedentary lifestyle; advancing age; ethnic groups of high predisposition for T2D or CVD			

Abbreviations: WHO, World Health Organization; AACE, American Association of Clinical Endocrinologists; AHA/NHLBI, American Heart Association/National Heart, Lung, and Blood Institute; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; IDF, International Diabetes Federation; BMI, body mass index; WC, waist circumference; TG, serum triglycerides; HDL-C, serum high-density lipoprotein cholesterol; EBP, elevated blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

CHAPTER 2: CONSUMPTION OF DAIRY AND METABOLIC SYNDROME RISK IN A CONVENIENCE SAMPLE OF MEXICAN COLLEGE APPLICANTS

ABSTRACT

Objective: The rise in MetS is accompanied by a decrease in milk and dairy consumption and an increase in sugar-sweetened beverage (SSB) consumption, with SSB possibly displacing dairy products in the diet. Our main objective was to determine whether individuals not meeting daily dairy recommendations of three servings per day were at greater risk for MetS.

Design: For this cross-sectional study, we included subjects with complete data on the validated 118-item Willett food frequency questionnaire adapted for the Mexican population, BMI, WC, blood pressure, fasting glucose, and lipoprotein profile from an ongoing collaborative project.

Setting: A primary health care center (University clinic) in San Luis Potosi, Mexico.

Subjects: Study participants were a subset of Mexican college applicants aged 18-25 years old (n=339) from a larger cohort.

Measures of Outcome: Dairy was defined as milk-based products only. MetS was diagnosed based on the International Diabetes Federation/American Heart Association (IDF/AHA) harmonized defining criteria.

Results: Overall, 77% of individuals were not meeting the recommended three daily servings of dairy per day. Overall prevalence of MetS was 10.6%. Individuals who failed to meet dairy recommendations may be at 2.9 times greater risk for MetS (95% CI 1.0–8.3, $p = 0.05$) when controlling for age, sex, family history of cardiovascular disease and type 2 diabetes, and physical activity, but this must be further investigated. Because of our study design, we could not determine whether SSB were displacing dairy products in the diet. Still, our data support the

importance of meeting daily dairy recommendations for the prevention of MetS in Mexican young adults.

INTRODUCTION

Over the last decade, Mexico has experienced the fastest rates of change for obesity globally, with overall prevalence of overweight and obesity approaching that of the United States (Barquera et al., 2008). Obesity rates are not only increasing in adults, but in children as well, causing a subsequent increase in obesity-related medical complications (Cook, Weitzman, Auinger, Nguyen, & Dietz, 2003). Obese individuals often exhibit abdominal obesity, insulin resistance, dyslipidemia, and hypertension, a cluster of risk factors known as MetS. MetS is becoming increasingly prevalent in children and adolescents, with some reports estimating anywhere from 9.3% to 29% of Mexican and Latino individuals affected (Castillo et al., 2007; Guerrero-Romero et al., 2010; Messiah et al., 2009). The alarming prevalence rates of MetS in this population have increased awareness of the contribution of dietary habits to the disease.

A fast nutritional transition is underway in Mexico, where the consumption of high-calorie beverages (not including milk) more than doubled for adolescents aged 12 to 18 years and tripled for adult women aged 19 to 48 years from 1999 to 2006 (Barquera et al., 2008). Several studies have shown that the increased consumption of high-calorie beverages is associated with overweight and obesity in adults, adolescents, and children (Ludwig, Peterson, & Gortmaker, 2001; Welsh et al., 2005). Although dairy products provide most of the daily requirement for dietary calcium, daily intake of calcium and dairy declines during the transition from adolescence to young adulthood (Larsson et al., 2009). It appears that regular consumption of milk is being replaced with greater consumption of other high-energy beverages that often do not provide any nutritional benefits and may be harmful to individual health.

Inverse relationships between dairy intake and its composite nutrients with central adiposity have been observed in children, adolescents, young adults, and older adults (Beydoun et al., 2008; Brooks, Rajeshwari, Nicklas, Yang, & Berenson, 2006; dos Santos, Cintra, Fisberg, & Martini, 2008; Mirmiran, Esmaillzadeh, & Azizi, 2005; Brooks et al., 2006; dos Santos et al., 2008). Higher consumption of dairy has even been associated with lower body fat in children as young as 2 to 5 years (Carruth & Skinner, 2001). Increased dietary calcium intake may reduce blood pressure and insulin levels, and increase HDL-C (Drouillet et al., 2007). Additionally, the risk of developing T2D can be reduced by long-term consumption of dairy products (Choi, Willett, Stampfer, Rimm, & Hu, 2005; Elwood et al., 2008). Higher intake of total calcium, both dietary and supplemental, was inversely related to the overall prevalence of MetS in women (Liu et al., 2005). Overall, high intake of dairy products seems to elicit a protective effect on MetS development (Lutsey, Steffen, & Stevens, 2008). However, some studies have shown that dairy consumption has no effect on MetS risk factors (Brooks, Rajeshwari, Nicklas, Yang, & Berenson, 2006; Newby, et al., 2004; Phillips, et al., 2003; Snijder, et al., 2007; Striegel-Moore, et al., 2006; Tam, et al., 2006), making it difficult for individuals to agree on and trust the dairy consumption recommendations. Given the heterogeneous nature of MetS and the diversity of dietary patterns, it becomes relevant to investigate the contribution of dairy consumption to risk of metabolic disease.

We hypothesized that individuals who were not meeting dairy recommendations would be at greater risk for presenting MetS or its components. This study aims to determine (1) the prevalence of MetS risk factors in Mexican college age individuals who were either meeting or not meeting the recommended three daily servings of dairy per day; (2) the contribution of dairy consumption to the relative risk of individual or combined components of MetS; and (3) the contribution of SSB to the diet to determine whether the consumption of SSB may be competing with dairy intake.

MATERIALS AND METHODS

Study Population and Procedure

Participants for the current study were selected from the larger UP AMIGOS (Universities of San Luis Potosí and Illinois: A Multidisciplinary Investigation on Genetics, Obesity, and Social-Environment) 2009 study cohort of 10,000 applicants aged 18 to 25 years to the Autonomous University of San Luis Potosí (Universidad Autónoma de San Luis Potosí [UASLP]) who were seeking admission for the 2010 school cycle between February and July of 2009. A participation schematic is shown in Figure 1. As part of the UASLP application process, all participants were submitted to a health screen at the university clinic. The health screen consisted of: (1) anthropometric measurements, consisting of height, weight, WC, and blood pressure; (2) a medical interview and physical exam executed by a physician; (3) a blood draw following an overnight fast for blood biomarkers; and (4) a food frequency questionnaire based upon the Willett food frequency questionnaire adapted for the Mexican population. Individuals willing to participate were apprised of study information and their rights for our ongoing collaborative project before signing the informed consent form. The protocol was reviewed and approved by both Institutional Review Boards at UASLP and at the University of Illinois at Urbana-Champaign.

Participant Selection

Participants for the current, smaller cross-sectional study were selected based upon the degree of completion of data available from the health clinic assessment, including a complete lipid profile, and from the food frequency questionnaire (Hernandez-Avila et al., 1998) (see Appendix A), of which 90% or more of the 118 items was completed. Individuals with calorie consumption ± 4 SD were excluded (n=4). Individuals with a BMI ≤ 18.49 kg/m^2 and ≥ 40.00

kg/m^2 were also excluded to prevent skewing results of the study. The final subset consisted of 339 individuals.

Anthropometric Measures

Anthropometric measures were conducted by trained health professionals at the UASLP health clinic. Height was measured twice in the same visit using a fixed stadiometer and was recorded to the nearest 0.5 cm, with the final measurement representing an average of the two measures. Weight was also collected twice in the same visit on a calibrated scale (attached to the stadiometer) (Torino, Tecno Lógica, Mexicana, Mexico) and recorded to the nearest 0.1 kg, with the final measurement representing an average of the two measures. BMI was calculated and classified according to the World Health Organization (WHO) as follows: underweight (≤ 18.49 kg/m^2), normal weight (18.50 – 24.99 kg/m^2), overweight (25.00 – 29.99 kg/m^2), and obese (≥ 30.00 kg/m^2) (World Health Organization, 2000). Waist circumference was measured using a flexible, non-stretching nylon tape at the level of the iliac crest following normal expiration with the subject in the standing position and was recorded to the nearest 0.1 cm. Waist circumference risk level for MetS was determined according to the IDF/AHA population-specific joint definition: at risk males, ≥ 90 cm, and at risk females, ≥ 80 cm (Alberti et al., 2009).

Blood Pressure

Blood pressure was measured by trained, certified health care providers according to a common protocol adapted from AHA-recommended procedures. It was taken on the dominant arm (right arm in most cases) in the seated position using appropriately sized Welch Allyn cuffs. According to the harmonized definition for MetS, EBP was defined as SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg (Alberti et al., 2009).

Blood Biomarkers

Following the medical examination, overnight (≥ 8 hours) fasting blood samples were collected. Fasting blood glucose was determined according to the glucose oxidase peroxidase method (Alcyon 300 autoanalyzer from Abbott [Chicago, IL] and reagents from Biosystems [Barcelona, Spain]). Impaired fasting glucose (IFG) was defined as having a fasting glucose > 100 mg/dL (Alberti et al., 2009). According to the data of this subset, we assumed that participants adhered to fasting guidelines, as no blood glucose values over 110 mg/dL were observed. The determination of serum lipid profiles was carried out by the same Alcyon 300 analyzer for diagnostic use *in vitro*, results are expressed in mg/dL. Serum TG were determined according to the glycerol phosphate oxidase peroxidase method, based on a colorimetric enzymatic reaction and measured in the Alcyon 300 analyzer. HDL-C was determined by a direct method in which a detergent solubilized the HDL-C, which was then quantified spectrophotometrically according to the cholesterol oxidase method. Hypertriglyceridemia was defined as having fasting serum TG ≥ 150 mg/dL, while low serum HDL-C was defined as having fasting HDL-C < 40 mg/dL (males) and < 50 mg/dL (females) (Alberti et al., 2009).

Metabolic Syndrome Definition

We diagnosed MetS according to the IDF/AHA harmonized criteria of having three or more of the following: (a) increased WC, at risk males ≥ 90 cm and at risk females ≥ 80 cm; (b) elevated SBP and/or DBP, SBP ≥ 130 mmHg and DBP ≥ 85 mmHg; (c) IFG, fasting glucose > 100 mg/dL; (d) hypertriglyceridemia, fasting serum TG ≥ 150 mg/dL; and (e) low serum HDL-C, fasting serum HDL-C < 40 mg/dL (males) and < 50 mg/dL (females) (Alberti et al., 2009).

Dietary Assessment

Participants completed a validated 118-item Willett food frequency questionnaire that was adapted for the Mexican population in order to include commonly consumed foods and beverages in Mexico (Hernandez-Avila et al., 1998) (see Appendix A). This survey was not developed to specialize in specifically capturing dairy intake, rather dietary intake overall. The questionnaires were administered in a group setting to ensure consistency of instructions. Questionnaire responses were entered into the SNUT (Sistema de Evaluacion de Habitos Nutricionales y Consumos de Nutrimientos; developed by the National Institute of Public Health, Mexico) nutrition software for nutrient analysis. Results from the nutrient analysis were calculated by the SNUT software and exported to SAS version 9.2 (SAS Institute Inc.; Cary, NC) for further data analysis. Frequency of consumption estimates were determined by using the following weights that correspond to survey responses: a) 6 for reported frequencies of 6 or more per day; b) 4.5 for 4-5 per day; c) 2.5 for 2-3 per day; d) 1 for 1 per day; e) 0.8 for 5-6 per week; f) 0.43 for 2-4 per week; g) 0.08 for 2-3 per month; and h) 0.016 for 1 or less per month (Hernandez-Avila et al., 1998). In order to calculate weekly consumption frequencies, the values obtained for daily consumption were multiplied by 7. Portion sizes of the foods included in the current study are shown in Table 2. Participants were categorized into two groups based upon the United States Department of Agriculture (USDA) recommendations: (1) meeting or (2) not meeting dairy recommendations if their total reported daily servings were $\geq$ 3/day or $<$ 3/day, respectively. Dairy items on the questionnaire constituted the following milk-based foods: cottage cheese, Oaxaca cheese, Manchego or Chihuahua cheese, cream cheese, yogurt, and ice cream. Cream cheese was included in this analysis because, as a white cheese, it is classified as a dairy product. We did not select dairy items based upon their calcium content. Sugar sweetened beverage items on the questionnaire included: soft drinks, flavored sugar water, atole with milk, and atole without milk. (Atole is a traditional cornstarch-based Mexican drink that typically consists of a mixture of cornstarch, water, sugar, cinnamon, and sometimes milk.) Alcohol intake (beer, wine, and rum, brandy, and/or tequila) was included in the analysis to observe whether there was a difference in consumption between the two dairy intake groups. Flour tortillas were included in descriptive analyses to compare the dietary contribution with that of corn tortillas, a source of calcium in the Mexican diet.

Physical Activity Questionnaire

Physical activity (PA) was assessed by administering the long version of the International Physical Activity Questionnaire (IPAQ) to each participant (Hallal & Victoria, 2004) (see Appendix B). Responses were categorized into three groups based on ever having engaged in PA: 1) low or no PA; 2) moderate PA; and 3) high or vigorous PA. Exercise duration was not included in this analysis.

Statistical Analysis

All data were analyzed by SAS version 9.2. All continuous variables were assessed for normality and log-transformed (log_{10}) to reduce skewness before performing any statistical analyses. Except for BMI, WC, SBP, DBP, fasting glucose, and total energy and calcium intake, the remaining variables were log-transformed in order to perform the analysis. One-way ANOVA was performed to compare differences between individuals meeting and not meeting daily dairy recommendations. Differences were considered significant where $p < 0.05$. Participants were categorized as previously stated. Total weekly dairy servings was calculated as the sum of weekly servings of cheese (cottage, Oaxaca, Manchego or Chihuahua, and cream cheese), yogurt, and ice cream. Total SSB servings was calculated as the sum of soft drinks, flavored sugar water, atole with milk, and atole without milk. Relative risk ratios to assess individual or combined components of MetS were estimated using modified Poisson logistic regressions and various adjustment models (Spiegelman & Hertzmark, 2005). Here, we report on three models: (1) adjusted for age and sex; (2) adjusted for age, sex, and energy intake; and (3) adjusted for age, sex, energy intake, family history of CVD and T2D, and PA. Due to the relationship between MetS risk factors and increasing age, we controlled for age to adjust for even minor differences. Classifications used in the Poisson logistic regressions were: (1) consumption of < 7 whole milk servings per week, to represent consumption of whole milk below one serving per day of the week; (2) consumption of < 7 cheese servings per week, to represent consumption of cheese below one serving per day of the week; and (3) not meeting dairy requirements of 21 dairy servings per week, or 3 servings per day of the week. The SAS package version 9.2 (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

RESULTS

Overall, MetS was present in 10.6% of the individuals (n= 36). The prevalence of MetS and individual risk factors are shown in Table 3. Low HDL-C was the most common risk factor observed (51.3%), followed by increased WC (45.2%). The prevalence of EBP, IFG, and hypertriglyceridemia were 19.5%, 12.5%, and 19.8%, respectively. After comparing the prevalence of MetS and individual risk factors between individuals who were meeting dairy recommendations and those who were not meeting recommendations, we observed that MetS and each of the individual risk factors were more prevalent in those who were not meeting dairy recommendations (Table 3).

Seventy-seven percent of individuals in this subset were not meeting the daily dairy recommendations of at least three dairy servings per day (n= 260). No differences in BMI or in any of the individual MetS component measures (WC, IFG, blood pressure, TG or HDL-C) were observed when comparing individuals who were meeting dairy recommendations to those who were not meeting dairy recommendations (Table 4). Individuals meeting dairy recommendations consumed more calories (2880 kcal vs. 2016 kcal per day, $p < 0.0001$) and total calcium (1145 mg vs. 600 mg per day, $p < 0.0001$), as well as all dairy products, except for ice cream (Table 5). Because cream cheese is high in fat and lower in calcium, its inclusion may be controversial; however, because it is a dairy source, it was included in the current analyses. Those meeting dairy recommendations also consumed slightly more flavored sugar water (4.3 vs. 4.2 servings per week, $p = 0.01$) and total SSB overall (9.5 vs. 9.3 servings per week, $p = 0.001$). Conversely, individuals who were not meeting dairy recommendations consumed more atole with milk (0.6 vs. 0.4 servings per week, $p = 0.01$) and atole without milk (0.3 vs. 0.2 servings per week, $p = 0.02$). However, such differences in weekly beverage consumption are quite minimal. Corn tortillas, a source of dietary calcium aside from dairy and other traditional dietary calcium sources, were consumed more frequently by individuals not meeting dairy recommendations (15.6 *vs.* 14.3 servings per week, $p = 0.01$). There were no differences in alcohol consumption between the two groups.

In this population, the two most common MetS risk factors observed were low HDL-C and increased WC. These two factors combined were present in 26.0% (n = 88) of the population, while 28.6% (n = 97) individuals had none of the MetS risk factors. When contrasting the two groups, individuals with low HDL-C and increased WC had significantly higher BMI, WC, and serum TG and no differences in SBP, DBP, and fasting glucose (Table 6). In general, there were no differences in energy, calcium or total dairy intake, and consumption of SSB, alcohol, or tortillas between the two groups (Table 6).

We evaluated the contribution of three dairy consumption patterns to the relative risk of presenting individual or combined components of MetS. The reference patterns included consumption of less than 7 servings per week of milk (1) or cheese (2) and not meeting dairy requirements (3). The first two patterns did not show differences in risk for individual or combined components of MetS. However, individuals not meeting dairy recommendations were at 3.7 times (95% CI 1.2–11.7, $p = 0.02$) greater risk for MetS than those meeting the recommendations, after controlling for age, sex, and energy intake (Table 7). Although not significant, this risk may remain after further adjustment for potential confounders (PA and family history of CVD and T2D).

DISCUSSION

The current study aimed to determine the prevalence of MetS and individual risk factors and to assess the potential risk for MetS when not meeting daily dairy recommendations. The young adults participating in this study were considered "healthy"; still, almost 11% had MetS. Our reported prevalence was similar to the 9.3% reported in Mexican children and adolescents (Guerrero-Romero et al., 2010), but higher than the reported 3.7% in a subset of Mexican young adults or Caucasians of similar age range (Fernandes & Lofgren, 2011; Gonzalez Deschamps et al., 2007). Notably, the prevalence of MetS was lower in individuals who were meeting dairy recommendations than in those who were not meeting recommendations (5.3% vs. 13.9%). Data from ENSANUT 2006 reported that in 2006, 49.8% of adults ages 20 years and older had MetS (Rojas et al., 2010), though it is important to mention that this higher prevalence is related to the inclusion of older individuals. Indeed, increased age is associated with higher prevalence of slowly developing MetS related diseases, such as hypertension and diabetes, which are the two main causes of death in the Mexican adult population.

Individuals meeting dairy recommendations also had lower prevalence of all individual MetS risk factors; however, the values of the diagnostic parameters themselves were not different between groups. Our finding of no difference in the values of individual MetS risk factors between subjects meeting and not meeting daily dairy recommendations is not unlike other observations. Although some studies have shown that there is no significant relationship between dairy consumption and BMI (Brooks, Rajeshwari, Nicklas, Yang, & Berenson, 2006; Snijder et al., 2007), we did observe that individuals who were not meeting dairy recommendations were approximately 3 times more likely to be at risk for MetS. Our results concur with international results from Tehranian adults and European populations that have shown that individuals who consume higher amounts of dairy have a lower prevalence of MetS (Azadbakht, Mirmiran, Esmaillzadeh, & Azizi, 2005; Elwood, Pickering, & Fehily, 2007; Fumeron et al., 2011).

Over three-fourths (77%) of the Mexican young adults participating in this study were not meeting the recommended three daily servings of dairy foods per day and had higher risk of presenting MetS. This low daily intake data is comparable to a study conducted in a U.S. representative sample of 1,956 adolescents ages 12 to 19 years, which found that only 25% of these individuals were meeting daily milk consumption recommendations (Sebastian, Wilkinson, & Goldman, 2009). Our observations also held with a recent report in which Mexicans eating the Westernized dietary pattern, of which low dairy consumption is a defining characteristic, have increased odds for obesity, abdominal obesity, and high body fat percent (Denova-Gutierrez et al., 2011).

The two most frequent MetS risk factors observed in this study were low HDL-C and increased WC. The combined prevalence of those two factors has been shown to be higher in Hispanic populations than in other ethnic groups (Messiah et al., 2009). We also found that abdominal obesity was more common in females than in males. This finding concurs with reports from ENSANUT 2006, which used the same IDF/AHA MetS defining criteria. Results from ENSANUT 2006 showed that 83.8% of females versus 62.9% of males had increased WC and 52.7% of females versus 46.4% of males had MetS (Rojas et al., 2010). We investigated if greater or lower consumption of dairy was associated with the presence of these two risk factors, but we did not find an association (see Appendix D).

Consumption of dairy products may also be protective to some MetS risk factors. Individuals consuming higher amounts of dairy have been shown to have lower body fat (Mennen et al., 2000), a relationship further supported by findings of an inverse relationship between dairy consumption and BMI in several studies (Marques-Vidal, Goncalves, & Dias, 2006; Mirmiran, Esmaillzadeh, & Azizi, 2005; Moore et al., 2010). Increased dairy consumption has also been shown to have a strong inverse association with insulin resistance syndrome among overweight adults and may also reduce the risk of T2D and CVD (Varenna, Binelli, Casari, Zucchi, & Sinigaglia, 2007). Although biological and molecular mechanisms remain a matter of debate, the current evidence suggests a negative association between dairy consumption and body weight (Pereira et al., 2002). Our study provides further support for the reduction of MetS risk when consuming dairy products at recommended levels.

In some populations, increased SSB consumption may be displacing the consumption of milk and contributing to adverse health conditions (Barquera et al., 2008; Dougkas, Reynolds, Givens, Elwood, & Minihane, 2011), while in others, consumption of SSB tends to level off after adolescence (Rampersaud, Bailey, & Kauwell, 2003). Higher SSB consumption has been associated with overall cardiometabolic risk, particularly, higher risk of increased WC, high low-density lipoprotein cholesterol (LDL-C), and high serum TG (Nelson, Neumark-Sztainer, Hannan, & Story, 2009). Here, we were unable to observe a displacement of milk by SSB in individuals not meeting dairy recommendations; in fact, individuals meeting dairy recommendations consumed slightly more SSB. However, it could be reasonable to speculate that individuals who did not meet dairy recommendations may have been replacing dairy products with SSB, while those meeting dairy recommendations were simply adding the extra SSB to their diet.

We observed a significant difference in energy intake between the two groups. Individuals meeting dairy recommendations consumed more daily calories (on average) than those not meeting dairy recommendations. Despite this difference, there was no difference in BMI or any individual MetS risk factors between these two groups. After further analysis to determine the source of additional energy intake (see Appendix D), the only foods consumed more by the group meeting dairy recommendations and substantially enough to contribute to the energy difference were the dairy foods – milk, cheese, and yogurt in particular. Additional analyses will be conducted in the future to investigate the possible contribution of fruits and vegetables or other food groups to the difference of energy intake between the two groups.

The strengths and weaknesses of this study need to be discussed. First, this study focuses on individuals aged 18 to 25 years, which tends to be a "medically neglected" age group due to the lack of regular health screening by a physician. Individuals may begin to see a physician for a preventive care visit infrequently prior to this age and as early as the age of 13 years (Nordin, Solberg, & Parker, 2010). These findings support the need not only for more prevention and intervention programs for adolescents and young adults, but for early detection strategies as well. Young adults tend to be more self-reliant, in which lifestyle changes may be more successful in order to prevent the development of MetS and/or reverse the development of other diseases in affected individuals. Furthermore, our data support a simple public health message that is easy to deliver and yields practical, positive results. Our limitations include the small sample size and our inability to directly measure eating patterns, precluding us to generalize our interpretation of the results. We considered the possibility of residual confounding; however, we determined that this phenomenon was unlikely due to the greater prevalence of MetS that was observed in individuals who were not meeting dairy recommendations, which supports the nearly 3 times greater risk for MetS in these individuals. Additionally, similar methodology has been applied to other studies with a greater number of individuals and wide age range finding that the MetS risk is associated with a Westernized dietary pattern (Denova-Gutierrez et al., 2010). The cross-sectional study design limits causality inferences, as individuals may have a number of reasons to restrict dairy in the diet. Aside from dietary changes, another reason for restriction of dairy is the incidence of lactose intolerance, an aspect on which we did not have data. Another limitation of this study is the self-reporting nature of our data collection. It is known that individuals generally tend to underreport calorie intake, with overweight and obese individuals underreporting more than their normal weight counterparts (Bedard, Shatenstein, & Nadon, 2004; Voss, Kroke, KlipsteinGrobusch, & Boeing, 1997). We also could not determine the amount of milk used to make the atole with milk that was consumed, so these quantities could not be added for group comparisons. Lastly, we did not measure or evaluate for differences in low-fat vs. high-fat dairy products due to the lack of familiarity of low-fat dairy in the typical Mexican diet.

CONCLUSION

To sum the findings of this study, Mexican college applicants who were not meeting daily dairy recommendations triplicated their risk for presenting MetS. Our results suggest that simply meeting dairy recommendations may serve as an effective dietary prevention and intervention measure to reduce individual risk for MetS. Adopting the USDA daily dairy recommendation as a habit early in life is a low cost approach to have a positive impact in maintaining health and decreasing metabolic disease risk.

Acknowledgments

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Figure 1. Participant Selection Schematic for Selection of Study College Applicants.

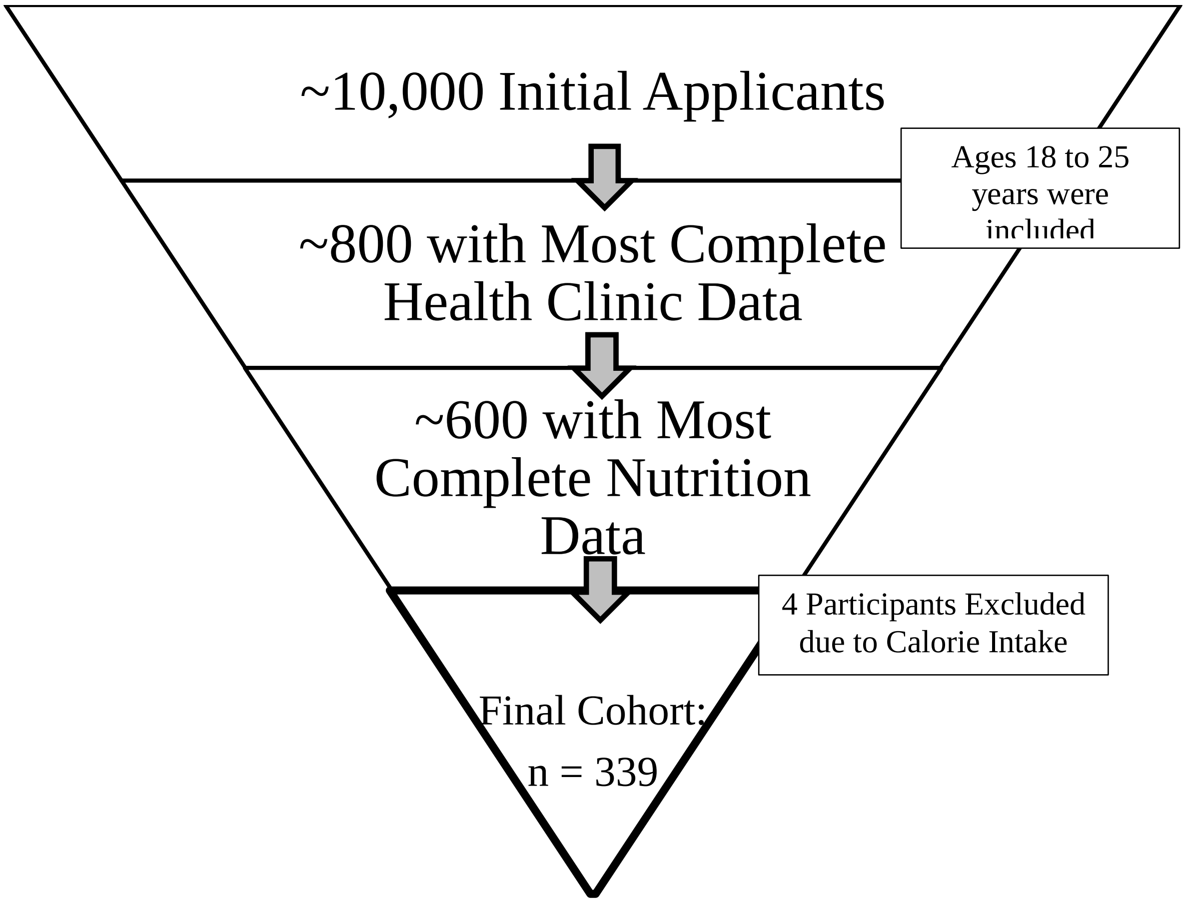

Table 2. List of food items analyzed in the current study from the validated 118-item Willett food frequency questionnaire adapted for the Mexican population and corresponding portion sizes.

	Food Item	Portion Size
Dairy Products	Whole milk	1 cup
	Cottage Cheese	½ cup
	Oaxaca cheese	1 slice
	Manchego or Chihuahua cheese	1 slice
	Cream cheese	1 tablespoon
	Yogurt	1 cup
	Milk ice cream	1 scoop in a cone
SSB	Soft drink	12 oz.
	Flavored sugar water	1 cup
	Atole with milk	1 cup
	Atole without milk	1 cup
Alcohol	Beer	12 oz.
	Wine	1 cup
	Rum, brandy, tequila	1.5 oz.
Tortillas	Corn tortillas	1- 4” tortilla
	Flour tortillas	1- 4” tortilla

Abbreviation: SSB, sugar-sweetened beverages.

Table 3. Prevalence rate of metabolic syndrome and individual risk factors in all individuals, those meeting dairy recommendations, and those not meeting recommendations (numbers shown are raw calculated percentages).

	All	**Meeting**	**Not Meeting**
n	339	79	260
Risk Factor		*Prevalence (%)*	
Metabolic Syndrome	10.6	5.3	13.9
Increased WC	45.2	8.8	36.4
Elevated BP	6.4	1.8	4.7
Impaired Fasting Glucose	12.5	2.9	9.6
Hypertriglyceridemia	19.6	4.1	15.7
Low HDL-C	51.3	11.1	40.2

Frequency cross-tabulations.
Abbreviations: WC, waist circumference; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol.

Table 4. Comparison of adjusted metabolic characteristics* of young Mexican adults (18-25 years) that were or were not meeting the daily dairy requirements.

	Meeting		**Not Meeting**		***p***
n (males/females)	79 (41/38)		260 (126/134)		
Subject characteristics	Mean	95% CI	Mean	95% CI	
Age, *years*	18.9	18.6, 19.2	18.9	18.7, 19.0	0.79
BMI, *kg/m²*	24.7	23.8, 25.6	25.1	24.6, 25.7	0.52
WC, *cm*	84.1	81.2, 87.1	84.1	82.6, 85.5	0.65
SBP, *mmHg*	112.9	111.1, 114.6	112.5	111.3, 113.6	0.96
DBP, *mmHg*	74.1	72.7, 75.6	73.1	72.3, 73.9	0.43
Glucose, *mg/dL*	90.5	88.4, 92.5	90.7	89.6, 91.7	0.92
TG, *mg/dL*	110.1	95.6, 124.6	120.8	113.8, 127.8	0.06
HDL-C, *mg/dL*	46.3	44.1, 48.4	47.9	46.2, 49.5	0.98

One-way ANOVA was used to detect significance at $p \leq 0.05$.
Abbreviations: BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, fasting serum triglycerides; HDL-C, fasting serum HDL cholesterol.
[*] All variables, except age, were adjusted for age, sex, and daily calorie intake. All individuals were fasting before blood draw.

Table 5. Comparison of selected food group consumption, including dairy products, between individuals meeting or not meeting daily dairy recommendations.

	Meeting		**Not Meeting**		***p***
n (males/females)	79 (41/38)		260 (126/134)		
Nutrient intake, *per day*	Mean	95% CI	Mean	95% CI	
Energy[*], *kcal*	2878	2626, 3134	2016	1904, 2129	<0.0001
Calcium, *mg*	1145	1061, 1229	600	566, 633	<0.0001
Dairy products, *servings per week*					
Whole milk	14.8	13.2, 16.4	3.6	3.2, 4.1	<0.0001
Cottage cheese	6.8	5.1, 8.5	2.0	1.7, 2.2	<0.0001
Oaxaca cheese	2.7	1.7, 3.8	0.8	0.6, 0.9	0.0004
Manchego or Chihuahua cheese	2.3	1.6, 3.0	0.5	0.4, 0.6	<0.0001
Cream cheese	1.7	1.1, 2.2	0.5	0.4, 0.7	<0.0001
Yogurt	4.1	2.9, 5.2	1.6	1.4, 1.9	<0.0001
Milk ice cream	0.9	0.6, 1.1	0.9	0.7, 1.1	n.s.
Total cheese†	11.8	9.2, 14.5	3.2	2.8, 3.6	<0.0001
Total dairy‡	32.4	29.5, 35.3	8.8	8.2, 9.5	<0.0001
SSB§, *servings per week*					
Soft drinks	4.5	2.8, 6.3	4.3	3.3, 5.3	0.004
Flavored sugar water	4.3	2.7, 5.9	4.2	3.4, 5.0	0.01
Atole with milk	0.4	0.3, 0.6	0.6	0.4, 0.7	0.01
Atole without milk	0.2	0.1, 0.2	0.3	0.2, 0.5	0.02
Total SSB‖	9.5	7.0, 11.9	9.3	8.0, 10.7	0.001
Alcohol, *servings per week*					
Beer	1.1	0.5, 1.6	0.6	0.3, 0.8	n.s.
Wine	0.5	0.0, 0.9	0.3	0.1, 0.4	n.s.
Rum, brandy, tequila	0.6	0.4, 0.9	0.5	0.2, 0.9	n.s.

Table 5 (cont.)

Tortillas, *servings per week*					
Corn tortillas	14.3	11.4, 17.3	15.6	13.9, 17.2	0.01
Flour tortillas	4.4	3.1, 5.7	3.7	2.9, 4.5	n.s.

One-way ANOVA was used to detect significance at $p \leq 0.05$.
n.s., non-significant differences
[*] Daily energy intake adjusted for age and sex.
†Total Cheese is the sum of Cottage, Oaxaca and Manchego or Chihuahua cheeses.
‡ Total Dairy is the sum of total cheese plus whole milk, yogurt, and ice cream.
§ SSB, sugar-sweetened beverages.
|| Total SSB is the sum of soft drinks, flavored sugar water, atole with milk, and atole without milk.

Table 6. Comparison of clinical and dietary intake characteristics between individuals without MetS risk factors and those with combined low HDL-C and increased WC.

	No MetS risk factors		**Large WC and Low HDL-C**		***p***
Participants, n (M/F)	97 (66/31)		88 (23/65)		
Participant characteristics	*Mean*	*95% CI*	*Mean*	*95% CI*	
Age (years)	18.9	18.6, 19.1	18.9	18.6, 19.2	0.84
BMI (kg/m^2)	22.6	22.0, 23.1	28.2	27.3, 29.1	<0.0001
WC (cm)	76.6	75.2, 78.0	92.8	90.8, 94.8	<0.0001
SBP (mmHg)	112.7	111.1, 114.4	112.4	110.5, 114.2	0.63
DBP (mmHg)	72.7	71.5, 73.9	73.8	72.4, 75.1	0.18
Glucose[†] (mg/dL)	91.2	89.0, 93.3	90.4	88.6, 92.2	0.37
TG[†] (mg/dL)	111.0	98.2, 123.7	128.7	115.1, 142.2	0.0008
HDL-C[†] (mg/dL)	54.9	52.9, 56.8	40.4	39.0, 41.8	<0.0001
Nutrient intakes					
Energy[‡] (kcal)	2252	2028, 2476	2239	2018, 2460	0.59
Calcium (mg)	750	671, 830	727	645, 810	0.42
Dairy products (servings per week)					
Whole milk	6.6	5.3, 7.8	6.2	4.6, 7.8	0.44
Cottage cheese	3.4	2.4, 4.4	3.6	2.3 4.9	0.81
Oaxaca cheese	1.1	0.7, 1.4	1.8	0.9 2.8	0.88
Manchego or Chihuahua cheese	1.0	0.6, 1.3	1.1	0.6, 1.7	0.60
Cream cheese	0.8	0.5, 1.1	0.7	0.3, 1.2	0.02
Yogurt	2.4	1.6, 3.2	2.1	1.5, 2.7	0.35
Milk ice cream	0.7	0.5, 0.9	0.9	0.6, 1.1	0.36
Total cheese [§]	5.5	4.2, 6.7	6.6	4.3, 8.9	0.56
Total dairy [‖]	15.2	12.6, 17.8	15.7	12.2, 19.2	0.36
SSB[¶] (servings per week)					
Soft drinks	4.4	2.8, 6.0	3.2	2.5, 3.9	0.55
Flavored sugar water	3.2	2.3, 4.1	4.6	2.9, 6.3	0.09
Atole with milk	0.5	0.3, 0.7	0.4	0.3, 0.6	0.35

Table 6 (cont.)

Atole without milk	0.3	0.1, 0.4	0.4	0.0, 0.8	0.23
Total SSB	8.4	6.5, 10.3	8.4	6.5, 10.2	0.29
Alcohol (servings per week)					
Beer	0.7	0.5, 1.0	0.8	0.0, 1.5	0.85
Wine	0.2	0.1, 0.3	0.4	-0.1, 0.7	0.74
Rum, brandy, tequila	0.6	0.2, 0.9	0.8	0.4, 0.9	0.27
Tortillas (servings per week)					
Corn tortillas	15.8	13.0, 18.7	12.7	10.4, 15.0	0.12
Flour tortillas	4.0	2.6, 5.4	3.6	2.3, 4.9	0.88

One-way ANOVA was used to detect significance at $p \leq 0.05$.

Abbreviations: MetS, metabolic syndrome; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, fasting serum triglycerides; HDL-C, fasting serum HDL cholesterol.

† All individuals were fasting before blood draw.

‡ Daily energy intake adjusted for age and sex.

§ Total Cheese is the sum of Cottage, Oaxaca and Manchego or Chihuahua cheeses.

|| Total Dairy is the sum of total cheese plus whole milk, yogurt, and ice cream.

¶ SSB, sugar-sweetened beverages.

** Total SSB is the sum of soft drinks, flavored sugar water, atole with milk, and atole without milk.

Table 7. Relative risk for individual and combined factors of MetS according to dairy intake in young Mexican adults (18-25 years).

	Model 1[†]			**Model 2**[‡]			**Model 3**[§]		
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***
Consumption of < 7 Whole Milk Servings per week									
WC ≥80 cm (F); ≥90 cm (M)	1.1	0.9, 1.4	0.47	1.0	0.8, 1.4	0.87	1.1	0.9, 1.5	0.31
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	1.2	0.5, 2.9	0.77	2.1	0.5, 10.0	0.34	1.4	0.6, 3.7	0.44
Glucose > 100 mg/dL	1.2	0.6, 2.2	0.57	1.2	0.6, 2.6	0.60	1.1	0.6, 2.0	0.81
Triglycerides ≥ 150 mg/dL	1.0	0.6, 1.6	0.99	1.2	0.7, 2.0	0.60	1.1	0.7, 1.7	0.77
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.0	0.8, 1.2	0.79	1.0	0.8, 1.4	0.87	1.0	0.8, 1.2	0.73
MetS (presence of 3 or more risk factors)	1.5	0.7, 3.0	0.29	1.6	0.7, 3.4	0.24	1.6	0.8, 3.4	0.23
Consumption of < 7 Cheese Servings per week									
WC ≥80 cm (F); ≥90 cm (M)	1.0	0.8, 1.3	0.93	1.2	0.8, 1.7	0.36	1.1	0.8, 1.4	0.73
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	1.7	0.5, 5.7	0.39	3.4	0.5, 23.5	0.21	2.6	0.9, 7.3	0.07
Glucose > 100 mg/dL	1.6	0.8, 3.5	0.20	1.2	0.5, 2.9	0.68	1.6	0.7, 3.8	0.24
Triglycerides ≥ 150 mg/dL	1.1	0.7, 1.9	0.67	1.5	0.7, 2.8	0.27	1.2	0.7, 2.2	0.46
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.2	0.9, 1.5	0.30	1.2	0.8, 1.7	0.36	1.2	0.9, 1.5	0.29
MetS (presence of 3 or more risk factors)	1.5	0.6, 3.4	0.36	1.7	0.7, 4.1	0.21	1.7	0.7, 4.0	0.25
Not Meeting Dairy Requirements									
WC ≥80 cm (F); ≥90 cm (M)	1.2	0.9, 1.7	0.17	1.4	0.9, 2.0	0.12	1.4	1.0, 1.9	0.06
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	0.9	0.4, 2.4	0.87	1.4	0.3, 6.2	0.65	1.3	0.4, 3.9	0.64
Glucose > 100 mg/dL	1.0	0.5, 2.0	0.93	1.0	0.4, 2.4	0.97	0.9	0.4, 1.8	0.68
Triglycerides ≥ 150 mg/dL	1.2	0.7, 2.1	0.45	1.5	0.8, 2.9	0.23	1.5	0.8, 2.7	0.22
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.1	0.8, 1.4	0.54	1.4	0.9, 2.0	0.12	1.1	0.8, 1.4	0.56
MetS (presence of 3 or more risk factors)	2.4	0.9, 6.5	0.09	3.7	1.2, 11.7	0.02[*]	2.9	1.0, 8.3	0.05

Relative risk ratios were estimated using a modified Poisson logistic regression.

Abbreviations: MetS, metabolic syndrome; WC, waist circumference; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, fasting serum triglycerides; HDL-C, fasting serum HDL-cholesterol.

[†] Model 1, adjusted for age and sex.

‡ Model 2, adjusted for age, sex, and total calorie intake.
§ Model 3, adjusted for age, sex, total calorie intake, family history of cardiovascular disease and type 2 diabetes, and physical activity.
* $p \leq 0.05$

CHAPTER 3: LOW PAPAYA CONSUMPTION MAY INCREASE RISK FOR LOW HIGH-DENSITY LIPOPROTEIN CHOLESTEROL IN MEXICAN COLLEGE APPLICANTS

ABSTRACT

Objective: Raising HDL-C via nutrition intervention is a challenge. Low in calorie, papaya fruit also contains many vitamins and minerals, as well as fiber, making it one of the healthier fruit options. Our objective was to determine whether individuals consuming less papaya were at greater risk for low HDL-C, hypertriglyceridemia, high LDL-C, and hypercholesterolemia.

Design: For the current cross-sectional study, we included subjects with complete data on a validated 118-item Willett food frequency questionnaire adapted for the Mexican population, BMI, and lipid and lipoprotein profile from UP AMIGOS.

Setting: A primary health care center (University clinic) in San Luis Potosi, Mexico.

Subjects: Study participants were a subset of Mexican college applicants aged 18-25 years old (n=339; 50.7% females) from the larger study cohort.

Measures of Outcome: Subjects were split into two consumption groups: < 3 or > 3 weekly papaya servings (mean intake 0.38 vs. 4.3 servings/week, $p < 0.0001$) based upon tertiles of consumption. Hypertriglyceridemia, low HDL-C, high LDL-C, and hypercholesterolemia were diagnosed based upon IDF and the NCEP ATP III criteria.

Results: Overall prevalence of low HDL-C was 51.6%. There were no differences in blood lipid profiles between the two groups; however, females who consumed < 3 servings of papaya per week may be at 1.52 times greater risk (95% CI 0.99-2.32, $p = 0.05$) of having low HDL-C after adjustment for age and family history of CVD and T2D, but because 1.0 in included in the confidence interval, there is a possibility that there is no relationship; therefore, this warrants further investigation. These findings were not observed in males. We did not observe risk for

other at-risk blood lipid measures. However, prevalence of low HDL-C, hypertriglyceridemia, high LDL-C, and hypercholesterolemia was higher in those consuming < 3 weekly servings of papaya. Those who consumed papaya more frequently also consumed more fruits and vegetables. Although preliminary, our results suggest that consumption of at least 3 servings of papaya per week may be indicative of a healthier overall diet and help prevent dyslipidemias in Mexican college age individuals.

INTRODUCTION

Results from ENSANUT 2006 show that the prevalence of low HDL-C in Mexican young adults aged 20 to 29 years in the year of the study (2005-2006) was 61.9% (Aguilar-Salinas et al., 2010). Out of hypercholesterolemia, hypertriglyceridemia, low HDL-C, and high LDL-C, low HDL-C was the most common lipid disorder in these individuals (Aguilar-Salinas et al., 2010). Given the fact that the prevalence of low HDL-C exceeds the prevalence of obesity alone, dietary modifications, particularly those aligned with current dietary trends (e.g. fruit and vegetable intake) that may increase HDL-C levels warrant further investigation.

A strong inverse relationship between HDL-C levels and the risk of coronary heart disease (CHD) has been shown in many epidemiological studies (Assmann & Schulte, 1988; de Freitas et al., 2011; Skretteberg et al., 2012). When compared to other markers of CHD risk, HDL-C may be the strongest predictor (Gordon, Castelli, Hjortland, Kannel, & Dawber, 1977; Menotti et al., 2011; Stampfer, Sacks, Salvini, Willett, & Hennekens, 1991). This can be illustrated by a longitudinal study of 2,650 disease-free men and women aged 35-74 years from central Italy that investigated the role of MetS in predicting CHD and CVD events. Although MetS predicted greater likelihood of CHD and CVD events, HDL-C and SBP were the only MetS risk factors contributing to the prediction (Menotti et al., 2011). The impact of HDL-C on CHD and CVD risk is most likely credited to its role in reverse cholesterol transport. In reverse cholesterol transport, high-density lipoprotein (HDL) mediates excess cholesterol efflux from other tissues and ultimately returns the cholesterol to the liver for recycling or breakdown (Lewis & Rader, 2005). Additionally, HDL has been shown to have anti-inflammatory, antioxidant, and anti-thrombotic properties, therefore eliciting protective effects on the endothelium and further preventing CVD risk (Assmann & Gotto, 2004). The expert consensus is that raising HDL-C should be one of the goals in the management of atherogenic dyslipidemias for CVD risk reduction (Marcason, 2011).

It is recommended that the first line treatment for increasing HDL-C levels is a combination of moderate intensity exercise three or more times per week, weight loss, smoking cessation, and mild to moderate alcohol consumption (Bhatt, Wells, Sperling, & Baer, 2010). However, this does not necessarily help individuals who already do not smoke or drink or those for whom weight loss is inappropriate. It has even been shown that physical activity may not influence HDL-C to the level of association with CHD. To explain, results of a longitudinal study of 1,357 healthy Norwegian men aged 44-69 years showed that the highest HDL-C level quartile was associated with lower risk of CHD, fatal CHD, fatal CVD, and all-cause death compared to those in the lowest HDL-C quartile. Moreover, the analysis revealed that physical fitness and changes in physical fitness had no impact on the ability of HDL to predict CHD (Skretteberg et al., 2012). The strong relationship between HDL-C and risk of CHD, CVD, and mortality provides justification for conducting research in this area, particularly on methods that align with the previously mentioned first-line treatment goals, which do not include use of pharmacotherapy.

Several pharmaceutical drugs have been shown to increase HDL-C. Pharmaceutical niacin, perhaps the most effective HDL-C raising agent currently available, can increase HDL-C levels by up to 35% (Expert Panel on Detection, Evaluation, and Treatment of High Blood & Cholesterol in Adults, 2001), while fibrates, such as Fenofibrate, modestly raise HDL by 12% (Belfort, Berria, Cornell, & Cusi, 2010). Two cholesteryl ester transfer protein (CETP) inhibitors are currently in later phases of clinical trials and show great promise. Anacetrapib and Evacetrapib have been shown to increase HDL-C by 138.1% and 128.8%, respectively (Cannon et al., 2010; Nicholls et al., 2011). Although pharmacotherapy has been shown to be effective, it can be costly, difficult to obtain, and may not be the preferred treatment for many individuals, especially young adults.

Lifestyle modification, the first step in raising HDL-C levels, involves both dietary and physical activity changes, providing an alternative to pharmacotherapy. It has been shown that moderate alcohol consumption may increase HDL-C, an effect also seen at the dose-response level (Brien, Ronksley, Turner, Mukamal, & Ghali, 2011). Consumption of 1-2 drinks per day increases HDL-C by 1.30 mg/dL; 2-4 drinks per day increases HDL-C by 1.86 mg/dL; and 5 or more drinks per day increases HDL-C by 2.54 mg/dL (Brien, Ronksley, Turner, Mukamal, & Ghali, 2011). When consuming 5 or more drinks per day, one must also consider the potential negative health effects of daily alcohol consumption in larger quantities. Other dietary modifications have been shown to increase HDL-C and may be more achievable, especially for those who do not consume alcohol or for the adolescent and young adult population who are legally unable to consume alcohol. Consumption of fish and omega-3 fatty acids, particularly eicosapentanoic acid (EPA) and docosahexanoic acid (DHA), can modestly increase HDL-C by 1-3% when consumed in amounts totaling 4 grams daily of combined EPA and DHA (Harris, 1997). The Mediterranean diet pattern, characterized by frequent consumption of fruits, vegetables, nuts, legumes, whole grains, and olive oil; low intake of saturated fat, dairy products, and red meat; several times weekly consumption of poultry, fish, and eggs; and moderate consumption of wine with meals, has repeatedly shown to be protective against CVD (de Lorgeril et al., 1999). Short-term adherence to this diet pattern has shown to increase HDL-C levels by 1.17 mg/dL (Kastorini et al., 2011). Another reasonable lifestyle modification, increasing physical activity, particularly aerobic exercise, can modestly increase HDL-C

(Fogelholm, 2010). The successful raising of HDL-C by over 100% by CETP inhibitors, albeit promising, may be unnecessary in the grand scheme of one's health, as this could also increase a person's total cholesterol levels if he or she is not adhering to other lifestyle modifications. Although increases in HDL-C resulting from dietary and lifestyle modifications are quite small when compared to those seen with pharmaceutical agents, making these small changes may improve HDL-C levels, as well as overall health. This is important because achieving optimal HDL-C levels has been associated with reducing CVD (Marcason, 2011).

Expanding the knowledge of alternative approaches to raising HDL-C for additional benefit could be important for those who seek prevention and treatment methods that are not pharmaceutical in nature. Potential benefits of the bioactive components in many accessible fruits and vegetables are still not completely understood to the extent necessary to make a health recommendation. In many cases, certain benefits of these "medicinal" fruits and vegetables may not have been experimentally investigated; rather, knowledge of their medicinal properties is derived from ancient literature. Papaya is an example of a traditional medicinal fruit, the various parts of which have been claimed to relieve obesity and diabetes. For many generations, Yoruba herbalists of South-West Nigeria have used the dry seeds of Carica papaya in the traditional management of suspected diabetic and obese patients (Adeneye & Olagunju, 2009); however, supporting scientific evidence of the use of Carica papaya in the management of diabetes mellitus, obesity, and dyslipidemia is lacking.

Initially originated in southern Mexico and Costa Rica, papaya has since been introduced as a plantation crop in Australia, Hawai'i, the Philippines, Sri Lanka, South Africa, India, and other tropical regions (Krishna, Paridhavi, & Patel, 2008). As with all fruits, papaya is relatively low in calories, but rich in vitamins, minerals, flavonoids, saponins, and carotenoids and contains enzymes, one of which is Carica papaya lipase (CPL) (Krishna, Paridhavi, & Patel, 2008). It has been shown that administration of Carica papaya seed extract significantly reduces fasting blood glucose, serum TG, total cholesterol (TC), LDL-C, and very low-density lipoprotein cholesterol levels and elevates HDL-C levels in Wistar rats; however, it must be noted that rats are not an ideal model for the study of blood lipids (Adeneye & Olagunju, 2009). Although a long-lived traditional medical practice in many countries, including Mexico, the consumption of papaya fruit for the prevention and treatment of obesity, diabetes, and dyslipidemias has not been made a general recommendation for individuals to follow. Due to the high prevalence of low HDL-C in Mexican young adults and the need for reasonable prevention and intervention strategies, we elected to investigate the effect of papaya consumption on HDL-C levels and other blood lipid parameters.

We hypothesized that individuals who consumed three or more servings of papaya per week would have higher HDL-C levels and a more favorable blood lipid profile compared to those who consumed fewer than three weekly servings. The current study aims to determine (1) the overall prevalence of low HDL-C and other blood lipid disorders in Mexican college-age individuals; (2) whether a difference in these parameters exists between individuals consuming three or more servings of papaya fruit per week and those consuming less than three servings per week; and (3) the risk for low HDL-C and other dyslipidemias when consuming less than 3 servings of papaya per week.

MATERIALS AND METHODS

Study Population and Procedure

Participants for the current study were selected from the larger UP AMIGOS (Universities of San Luis Potosí and Illinois: A Multidisciplinary Investigation on Genetics, Obesity, and Social-Environment) 2009 study cohort of college applicants aged 18 to 25 years to the Autonomous University of San Luis Potosí (Universidad Autónoma de San Luis Potosí [UASLP]) who were seeking admission for the 2010 school cycle between February and July of 2009 (for participant selection schematic, see Chapter 2, Figure 1). As part of the UASLP application process, all participants were submitted to a health screen at the university clinic. The health screen consisted of: (1) anthropometric measurements, including height, weight, waist circumference, and blood pressure; (2) a medical interview and physical exam executed by a physician; (3) a blood draw following an overnight fast for blood biomarkers; and (4) a food frequency questionnaire based upon the Willett food frequency questionnaire adapted for the Mexican population. Individuals willing to participate were apprised of study information and their rights for our ongoing collaborative project before signing the informed consent form. The protocol was reviewed and approved by both Institutional Review Boards at UASLP and at the University of Illinois at Urbana-Champaign.

Participant Selection

Participants for the current cross-sectional study were selected based upon the degree of completion of data available from the health clinic assessment, including a complete lipid profile, and from the food frequency questionnaire (Hernandez-Avila et al., 1998) (see Appendix A), of which 90% or more of the 118 items was completed. Individuals with calorie consumption ± 4 SD were excluded (n=4). Individuals with a BMI ≤ 18.49 kg/m^2 and ≥ 40.00 kg/m^2 were also excluded to prevent skewing results of the study. The final subset consisted of 339 individuals, as in the previous study.

Anthropometric Measures

Anthropometric measures were conducted by trained health professionals at the UASLP health clinic. Height was measured twice in the same visit using a fixed stadiometer and was recorded to the nearest 0.5 cm, with the final measurement representing an average of the two measures. Weight was also collected twice in the same visit on a calibrated scale (attached to the stadiometer) (Torino, Tecno Lógica, Mexicana, Mexico) and recorded to the nearest 0.1 kg, with the final measurement representing an average of the two measures. BMI was calculated and classified according to the WHO (World Health Organization, 2000) as follows: underweight (≤ 18.49 kg/m^2), normal weight (18.50 – 24.99 kg/m^2), overweight (25.00 – 29.99 kg/m^2), and obese (≥ 30.00 kg/m^2).

Blood Biomarkers

Following the medical examination, overnight (≥ 8 hours) fasting blood samples were collected. Fasting blood glucose was determined according to the glucose oxidase peroxidase method (Alcyon 300 autoanalyzer from Abbott [Chicago, IL] and reagents from Biosystems [Barcelona, Spain]). Impaired fasting glucose (IFG) was defined as having a fasting glucose > 100 mg/dL (Alberti et al., 2009). According to the data of this subset, we assumed that participants adhered to fasting guidelines, as no blood glucose values over 110 mg/dL were observed. The determination of serum lipid profiles was carried out by the same Alcyon 300 analyzer for diagnostic use *in vitro* (results are expressed in mg/dL). Serum TG and total cholesterol (TC) were determined according to the glycerol phosphate oxidase peroxidase method, based on a colorimetric enzymatic reaction and measured in the Alcyon 300 analyzer. HDL-C was determined by a direct method in which a detergent solubilized the HDL-C, which was then quantified spectrophotometrically according to the cholesterol oxidase method. LDL-C was calculated based upon the Friedewald equation (Warnick, Knopp, Fitzpatrick, & Branson, 1990). Hypertriglyceridemia was defined as having fasting serum TG ≥ 150 mg/dL; low HDL-C was defined as having fasting HDL-C < 40 mg/dL (males) and < 50 mg/dL (females); high LDL-C was defined as having fasting LDL-C > 130 mg/dL; and hypercholesterolemia was defined as having fasting TC > 200 mg/dL (Alberti et al., 2009). It bears noting that, according to the AHA, the higher HDL-C cutoff in females is due to the greater presence (during childbearing years) of the female sex hormone, estrogen, which tends to raise HDL-C.

Dietary Assessment

Participants completed a validated 118-item Willett food frequency questionnaire that was adapted for the Mexican population in order to include commonly consumed foods and beverages in Mexico (Hernandez-Avila et al., 1998) (see Appendix A). Questionnaire responses were entered into the SNUT (Sistema de Evaluacion de Habitos Nutricionales y Consumos de Nutrimientos; developed by the National Institute of Public Health, Mexico) nutrition software for nutrient analysis. Results from the nutrient analysis were calculated by the SNUT software and exported to SAS version 9.2 (SAS Institute Inc.; Cary, NC) for further data analysis. Frequency of consumption estimates were determined by using the following weights that correspond to survey responses: a) 6 for reported frequencies of 6 or more per day; b) 4.5 for 4-5 per day; c) 2.5 for 2-3 per day; d) 1 for 1 per day; e) 0.8 for 5-6 per week; f) 0.43 for 2-4 per week; g) 0.08 for 2-3 per month; and h) 0.016 for 1 or less per month (Hernandez-Avila et al., 1998). In order to calculate weekly consumption frequencies, the values obtained for daily consumption were multiplied by 7. The fruits and vegetables included in the analyses were: banana, orange, orange juice, melon, apple, watermelon, pineapple, papaya, pear, mango, tangerine, strawberries, peach, grapes, prickly pear, plum, mamey sapote, sapote, tomato sauce, tomato, potato, carrots, lettuce, spinach, squash, cactus, peppers, vegetable soup, avocado, pumpkin, cauliflower, green beans, and dried chilis. Corn was also included due to its carotenoid content. Participants were categorized into two groups based upon the level of consumption of papaya as denoted by the third quartile of consumption: (1) less than 3 servings, or 75% of the subset; and (2) 3 or more servings, a criterion met by 25% of the subset.

Physical Activity Questionnaire

PA was assessed by administering the long version of the IPAQ to each participant (Hallal & Victoria, 2004) (see Appendix B). As in the previous study, responses were categorized into three groups based on ever having engaged in PA: 1) low or no PA; 2) moderate PA; and 3) high or vigorous PA. We did not include exercise duration in this analysis.

Statistical Analysis

All data were analyzed by SAS version 9.2. Continuous variables were assessed for normality and log-transformed ($\log_{10}$) to reduce skewness before performing any statistical analyses. Except for BMI and total energy, the remaining variables were log-transformed in order to perform the analysis. One-way ANOVA was performed to compare differences between individuals consuming < 3 servings or ≥ 3 servings of papaya per week. Differences were considered significant where $p < 0.05$. Participants were categorized as previously stated. Relative risk ratios to assess low HDL-C and other blood lipid parameters were estimated using modified Poisson logistic regressions and various adjustment models (Spiegelman & Hertzmark, 2005). The following blood lipid parameters were assessed: (1) hypertriglyceridemia, fasting serum TG ≥ 150 mg/dL; (2) fasting serum HDL-C < 40 mg/dL (males) and < 50 mg/dL (females); (3) fasting LDL-C > 130 mg/dL (calculated using the Friedewald equation, cited above); and (4) fasting serum TC > 200 mg/dL. In the current study, we report on two Poisson logistic regression models: (1) adjusted for age; and (2) adjusted for age and family history of

CVD. Due to the relationship between cholesterol levels and increasing age, we controlled for age to adjust for even minor differences. The classification used in the Poisson logistic regressions was consumption of < 3 servings of papaya per week. The SAS package version 9.2 (SAS Institute, Cary, NC, USA) was used for all statistical analyses.

RESULTS

Slightly more than half of the participants (51.6%, n = 176) had low HDL-C. Table 8 summarizes the prevalence (represented in raw calculated percentages) of the dyslipidemias measured in the current study. The overall prevalence of hypertriglyceridemia, high LDL-C, and hypercholesterolemia were 19.5%, 48.4%, and 20.4%, respectively. After comparing males and females, the prevalence of low HDL-C, hypertriglyceridemia, high LDL-C, and hypercholesterolemia were only slightly higher in females. Between papaya consumption groups, there were differences in the prevalence of dyslipidemias. In individuals consuming < 3 servings of papaya per week, the prevalence of hypertriglyceridemia was 17.1%, a 7-fold increase in prevalence than was observed in those who consumed ≥ 3 servings of papaya per week. Further, the prevalence of low HDL-C, high LDL-C, and hypercholesterolemia in those who consumed < 3 servings of papaya per week were 44.3%, 41.3%, and 16.2%, respectively. Low HDL-C and high LDL-C each occurred in six times as many individuals who consumed < 3 servings of papaya per week compared to those who consumed ≥ 3 servings of papaya per week, while hypercholesterolemia occurred in four times as many individuals who consumed < 3 servings of papaya per week compared to those who consumed ≥ 3 servings of papaya per week.

Due to the differing cutoffs for HDL-C in males and females, we also compared the general characteristics of the study participants between males and females (Table 9). As expected, females had higher levels of HDL-C compared to males (p = 0.002). However, no other significant differences in blood lipid parameters were observed between the sexes. Nutritionally, males consumed more calories and fiber daily than did females ($p = 0.016$ and $p = 0.025$, respectively). We did not observe a significance difference in daily niacin intake between males and females.

We compared general characteristics of the study participants according to the papaya consumption groups (Table 10). We observed no differences in age, BMI, serum TG, HDL-C, calculated LDL-C, or TC between the two groups. After comparing total nutrient consumption between those consuming < 3 and ≥ 3 servings of papaya per week, we observed significant differences in total calorie intake, which was higher in the group consuming ≥ 3 servings of papaya per week (A difference of 459 calories/day, $p = 0.002$).

We evaluated the contribution of the level of papaya consumption to the relative risk for dyslipidemias in males and females separately using the reference papaya consumption of < 3 servings of papaya fruit per week (Table 11). No risk was observed for hypertriglyceridemia, high LDL-C, or hypercholesterolemia in either males or females for either of the models used. However, in females only, it was observed that those who consumed < 3 servings of papaya per week may be at 1.5 times greater risk for low HDL-C (95% CI 1.0–2.3, $p = 0.05$) after adjustment for age and family history of CVD; however, this finding is inconclusive due to 1.0 being contained within the confidence interval. (Other relative risk models can be found in Appendix E.)

Lastly, to assess overall fruit and vegetable intake, we evaluated carotenoid intake and compared these intake values between the two papaya consumption groups. Fruits and vegetables were compared between the two papaya consumption groups by males and females separately. Individuals who consumed ≥ 3 servings of papaya per week consumed more alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein, and overall total carotenoids, indicative of overall higher total carotenoid intake (Table 12). To confirm this notion, we compared fruit and vegetable intake between the two papaya consumption groups (Table 13). When comparing fruit and vegetable intake in males, those who consumed ≥ 3 servings of papaya per week consumed more total fruit and vegetable servings per week (78.9 servings vs. 35.9 servings, $p < 0.0001$). They also consumed more servings of orange juice, melon, apple, pineapple, papaya, pear, mango, strawberries, peach, grapes, prickly pear, plum, carrots, lettuce, spinach, squash, peppers, vegetable soup, and avocado. There were no differences in intake of banana, orange, tangerine, mamey sapote, sapote, tomato sauce, tomato, potato, cactus, pumpkin, cauliflower, green beans, dried chilis, or corn. Females who consumed ≥ 3 servings of papaya per week also consumed more total servings of fruits and vegetables per week than those who consumed fewer than 3 servings of papaya per week (72.9 servings vs. 48.6 servings, $p = 0.002$). These individuals also consumed more weekly servings of melon, watermelon, pineapple, papaya, pear, peach, lettuce, spinach, squash, and cauliflower, but not of the other fruits or vegetables that were included in the analysis. Indeed, individuals who consume ≥ 3 servings of papaya per week consume more fruits and vegetables; therefore, more frequent papaya consumption may be an indicator for a healthier, more varietal dietary intake overall, particularly consumption of fruits and vegetables.

DISCUSSION

The current study had a goal to address part of the ancient medicinal claim that consuming more papaya fruit may relieve obesity and obesity-related diseases. The aims included determining the overall prevalence of dyslipidemias in Mexican young adults, detecting a potential difference in blood lipid parameters between individuals consuming < 3 servings of papaya per week and those consuming ≥ 3 servings of papaya per week, and evaluating the risk for low HDL-C and other dyslipidemias according to the level of papaya consumption. More than half (51.6%) of the young adults in the current study had low HDL-C, which was slightly below the ENSANUT 2006 report of low HDL-C present in 61.9% of individuals aged 20 to 29 years (Aguilar-Salinas et al., 2010). We also observed overall prevalence of 19.5%, 48.4%, and 20.4% of hypertriglyceridemia, high LDL-C, and hypercholesterolemia, respectively. The rates we observed for hypertriglyceridemia and hypercholesterolemia were lower than was previously reported from ENSANUT 2006 for the 20 to 29 year-old age group; however, the prevalence of high LDL-C in our study was higher than the rate observed in the national report (Aguilar-Salinas et al., 2010). Interestingly, ENSANUT 2006 reports higher prevalence of hypertriglyceridemia and low HDL-C in men (Aguilar-Salinas et al., 2010). In our study, after comparing males and females, the prevalence of hypertriglyceridemia, low HDL-C, high LDL-C, and hypercholesterolemia were only slightly higher in females than in males.

After categorizing participants based upon the third quartile of papaya fruit consumption per week, we compared the prevalence of the dyslipidemias between individuals consuming < 3 servings of papaya per week and those consuming ≥ 3 or more servings of papaya per week. Across the four dyslipidemias, individuals who consumed < 3 servings of papaya per week had higher prevalence rates than those who consumed ≥ 3 or more servings of papaya per week. Hypertriglyceridemia was present in 2.4% of those consuming ≥ 3 or more servings per week, while 17.1% of those consuming < 3 servings per week had hypertriglyceridemia, a 7-fold increase in prevalence. The prevalence of low HDL-C and high LDL-C were six times higher in those consuming < 3 servings of papaya per week, while the prevalence of hypercholesterolemia was four times higher in this group. To the best of our knowledge, this study is the first to investigate a relationship of papaya consumption and prevalence of dyslipidemia. Therefore, our findings cannot be compared to data in the current literature and must be replicated.

To complete the final objective of the study, we evaluated the contribution of the level of papaya consumption to the relative risk for dyslipidemias in males and females separately. Using the reference papaya consumption of < 3 servings of papaya fruit per week, we observed no risks for dyslipidemias we investigated. One study that investigated dietary patterns and MetS risk in adult Samoans concluded that those consuming the neo-traditional dietary pattern (with papaya fruit being a defining characteristic) had increased serum concentrations of HDL-C and lower prevalence of MetS than those consuming the modern dietary pattern (DiBello et al., 2009). The authors noted that papaya and papaya soup, common to the neo-traditional dietary pattern, represented an important source of fiber in the Samoan Islands diet, potentially contributing to some of the findings (DiBello et al., 2009). However, in our study, we observed no significant difference in fiber intake between papaya consumption groups, so we suspect that there may be more explanations for our findings.

To further explore our findings, we evaluated and compared carotenoid and fruit and vegetable intake between the two papaya consumption groups. Individuals who consumed ≥ 3 servings of papaya per week consumed more total carotenoids, indicating that they may consume more total fruits and vegetables overall. After comparing males and females separately, the males and females who consumed ≥ 3 servings of papaya per week did in fact consume more total fruits and vegetables on a weekly basis, particularly those of more variety. Papaya intake above 3 servings per week may be indicative of a more nutritional and varietal diet overall. Because fruit and vegetable intake has been shown to be protective against various metabolic risk factors, it is recommended that all individuals meet fruit and vegetable intake guidelines while incorporating a variety as well (Hong, et al., 2012).

It warrants mentioning that we observed a significant difference in energy intake between the two groups. Individuals who consumed ≥ 3 or more servings of papaya per week consumed ~450 calories more per day (on average) than those who consumed < 3 servings per week. Despite this dissimilarity, we observed no significant differences in BMI or in any of the mean lipid concentrations between the two papaya consumption groups (although the prevalence of dyslipidemias were higher in the low papaya intake group). After further analysis to determine the source of additional energy intake (data not shown), the only foods consumed more by the group consuming ≥ 3 or more servings of papaya per week and substantially enough to contribute to the energy difference were the dairy foods, particularly milk, cheese, and yogurt. Future analyses should be considered to investigate a potential positive interaction between dairy and fruit and vegetable consumption on the health of Mexican young adults.

The strengths and weaknesses of this study need to be discussed. First, to our knowledge, this is the first study to investigate the potential beneficial relationship between papaya consumption and dyslipidemias, specifically low HDL-C. Low HDL-C is quite prevalent in Hispanic populations, particularly in young adults (Aguilar-Salinas et al., 2010). Although preliminary, the results of the current study show promise and should be further investigated through randomized controlled trials to determine whether papaya consumption could be an effective dietary prevention and intervention option for low HDL-C. Furthermore, this study focuses on individuals aged 18 to 25 years, who usually do not have access to regular health screening by a physician. Individuals may begin to see a physician for a preventive care visit infrequently prior to this age and even as early as age of 13 (Nordin, Solberg, & Parker, 2010).

These findings support the need for early detection, prevention, and treatment strategies for low HDL-C and other dyslipidemias. It is crucial to detect this condition early, as it may just be the tip of the iceberg; other metabolic disease may be present or in the process of development. The consumption of papaya fruit is a simple dietary modification that may help maintain HDL-C levels within normal range. On the other hand, the limitations of this study are worth mentioning. The cross-sectional design, small sample size, and our inability to determine reasons for papaya consumption or lack thereof primarily limit our capacity to infer more from the results. One important factor that must be considered is the timing of the seasonal availability of papaya in Mexico with the time of data collection, which occurred between February and July of 2009. This may have a slight effect on the results and must be considered when interpreting the results. Another limitation of the current study is the self-reporting methodology used for our data collection. It is known that individuals tend to underreport calorie intake and that overweight and obese individuals underreport more than normal weight individuals (Bedard, Shatenstein, & Nadon, 2004; Voss, Kroke, Klipstein Grobusch, & Boeing, 1997).

After considering the disparities in prevalence between the two papaya consumption groups and the risk observed, it is important to search for more insight and to conduct future research to investigate the relationship between papaya consumption and risk for dyslipidemias, as it may be an effective dietary modification in the prevention and treatment of lipid disorders.

CONCLUSION

Overall, we observed that individuals who consumed more servings of papaya had lower prevalence of dyslipidemias. Since these individuals also consumed more fruits and vegetables, it will be important to investigate the possible protective effect of fruit and vegetable intake on MetS in Mexican young adults. To further support the efficacy of this dietary modification, future studies need to be conducted to investigate this claim that has begun to re-emerge from ancient Ayurvedic literature.

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Table 8. Prevalence of low HDL-C (presented in raw calculated percentages) and other blood lipid parameters in all individuals, males and females, those consuming < 3 servings of papaya/week, and those consuming ≥ 3 servings of papaya/week.

	All	**Males**	**Females**	**< 3 servings**	**≥ 3 servings**
n (males/females)	339 (167/172)	167	172	285 (143/142)	54 (24/30)
Blood Lipid Parameter			*Prevalence (%)*		
Hypertriglyceridemia	19.5	9.1	10.3	17.1	2.4
Low HDL-C	51.6	20.4	31.3	44.3	7.4
High LDL-C	48.4	23.6	24.8	41.3	7.1
Hypercholesterolemia	20.4	8.9	11.5	16.2	4.1

Frequency cross-tabulations.
Abbreviations: HDL-C, fasting serum HDL cholesterol; LDL-C, fasting serum LDL cholesterol.

Table 9. Comparison of blood lipid measures and nutrient intake between male and female Mexican college applicants.

	All		Males		Females		***p***
Participants, n	339		167		172		
Participant Characteristics	*Mean*	*95% CI*	*Mean*	*95% CI*	*Mean*	*95% CI*	
Age, *years*	18.9	18.7, 19.0	18.8	18.6, 18.9	19.0	18.8, 19.2	0.12
BMI, *kg/m²*	25.0	24.6, 25.5	25.1	24.4, 25.7	25.0	24.3, 25.7	0.83
TG, *mg/dL*	118.3	112.0, 124.6	118.8	109.3, 128.2	117.9	109.5, 126.4	0.64
HDL-C, *mg/dL*	47.5	46.1, 48.8	45.3	43.5, 47.1	49.7	47.7, 51.6	0.002
LDL-C, *mg/dL*	103.7	100.7, 106.7	103.4	99.4, 107.5	104.0	99.6, 108.4	0.99
Total cholesterol, *mg/dL*	174.8	171.1, 178.6	172.5	167.5, 177.4	177.2	171.5, 182.9	0.42
Nutrient Intake	*Mean*	*95% CI*	*Mean*	*95% CI*	*Mean*	*95% CI*	
Papaya, *servings per week*	1.0	0.8, 1.2	0.8	0.6, 1.1	1.2	0.9, 1.5	
Calories	2217	2106, 2329	2357	2174, 2539	2082	1954, 2209	0.016
Fiber, *g*	25.6	24.1, 27.0	26.0	23.8, 28.2	25.2	23.3, 27.1	0.025
Niacin, *mg*	19.2	18.0, 20.4	20.6	18.6, 23.0	17.8	16.6, 19.1	0.72

One-way ANOVA was used to detect significance at $p \leq 0.05$.
Abbreviations: BMI, body mass index; TG, fasting serum TG; HDL-C, fasting serum HDL cholesterol; LDL-C, fasting serum LDL cholesterol.
*Calorie intake was adjusted by age and sex.
† All variables, except age, were adjusted for age, sex, and daily calorie intake.

Table 10. Comparison of blood lipid measures and nutrient intake of Mexican college applicants between individuals consuming < 3 servings of papaya per week and ≥ 3 servings of papaya per week.

	< 3 Servings Papaya/Wk (Mean, 95% CI 0.4, 0.3-0.4)		**≥ 3 Servings Papaya/Wk** (Mean, 95% CI 4.3, 3.7-4.9)		***p***
Participants, n (M/F)	285 (143/142)		54 (24/30)		
Participant Characteristics	*Mean*	*95% CI*	*Mean*	*95% CI*	
Age, *years*	18.9	18.7, 19.1	18.7	18.4, 19.0	0.20
BMI, kg/m^2	25.0	24.5, 25.5	25.4	24.2, 26.6	0.45
TG, *mg/dL*	120.9	113.8, 128.1	104.9	93.5, 116.3	0.10
HDL-C, *mg/dL*	47.3	45.8, 48.8	48.5	45.2, 51.9	0.31
Males	45.5	43.6, 47.4	44.0	38.4, 49.6	0.74
Females	49.1	46.9, 51.3	52.1	48.3, 56.0	0.14
LDL-C, *mg/dL*	103.6	100.4, 106.8	104.4	96.4, 112.4	0.97
Total cholesterol, *mg/dL*	175.0	170.9, 179.2	173.9	164.1, 183.7	0.82
Nutrient Intake	*Mean*	*95% CI*	*Mean*	*95% CI*	
Calories	2144	2030, 2258	2603	2259, 2946	0.002
Fiber, *g*	24.5	23.0, 26.0	31.2	26.6, 35.7	0.12
Niacin, *mg*	18.3	17.1, 19.5	24.0	20.1, 27.8	0.10

One-way ANOVA was used to detect significance at $p \leq 0.05$.
Abbreviations: BMI, body mass index; TG, fasting serum TG; HDL-C, fasting serum HDL cholesterol; LDL-C, fasting serum LDL cholesterol.
*Calorie intake was adjusted by age and sex.
† All variables, except age, were adjusted for age, sex, and daily calorie intake.

Table 11. Relative risk for blood lipid parameters according to papaya consumption in young Mexican adults (18-25 years).

Consumption of < 3 Papaya Servings per week	Model 1[†]			Model 2[‡]		
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***
Males						
Triglycerides ≥ 150 mg/dL	1.1	0.4, 3.0	0.80	1.1	0.4, 2.9	0.80
HDL-C < 40 mg/dL	0.8	0.5, 1.2	0.31	0.8	0.5, 1.2	0.31
LDL-C > 130 mg/dL	0.9	0.6, 1.3	0.53	0.9	0.6, 1.3	0.53
Total Cholesterol > 200 mg/dL	0.9	0.4, 2.1	0.76	0.9	0.4, 2.1	0.73
Females						
Triglycerides ≥ 150 mg/dL	1.7	0.6, 4.3	0.31	1.7	0.6, 4.3	0.30
HDL-C < 50 mg/dL	1.5	1.5, 2.3	0.06	1.5	1.0, 2.3	0.05
LDL-C > 130 mg/dL	1.4	0.9, 2.4	0.16	1.4	0.9, 2.4	0.15
Total Cholesterol > 200 mg/dL	0.7	0.4, 1.3	0.26	0.7	0.4, 1.3	0.26

Relative risk ratios were estimated using a modified Poisson logistic regression.
Abbreviations: TG, fasting serum TG; HDL-C, fasting serum HDL cholesterol; LDL-C, fasting serum LDL cholesterol.
[†] Model 1 adjusted for age.
[‡] Model 2 adjusted for age and family history of cardiovascular disease.

Table 12. Comparison of carotenoid intake of Mexican college applicants between individuals consuming < 3 servings of papaya per week and ≥ 3 servings of papaya per week.

	< 3 Servings Papaya/Wk (Mean, 95% CI 0.4, 0.3-0.4)		**≥ 3 Servings Papaya/Wk** (Mean, 95% CI 4.3, 3.7-4.9)		***p***
Participants, n (M/F)	285 (143/142)		54 (24/30)		
Participant Characteristics	*Mean*	*95% CI*	*Mean*	*95% CI*	
Total Carotenoids, *mg*	4453	4013, 4984	8235	6444, 10,026	<0.0001
Alpha-carotene, *mg*	265	231, 300	467	319, 615	0.003
Beta-carotene, *mg*	1969	1764, 2174	3577	2816, 4338	<0.0001
Beta-cryptoxanthin, *mg*	261	216, 307	799	652, 946	<0.0001
Lycopene, *mg*	4985	4382, 5587	7376	5801, 8951	0.005
Lutein, *mg*	906	804, 1007	2124	1513, 2734	<0.0001

One-way ANOVA was used to detect significance at p ≤ 0.05.

Table 13. Comparison of weekly fruit and vegetable* intake of Mexican college applicants between males and females (separately) consuming < 3 servings of papaya per week and ≥ 3 servings of papaya per week.

	< 3 Servings Papaya/Wk		**≥ 3 Servings Papaya/Wk**		***p***
Males, n	143		24		
Food Item	*Mean*	*95% CI*	*Mean*	*95% CI*	
Total F&V Intake**	35.9	31.4, 40.5	78.9	53.8, 104.1	<0.0001
Banana	2.3	1.8, 2.6	4.4	2.1, 6.7	0.10
Orange	2.3	1.7, 2.8	3.4	2.7, 4.2	0.41
Orange Juice	1.7	1.3, 2.1	3.3	1.8, 4.9	0.02
Melon	0.8	0.5, 1.1	1.9	1.1, 2.6	<0.0001
Apple	2.0	1.5, 2.4	4.0	2.1, 5.9	0.01
Watermelon	0.9	0.4, 1.4	2.0	1.2, 2.8	<0.0001
Pineapple	0.6	0.4, 0.8	2.3	0.8, 3.7	<0.0001
Papaya	0.34	0.3, 0.4	3.8	3.3, 4.4	<0.0001
Pear	0.5	0.4, 0.7	1.7	0.9, 2.4	0.0002
Mango	1.0	0.7, 1.4	4.2	1.3, 7.1	0.003
Tangerine	2.5	1.6, 3.4	3.0	1.4, 4.6	0.52
Strawberries	0.6	0.4, 0.8	3.8	0.2, 7.4	0.0006
Peach	0.5	0.4, 0.6	2.3	0.7, 4.0	0.005

Table 13 (cont.)

Grapes	0.7	0.5, 0.9	1.4	0.6, 2.2	0.02
Prickly Pear	0.4	0.3, 0.5	0.7	0.3, 1.0	0.05
Plum	0.3	0.2, 0.5	2.1	-0.6, 4.8	0.0004
Mamey Sapote	0.1	0.1, 0.2	0.4	0.1, 0.6	0.27
Sapote	0.1	0.0, 0.1	0.3	0.0, 0.7	0.18
Tomato Sauce	3.7	2.9, 4.4	4.4	2.1, 6.7	0.83
Tomato	2.3	1.7, 2.8	2.7	1.7, 3.7	0.89
Potato	2.2	1.5, 2.9	2.3	1.5, 3.0	0.15
Carrots	1.0	0.8, 1.2	1.6	1.0, 2.0	0.005
Lettuce	1.6	1.3, 1.8	3.6	1.6, 5.6	0.04
Spinach	0.7	0.5, 0.9	2.6	0.9, 4.3	0.002
Squash	0.7	0.5, 0.9	2.2	0.6, 3.7	0.03
Cactus	0.7	0.5, 0.9	1.2	0.5, 1.9	0.11
Peppers	0.4	0.3, 0.5	0.8	0.4, 1.2	0.01
Vegetable Soup	0.7	0.5, 0.9	2.0	0.4, 3.6	0.03
Avocado	1.6	1.1, 2.0	3.6	1.6, 5.6	0.01
Pumpkin	0.3	0.2, 0.5	1.2	-0.4, 2.7	0.18
Cauliflower	0.4	0.3, 0.5	1.0	0.3, 1.7	0.06
Green Beans	0.4	0.3, 0.6	0.8	0.3, 1.4	0.17
Dried Chilis	1.6	0.7, 2.5	1.8	0.2, 3.3	0.94

Table 13 (cont.)

Corn	1.0	0.7, 1.3	1.4	0.7, 2.1	0.48
Females, n	142		30		
Food Item	*Mean*	*95% CI*	*Mean*	*95% CI*	
Total F&V Intake**	48.6	42.1, 55.1	72.9	55.6, 90.1	0.002
Banana	2.0	1.3, 2.7	1.3	0.8, 1.8	0.77
Orange	3.1	2.3, 4.0	3.9	2.4, 5.5	0.23
Orange Juice	3.1	2.1, 4.2	3.2	1.9, 4.6	0.45
Melon	1.0	0.6, 1.5	1.9	1.1, 2.7	0.01
Apple	2.8	2.3, 3.4	3.5	2.2, 4.8	0.80
Watermelon	0.7	0.5, 0.8	2.7	1.3, 4.1	0.0001
Pineapple	0.7	0.5, 0.8	1.6	1.0, 2.2	0.0004
Papaya	0.4	0.4, 0.5	4.7	3.6, 5.8	<0.0001
Pear	0.6	0.4, 0.7	1.5	0.7, 2.2	0.004
Mango	1.3	0.6, 2.0	2.2	0.8, 3.6	0.09
Tangerine	3.6	2.4, 4.8	4.9	2.3, 7.4	0.17
Strawberries	1.3	0.6, 2.1	1.9	0.6, 3.2	0.07
Peach	0.7	0.5, 0.9	1.2	0.6, 1.8	0.02
Grapes	1.0	0.7, 1.3	2.1	0.8, 3.4	0.06
Prickly Pear	0.7	0.1, 1.3	0.8	0.2, 1.4	0.69
Plum	0.6	0.0, 1.2	0.9	0.3, 1.5	0.61

Table 13 (cont.)

Mamey Sapote	0.1	0.0, 0.1	0.5	-0.1, 1.1	0.08
Sapote	0.1	0.0, 0.2	0.5	-0.2, 1.0	0.88
Tomato Sauce	5.7	4.5, 6.8	4.3	2.5, 6.2	0.17
Tomato	3.4	2.7, 4.1	3.9	2.3, 5.5	0.64
Potato	1.9	1.6, 2.2	2.5	1.3, 3.7	0.87
Carrots	1.4	0.9, 1.9	2.3	1.2, 3.5	0.07
Lettuce	2.5	2.0, 3.0	5.0	3.3, 6.8	0.002
Spinach	1.0	0.5, 1.5	2.3	1.0, 3.7	0.01
Squash	0.9	0.7, 1.1	2.3	1.1, 3.6	0.0003
Cactus	0.9	0.7, 1.1	1.2	0.7, 1.7	0.72
Peppers	0.3	0.2, 0.5	0.5	0.1, 0.8	0.65
Vegetable Soup	0.8	0.6, 1.0	1.5	0.3, 2.7	0.15
Avocado	1.5	1.2, 1.8	1.9	1.3, 2.6	0.18
Pumpkin	0.5	0.2, 0.8	0.5	0.2, 0.8	0.98
Cauliflower	0.6	0.4, 0.7	1.5	0.3, 2.7	0.03
Green Beans	1.2	0.4, 1.9	1.5	0.3, 2.7	0.44
Dried Chilis	1.7	0.9, 2.5	2.0	0.7, 3.3	0.55
Corn	1.2	0.9, 1.6	2.0	0.7, 3.2	0.18

One-way ANOVA was used to detect significance at $p \leq 0.05$.
*Corn was included due to its carotenoid content.
**Total F&V Intake is the sum of weekly consumption of all fruits and vegetables included in the table.

Abbreviation: F&V, fruit and vegetable.

CHAPTER 4: CONCLUDING REMARKS AND FUTURE DIRECTIONS

Concluding Remarks

Similar to the United States, Mexico's rates of overweight and obesity are quite high. In fact, the prevalence of overweight and obesity in Mexico slightly surpasses that of the United States, with 72% of adults aged 20 years and older (Barquera, Campos-Nonato et al., 2009) and 26% of children and adolescents affected (Bonvecchio et al., 2009). A crucial time period of development is the transition from adolescence to adulthood; the time in which many young adults attend a college or university. During this time, many young adults do not regularly see a physician, allowing any present risk factors to go undetected. Current estimates of Mexican college age individuals aged 20 to 29 years report a prevalence of 55.8% for overweight and obesity combined, which translates to approximately 5.9 million people (Barquera, Campos-Nonato et al., 2009).

Because obesity is related to the development of other unfavorable conditions, it is necessary to evaluate individuals using markers that may indicate risk. Abdominal obesity, characterized by excess fat in the abdominal area, is closely associated with the development of CVD, T2D, and other metabolic risk factors (Bjorntorp, 1992). Measuring WC has proven an effective marker of total and abdominal fat, an independent predictor of insulin control, and the single most important predictor of MetS in younger individuals (Lee, Bacha, Gungor, & Arslanian, 2006). The prevalence of abdominal obesity has increased over time along with the growing rates of overweight and obesity. A 2009 estimation of the prevalence of abdominal obesity in Mexican and Mexican American women was 45% (Vella, Zubia, Ontiveros, & Cruz, 2009). These individuals are at greater risk for metabolic diseases, specifically for the conditions that constitute MetS.

MetS, a clustering of abdominal obesity, dyslipidemia, EBP, and T2D that affects millions of individuals, was identified as a result of the growing obesity epidemic (Reaven, 1988). Although controversial, MetS is a useful tool to identify at-risk individuals early so that intervention strategies can be implemented sooner rather than later. Thirty-six percent of Mexican individuals aged 20 to 39 years have MetS (Rojas et al., 2010); a rate that makes any concerned individual fearful of what is to come if effective prevention and intervention strategies are not established. However, in order to develop such strategies, it is important to understand the origin of obesity and obesity-related risk factors.

The origin, or "cause," of obesity and obesity-related diseases is a complex combination of environmental, social, and genetic factors, all of which have been shaped by the evolution and adaptation of humankind. Changes in the diet that have occurred since the dawning of the industrial revolution have drastically increased life-threatening conditions, including obesity, hypertension, T2D, and dyslipidemias. These responses are typically a result from adaption to a diet pattern characterized by characterized by high refined grain, pastry, fast food, and soda intake and low whole grain cereal, seafood, and dairy consumption. The true adaptation is observed in healthy individuals who manage to maintain a normal, healthy weight in the absence of other obesity-related conditions. Provided the human body stays true to history, perhaps we need to change the type of foods available and the accessibility of those foods as well. For Mexico specifically, shifting back toward a traditional dietary pattern may be a step toward better health, as it was shown to be associated with lower disease risk (Denova-Gutierrez et al., 2010; Denova-Gutierrez et al., 2011; Flores et al., 2010). However, these changes do not occur rapidly; small, attainable steps must be taken to achieve healthful dietary modification. If this is possible, the genetic variants related to certain diseases may not weigh in as heavy a contributor to the development of obesity-related diseases and the trajectory of overall health can shift away from such diseases. The ultimate solution may be improving the diet our bodies need to healthfully adapt to the environment instead of providing a series of additional “supplements” to be taken twice by mouth daily with the potential of causing side effects more severe than those conditions they aim to treat.

Feasible dietary modifications were investigated to evaluate their potential for incorporation into prevention and intervention strategies for Mexican young adults. After analysis of the association between dairy consumption and MetS in Chapter 2, which was prevalent in 10.6% of our study sample, we observed that individuals who were not meeting the USDA recommendation of three servings of dairy per day may be at three times greater risk for having MetS. Whether SSB consumption was instrumental in leading to reduced dairy intake was undeterminable. Nevertheless, our findings indicate that simply meeting dairy recommendations may serve as an effective dietary prevention and intervention strategy to reduce individual risk for MetS.

The second potential dietary modification we explored, reported in Chapter 3, was the relationship between papaya consumption and low HDL-C and other dyslipidemias. Papaya consumption at the third quartile, three servings per week, was selected as a cutoff in order to provide a comprehensible, positive, potential health message that could be easily delivered to the public. Individuals who consumed < 3 servings of papaya per week had higher rates of hypertriglyceridemia, low HDL-C, high LDL-C, and hypercholesterolemia than those who consumed ≥ 3 servings of papaya per week. Additionally, females who consumed < 3 servings of papaya per week may be at 1.5 times greater risk for low HDL-C; however, our findings were inconclusive. It is possible that the higher fruit and vegetable intake of individuals who consumed more papaya may play a role in this relationship.

Further research needs to be conducted to investigate these findings so that they can be properly incorporated into prevention and intervention strategies for Mexican young adults.

Future Directions

In order to accurately determine whether the consumption of dairy three times per day is a feasible prevention and intervention measure for Mexican young adults, it would be ideal to conduct a randomized, controlled trial with an extended follow-up period. If the findings reported in Chapter 2 are confirmed, then this simple dietary modification can be incorporated into the framework for obesity and obesity-related disease prevention in Mexican young adults aged 18 to 25 years. One aspect that we were unable to explore, low-fat vs. high-fat dairy consumption, would be an asset to the randomized, controlled trial to observe any differences or benefits of the two types of dairy.

Similarly, to justify the findings we reported in Chapter 3, a great deal of progress must be made, as this is a topic in which supporting literature is lacking. However, in this case, testing this hypothesis in a randomized, controlled trial would help confirm whether consumption of papaya and other fruits and vegetables at various levels reduces risk of dyslipidemias in Mexican young adults of the same age. By maintaining an extended follow-up period, the long-term effects of papaya consumption on blood lipid parameters can be observed for monitoring of CHD and CVD risk as study participants age.

Ideally, after further data analysis investigating the interaction between dairy and papaya (and total fruit and vegetable) consumption, a randomized, controlled trial combining these two dietary modifications may help determine any positive or negative effects that may occur. The overall goal of this research is to prevent obesity and obesity-related conditions in this population, as well as to treat existing conditions, to improve the health status of the state of Mexico, with potential impact on the United States.

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APPENDIX A: FOOD FREQUENCY QUESTIONNAIRE USED TO CAPTURE DIETARY INTAKE DATA

Clave única:____________________ **Folio:**__________ [illegible]

CONSENTIMIENTO PARA PARTICIPAR EN EL PROYECTO:

"Detección del estilo de vida, fenotipo y genotipo de riesgo para prevenir enfermedades crónico-metabólicas: Diabetes Mellitus y Arteriosclerosis en adultos jóvenes de San Luis Potosí."

Yo ______________________________ Entendido la información y las características de este estudio de investigación, por lo tanto acepto participar voluntariamente en este estudio de investigación.

______________________________ FECHA____________

Firma

Datos adicionales:

Dirección______________________________________

Calle No. COL. CP.

Teléfono:________________

Por favor lee cuidadosamente y conteste cada una de las siguientes preguntas

1.- Lugar de Nacimiento:________________

2.- Peso al nacer ________________

3.- Fuma? SI NO cuantos /día ________

4.- Edad en que inicio a fumar ________________

5.- Hs frente al televisor ________/día

6- Horas con videojuegos o computadora______/día

Marque con una X la respuesta correspondiente

1. ¿Cuál es el total de cuartos, piezas o habitaciones con que cuenta su hogar? (Por favor no incluya baños, pasillos y zotehuelas)

1	2	3	4	5	6	7 o más

2. ¿Cuántos baños completos con regadera y W.C. (excusado) hay para uso exclusivo de los integrantes de su hogar?

1	2	3	4 o más

3. En su hogar ¿Cuenta con regadera funcionando en alguno de los baños?

No tiene	Si tiene

4. Contando todos los focos que utiliza para iluminar su hogar, incluyendo techo, paredes y lámparas de buro o piso ¿Cuántos fosos tiene su vivienda?

0-5	6-10	10-15	16-20	21 o más

5. El piso de su hogar es predominantemente de tierra, de cemento o de otro tipo de acabado?

Tierra o cemento firme	Otro tipo de material o acabado

6. ¿Cuántos automóviles propios, excluyendo taxis, tiene su hogar?

0	1	2	3 o más

7. ¿Cuántas televisiones a color funcionando tiene su hogar?

0	1	2	3 o más

8. ¿Cuántas computadoras personales, ya sea de escritorio o laptop funcionando tiene su hogar?

0	1	2	3 o más

9. En su hogar, ¿Cuenta con estufa de gas o eléctrica?

No tiene	Si tiene

10. Pensando en la persona que aporta la mayor parte del ingreso en su hogar, **¿Cuál fue el último año de estudios que completó?**

No Estudio	Primaria Incompleta	Primaria Completa	Secundaria Incompleta	Secundaria Completa	Carrera comercial	Carrera Técnica	Preparatoria incompleta	Preparatoria Completa	Licenciatura incompleta	Licenciatura completa	Diplomado o Maestría	Doctorado

CUESTIONARIO DE ALIMENTACION (FRECUENCIA DE CONSUMO). *Adaptado del Instituto Nacional de Salud Pública. Centro de Investigación en Salud Pública.*

Por favor indique con una cruz en la columna que corresponda a la opción más cercana a su realidad y en la columna de la derecha registre el número correspondiente a la frecuencia de consumo reportada.

FRECUENCIA DE CONSUMO

	ALIMENTO **Productos lácteos**	NUNCA	MENOS DE UNA VEZ AL MES	VECES AL MES	VECES A LA SEMANA			VECES AI DIA				**CLAVE**
		(01)	(02)	1-3 (03)	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
1	Un vaso de leche entera											
2	Una rebanada de queso fresco o ½ taza de queso cottage											
3	Una rebanada de queso Oaxaca											
4	Una rebanada de queso Manchego o Chihuahua											
5	Una cucharada de queso crema											
6	Una taza de yogurt o búlgaros											
7	Un barquillo helado de leche											

Durante el año previo a este día ¿Con que frecuencia consumió usted FRUTAS? Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad. Incluya las frutas que estuvieron disponibles solo en temporada.

FRECUENCIA DE CONSUMO

	ALIMENTO **Frutas**	NUNCA	MENOS DE UNA VEZ AL MES	VECES AL MES	VECES A LA SEMANA			VECES AI DIA				**CLAVE**
		(01)	(02)	1-3 (03)	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
8	Un plátano											
9	Una naranja											
10	Un vaso con jugo de naranja o toronja											
11	Una rebanada de melón											
12	Una manzana fresca											
13	Una rebanada de sandia											
14	Una rebanada de piña											
15	Una rebanada de papaya											
16	Una pera											
17	Un mango											
18	Una mandarina											
19	Una porción de fresas (~10)											
20	Un durazno, chabacano o nectarina											
21	Una porción de uvas (de 10 a 15)											
22	Una tuna											
23	Una porción de ciruelas (~6)											
24	Una rebanada de mamey											
25	Un zapote											

Durante el año previo a este día ¿Con que frecuencia consumió usted CARNES, HUEVO Y EMBUTIDOS? Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad.

FRECUENCIA DE CONSUMO

ALIMENTO **Carnes, huevo y embutidos**	NUNCA (01)	MENOS DE UNA VEZ AL MES (02)	VECES AL MES 1-3 (03)	VECES A LA SEMANA 1 (04)	 2-4 (05)	 5-6 (06)	VECES AI DIA 1 (07)	 2-3 (08)	 4-5 (09)	 6 (10)	CLAVE
26 Un huevo de gallina											
27 Una pieza de pollo											
28 Una rebanada de jamón											
29 Un plato de carne de res											
30 Un plato de carne de cerdo											
31 Una porción de atún											
32 Un pedazo de chicharrón											
33 Una salchicha											
34 Una rebanada de tocino											
35 Un bistec de hígado o hígados de pollo											
36 Un trozo de chorizo o longaniza											
37 Un plato de carne de pescado fresco (i.e. mojarra)											
38 Un plato de sardinas en tomate											
39 Media taza de mariscos											
40 Un plato de carnitas											
41 Un plato de barbacoa											

Durante el año previo a este día ¿Con que frecuencia consumió usted VERDURAS? Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad.

FRECUENCIA DE CONSUMO

ALIMENTO **Verduras**	NUNCA (01)	MENOS DE UNA VEZ AL MES (02)	VECES AL MES 1-3 (03)	VECES A LA SEMANA 1 (04)	 2-4 (05)	 5-6 (06)	VECES AI DIA 1 (07)	 2-3 (08)	 4-5 (09)	 6 (10)	CLAVE
42 Un jitomate en salsa o guisado											
43 Un jitomate crudo o en ensalada											
44 Una papa o camote											
45 Media taza de zanahoria											
46 Una hoja de lechuga											
47 Media taza de espinacas u otra verdura de hoja verde (acelgas)											
48 Media taza de calabacitas o chayotes											
49 Media taza de nopalitos											
50 Una rebanada de tocino											
51 Un plato de sopa crema de verduras											
52 Medio aguacate											
53 Media taza de flor de calabaza											
54 Media taza de coliflor											
55 Media taza de ejotes											
56 Una cucharadita de salsa picante o chiles con sus alimentos											
57 Un platillo con chile seco											
58 Un elote											

Durante el año previo a este día ¿Con que frecuencia consumió usted LEGUMINOSAS o CEREALES? Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad.

FRECUENCIA DE CONSUMO

ALIMENTO **Leguminosas**	NUNCA	MENOS DE UNA VEZ AL MES	VECES AL MES	VECES A LA SEMANA			VECES AI DIA				CLAVE
	(01)	(02)	1-3 (03)	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
59 Un plato de frijoles											
60 Media taza de chicharos											
61 Un plato de habas verdes											
62 Un plato de habas secas											
63 Un plato de lentejas o garbanzos											

FRECUENCIA DE CONSUMO

ALIMENTO **Cereales**	NUNCA	MENOS DE UNA VEZ AL MES	VECES AL MES	VECES A LA SEMANA			VECES AI DIA				CLAVE
	(01)	(02)	1-3 (03)	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
64 Una tortilla de maíz											
65 Una tortilla de trigo (tortilla de harina)											
66 Una rebanada de pan de caja (tipo Bimbo)											
67 Una rebanada de pan de caja integral											
68 Un bolillo o telera											
69 Una pieza de pan de dulce											
70 Un plato de arroz											
71 Un plato de sopa de pasta											
72 Un plato de avena											
73 Un tazón de cereal de caja (tipo hojuelas de maíz) ¿Qué tipo?________											
74 Cereal alto en fibra ¿Cuál? ________											

Durante el año previo a este día ¿Con que frecuencia consumió usted GOLOSINAS o POSTRES? Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad.

FRECUENCIA DE CONSUMO

ALIMENTO **Golosinas o postres**	NUNCA	MENOS DE UNA VEZ AL MES	VECES AL MES	VECES A LA SEMANA			VECES AI DIA				CLAVE
	(01)	(02)	1-3 (03)	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
75 Una rebanada de pastel											
76 Una cucharadita de ate, miel, mermelada, cajeta o leche condensada											
77 Una cucharadita de chocolate en polvo											
78 Una tablilla/barra de chocolate											
79 Una bolsa de frituras											

Durante el año previo a este día ¿Con que frecuencia consumió usted las siguientes BEBIDAS? Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad.

FRECUENCIA DE CONSUMO

ALIMENTO **Bebidas**	NUNCA	MENOS DE UNA VEZ AL MES	VECES AL MES	VECES A LA SEMANA			VECES AI DIA				**CLAVE**
	(01)	(02)	1-3 (03)	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
80 Un refresco de cola mediano											
81 Un refresco gaseoso de sabor											
82 Un refresco dietético											
83 Un vaso con agua de sabor azucarada											
84 Una taza de café sin azúcar											
85 Una taza de atole sin leche											
86 Una taza de atole con leche											
87 Una cerveza											
88 Una copa de vino de mesa											
89 Una bebida con ron, brandy o tequila											

Durante el año previo a este día ¿Con que frecuencia consumió usted GRASAS y qué tipo de ACEITE utiliza para cocinar? Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad.

FRECUENCIA DE CONSUMO

ALIMENTO **Aceites y grasas**	NUNCA	MENOS DE UNA VEZ AL MES	VECES AL MES	VECES A LA SEMANA			VECES AI DIA				**CLAVE**
	(01)	(02)	1-3 (03)	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
90 Aceite de maíz											
91 Aceite de soya											
92 Aceite de girasol											
93 Aceite de cartamo											
94 Aceite de oliva											
95 Una cucharadita de margarina											
96 Una cucharadita de mantequilla											
97 Una cucharadita de crema											
98 Una cucharadita de mayonesa											
99 Una cucharadita de manteca vegetal											
100 Una cucharadita de manteca animal											

Durante el año previo a este día ¿Con que frecuencia consumió usted los ANTOJITOS MEXICANOS que se enlistan a continuación? Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad.

FRECUENCIA DE CONSUMO

ALIMENTO **Antojitos**	NUNCA	MENOS DE UNA VEZ AL MES	VECES AL MES	VECES A LA SEMANA			VECES AI DIA				**CLAVE**
	(01)	(02)	1-3 (03)	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
101 Un taco al pastor											
102 Un sope o quesadilla											
103 Un plato con pozole											
104 Un tamal											

Por favor, indique cualquier otro alimento que usted consumió al menos una vez por semana y que no encontró en los alimentos anteriores, además de la siguiente lista, al año previo a este día. Por favor indique con una cruz, en la columna de frecuencias, la opción que considere más cercana a su realidad.

FRECUENCIA DE CONSUMO								
ALIMENTO **Otros**	VECES A LA SEMANA			VECES Al DIA				**CLAVE**
	1 (04)	2-4 (05)	5-6 (06)	1 (07)	2-3 (08)	4-5 (09)	6 (10)	
Charales secos	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]
Aceite de hígado de bacalao	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]
Salmon fresco	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]
Salmon enlatado	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]
Sardina en aceite	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]
	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]
	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]
	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]
	[__]	[__]	[__]	[__]	[__]	[__]	[__]	[__][__]

OTRAS PREGUNTAS

			CLAVE
¿Cuántas cucharaditas de azúcar le agrega usted a su alimentos al o largo del día? Tome en cuenta lo que le pone al café, licuado, otras bebidas, etc.		Cucharaditas	[__][__]
¿Le agrega usted sal a sus alimentos antes de probarlos?	a) Si	b) No	[__]
¿Se come usted el pellejo del pollo?	a) Si	b) No	[__]
¿Se come usted el "gordito" de la carne?	a) Si	b) No	[__]
¿Cuántos meses del año pasado consumió usted vitaminas? ¿Cuál o cuáles? ____	0 a, 1-2 b, 3-4 c, 5-6 d, 7-8 e, 9-10 f, 11-12 g		[__]
¿Cuántos meses del año pasado consumió usted suplemento de calcio? ¿Cuál o cuáles? ____	0 a, 1-2 b, 3-4 c, 5-6 d, 7-8 e, 9-10 f, 11-12 g		[__]
¿Considera usted que su alimentación ha cambiado durante el ultimo año?	a) Si	b) No	[__]

Si ha cambiado ¿Por qué?

____

____

____

Observaciones

____

____

____

APPENDIX B: INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE USED TO CAPTURE PHYSICAL ACTIVITY DATA

CUESTIONARIO INTERNACIONAL DE ACTIVIDAD FÍSICA

Estamos interesados en saber acerca de la clase de actividad física que la gente hace como parte de su vida diaria. Las preguntas se referirán acerca del tiempo que usted utilizó siendo físicamente activo(a) en los **últimos 7 días**. Por favor responda cada pregunta aún si usted no se considera una persona activa. Por favor piense en aquellas actividades que usted hace como parte del trabajo, en el jardín y en la casa, para ir de un sitio a otro, y en su tiempo libre de descanso, ejercicio o deporte.

Piense acerca de todas aquellas actividades **vigorosas** y **moderadas** que usted realizó en los **últimos 7 días**. Actividades **vigorosas** son las que requieren un esfuerzo físico fuerte y le hacen respirar mucho más fuerte que lo normal. Actividades **moderadas** son aquellas que requieren un esfuerzo físico moderado y le hace respirar algo más fuerte que lo normal.

PARTE 1: ACTIVIDAD FÍSICA RELACIONADA CON EL TRABAJO

La primera sección es relacionada con su trabajo. Esto incluye trabajos con salario, agrícola, trabajo voluntario, clases, y cualquier otra clase de trabajo no pago que usted hizo fuera de su casa. No incluya trabajo sin pago que usted hizo en su casa, tal como limpiar la casa, trabajo en el jardín, mantenimiento general, y el cuidado de su familia. Estas actividades serán preguntadas en la parte 3

1. ¿Tiene usted actualmente un trabajo o hace algún trabajo sin pago fuera de su casa?
   a) Sí
   b) No→***Pase a la PARTE 2: TRANSPORTE*** [___]

Las siguientes preguntas se refieren a todas las actividades físicas que usted hizo en los **últimos 7 días** como parte de su trabajo pago o no pago. Esto no incluye ir y venir del trabajo.

2. Durante los **últimos 7 días**, ¿Cuántos días realizó usted actividades físicas **vigorosas** como levantar objetos pesados, excavar, construcción pesada, o subir escaleras **como parte de su trabajo**? Piense solamente en esas actividades que usted hizo por lo menos 10 minutos continuos.
   Días por semana [___]
   a) Ninguna actividad física vigorosa relacionada con el trabajo ***→Pase a la pregunta 4***
   b) No sabe/No está seguro(a) [___]

3. ¿Cuánto tiempo en total usualmente le toma realizar actividades físicas **vigorosas** en uno de esos días que las realiza como parte de su trabajo?
   Horas por día [____] **Minutos por día** [____]
   a) No sabe/No está seguro(a) [____]

4. Nuevamente, piense solamente en esas actividades que usted hizo por lo menos 10 minutos continuos. Durante **los últimos 7 días**, ¿Cuántos días hizo Usted actividades físicas **moderadas como** cargar cosas ligeras **como parte de su trabajo**? Por favor no incluya caminar.
   Días por semana [___]
   a) No actividad física moderada relacionada con el trabajo ***→Pase a la pregunta 6***
   b) No sabe/No está seguro(a) [___]

5. ¿Cuánto tiempo en total usualmente le toma realizar actividades físicas **moderadas** en uno de esos días que las realiza como parte de su trabajo?
   Horas por día [____] **Minutos por día** [____]
   a) No sabe/No está seguro(a) [____]

6. Durante **los últimos 7 días**, ¿Cuántos días **caminó** usted por lo menos 10 minutos continuos **como parte de su trabajo**? Por favor no incluya ninguna caminata que usted hizo para desplazarse de o a su trabajo.
   Días por semana [___]
   a) Ninguna caminata relacionada con trabajo → **Pase a la PARTE 2: TRANSPORTE**
   b) No sabe/No está seguro(a) [___]

7. ¿Cuánto tiempo en total pasó generalmente **caminado** en uno de esos días como parte de su trabajo?
   Horas por día [____] **Minutos por día** [____]
   a) No sabe/No está seguro(a) [____]

PARTE 2: ACTIVIDAD FíSICA RELACIONADA CON TRANSPORTE

Estas preguntas se refieren a la forma como usted se desplazó de un lugar a otro, incluyendo lugares como el trabajo, las tiendas, el cine, entre otros.

8. Durante los **últimos 7 días**, ¿Cuántos días **viajó usted en un vehículo de motor** como un tren, bus, automóvil, o tranvía?

   a) No viajó en vehículo de motor →***Pase a la pregunta 10*** **Días por semana** [___]

Las siguientes preguntas se refieren a todas las actividades físicas que usted hizo en los **últimos 7 días** como parte de su trabajo pago o no pago. Esto no incluye ir y venir del trabajo.

9. Usualmente, ¿Cuánto tiempo gastó usted en uno de esos días viajando en un tren, bus, automóvil, tranvía u otra clase de vehículo de motor?

   Horas por día [____] **Minutos por día** [____]

   a) No sabe/No está seguro(a) [____]

Ahora piense únicamente acerca de montar en bicicleta o caminatas que usted hizo para desplazarse a o del trabajo, haciendo mandados, o para ir de un lugar a otro.

10. Durante los **últimos 7 días**, ¿Cuántos días **montó usted en bicicleta** por al menos 10 minutos continuos para **ir de un lugar a otro**?

    a) No montó en bicicleta de un sitio a otro →***Pase a la pregunta 12*** **Días por semana** [___]

11. Usualmente, ¿Cuánto tiempo gastó usted en uno de esos días montando en bicicleta de un lugar a otro?

    Horas por día [____] **Minutos por día** [____]

    a) No sabe/No está seguro(a) [____]

12. En los **últimos 7 días**¿Cuántos días caminó usted por al menos 10 minutos continuos para ir **de un sitio a otro**?

    a) No caminatas de un sitio a otro → ***Pase a la PARTE 3: TRABAJO DE LA CASA, MANTENIMIENTO DE LA CASA, Y CUIDADO DE LA FAMILIA*** **Días por semana** [___]

13. Usualmente, ¿Cuánto tiempo gastó usted en uno de esos días **caminando** de un sitio a otro?

    Horas por día [____] **Minutos por día** [____]

    a) No sabe/No está seguro(a) [____]

PARTE 3: TRABAJO DE LA CASA, MANTENIMIENTO DE LA CASA, Y CUIDADO DE LA FAMILIA

Esta sección se refiere a algunas actividades físicas que usted hizo en los **últimos 7 días** en y alrededor de su casa tal como arreglo de la casa, jardinería, trabajo en el césped, trabajo general de mantenimiento, y el cuidado de su familia.

14. Piense únicamente acerca de esas actividades físicas que hizo por lo menos 10 minutos continuos. Durante los **últimos 7 días**, ¿Cuántos días hizo usted actividades físicas **vigorosas** tal como levantar objetos pesados, cortar madera, palear nieve, o excavar **en el jardín o patio**?

    Días por semana [___]

    a) Ninguna actvidad física vigorosa en el jardín o patio →***Pase a la pregunta 16***

    b) No sabe/No está seguro(a) [___]

15. Usualmente, ¿Cuánto tiempo dedica usted en uno de esos días haciendo actividades físicas **vigorosas** en el jardín o patio?

    Horas por día [____] **Minutos por día** [____]

    a) No sabe/No está seguro(a) [____]

16. Nuevamente, piense únicamente acerca de esas actividades físicas que hizo por lo menos 10 minutos continuos. Durante los **últimos 7 días**, ¿Cuántos días hizo usted actividades físicas **moderadas** tal como cargar objetos livianos, barrer, lavar ventanas, y rastrillar **en el jardín o patio**?

    a) Ninguna actvidad física moderada en el jardín o patio →***Pase a la pregunta 18*** **Días por semana** [___]

17. Usualmente, ¿Cuánto tiempo dedica usted en uno de esos días haciendo actividades físicas **moderadas** en el jardín o patio?

    Horas por día [____] **Minutos por día** [____]

    a) No sabe/No está seguro(a) [____]

18. Durante **los últimos 7 días**, ¿Cuántos días **caminó** usted por lo menos 10 minutos continuos **como parte de su trabajo**? Por favor no incluya ninguna caminata que usted hizo para desplazarse de o a su trabajo.

a) Ninguna actividad física moderada dentro de la casa **Días por semana** [___]
→ ***Pase a la PARTE 4: ACTIVIDADES FÍSICAS DE RECREACIÓN, DEPORTE Y TIEMPO LIBRE***

19. Usualmente, ¿Cuánto tiempo dedica usted en uno de esos días haciendo actividades físicas **moderadas** dentro de su casa?

Horas por día [____] **Minutos por día** [____]
a) No sabe/No está seguro(a) [____]

PARTE 4: ACTIVIDADES FÍSICAS DE RECREACIÓN, DEPORTE Y TIEMPO LIBRE

Esta sección se refiere a todas aquellas actividades físicas que usted hizo en los últimos 7 días únicamente por recreación, deporte, ejercicio o placer. Por favor no incluya ninguna de las actividades que ya haya mencionado

20. Sin contar cualquier caminata que ya haya usted mencionado, durante los **últimos 7 días**, ¿Cuántos días **caminó** usted por lo menos 10 minutos continuos **en su tiempo libre**?

a) Ninguna caminata en tiempo libre →***Pase a la pregunta 22*** **Días por semana** [___]

21. Usualmente, ¿Cuánto tiempo gastó usted en uno de esos días **caminando** en su tiempo libre?

Horas por día [____] **Minutos por día** [____]
a) No sabe/No está seguro(a) [____]

22. Piense únicamente acerca de esas actividades físicas que hizo por lo menos 10 minutos continuos. Durante los **últimos 7 días**, ¿Cuántos días hizo usted actividades físicas **vigorosas** tal como aeróbicos, correr, pedalear rápido en bicicleta, o nadar rápido en su **tiempo libre**?

a) Ninguna actividad física vigorosa en tiempo libre →***Pase a la pregunta 24*** **Días por semana** [___]

23. Usualmente, ¿Cuánto tiempo dedica usted en uno de esos días haciendo actividades físicas **vigorosas** en su tiempo libre?

Horas por día [____] **Minutos por día** [____]
a) No sabe/No está seguro(a) [____]

24. Ahora, piense únicamente acerca de esas actividades físicas que hizo por lo menos 10 minutos continuos. Durante los **últimos 7 días**, ¿Cuántos días hizo usted actividades físicas **moderadas** tal como pedalear en bicicleta a paso regular, nadar a paso regular, jugar dobles de tenis, **en su tiempo libre**?

a) Ninguna actividad física moderada en tiempo libre → ***Pase a la PARTE 5: TIEMPO DEDICADO A ESTAR SENTADO(A)*** **Días por semana** [___]

25. Usualmente, ¿Cuánto tiempo dedica usted en uno de esos días haciendo actividades físicas **moderadas** en su tiempo libre?

Horas por día [____] **Minutos por día** [____]
a) No sabe/No está seguro(a) [____]

PARTE 5: TIEMPO DEDICADO A ESTAR SENTADO(A)

Las últimas preguntas se refieren al tiempo que usted permanece sentado(a) en el trabajo, la casa, estudiando, y en su tiempo libre. Esto incluye tiempo sentado(a) en un escritorio, visitando amigos(as), leyendo o permanecer sentado(a) o acostado(a) mirando televisión. No incluya el tiempo que permanece sentado(a) en un vehículo de motor que ya haya mencionado anteriormente.

26. Durante los **últimos 7 días**, ¿Cuánto tiempo permaneció **sentado(a)** en un **día en la semana**?

Horas por día [____] **Minutos por día** [____]
a) No sabe/No está seguro(a) [____]

27. Durante los **últimos 7 días**, ¿Cuánto tiempo permaneció **sentado(a)** en un **día del fin de semana**?

Horas por día [____] **Minutos por día** [____]
a) No sabe/No está seguro(a) [____]

Este es el final de este cuestionario, gracias por su participación.

APPENDIX C: CHAPTER 2 DAIRY LITERATURE REVIEW TABLE

Author	Subjects	Methods	Key Findings
(Astrup, Chaput, Gilbert, & Lorenzen, 2010)	Selected observational and intervention studies	Review Paper	Observational studies indicate that dairy beverage consumption is inversely associated with body weight and body fat. The results of intervention studies are inconclusive.
(Azadbakht, Mirmiran, Esmaillzadeh, & Azizi, 2005)	827 Iranian subjects aged 18–74y	Dietary intake was assessed with the use of a 168-item semiquantitative FFQ; MetS was defined according to guidelines of the Adult Treatment Panel III	Dairy consumption was inversely associated with the risk of having MetS
(Berkey, Rockett, Willett, & Colditz, 2005)	12,829 US children, aged 9-14y in 1996, who returned questionnaires by mail through 1999	Children annually reported their height and weight and completed FFQs regarding typical past-year intakes	Children who drank the most milk gained more weight, but the added calories appeared responsible; dietary calcium and skim and 1% milk were associated with weight gain, but dairy fat was not.
(Beydoun et al., 2008)	US adults from NHANES 1999 –2004 data; sample sizes ranged from 4,519 for MetS to 14,618 for obesity	Direct anthropometric assessments, blood pressure, and laboratory tests were constructed from the NHANES 1999-2004 survey data; associations between diet (assessed using 24-h recalls) and metabolic and other outcomes were tested	There was a significant inverse association between intake of whole milk, yogurt, calcium, and magnesium and metabolic disorders; differences in BMI between the NH black and NH whites were explained in small but significant part by dairy-related nutrients, particularly higher intakes of calcium and magnesium, and lower phosphorus intake; in terms of SBP, differences between

		using multivariate linear and logistic models and structural equation models	NH blacks and NH whites were also partly explained by dairy-related nutrients; a similar pattern was observed for SBP when comparing Mexican Americans with NH whites
(Brooks, Rajeshwari, Nicklas, Yang, & Berenson, 2006)	1,306 young adults aged 19–38y who participated in the 1995–1996 Bogalusa Heart Study	Intakes of calcium were obtained from data collected from a Youth and Adolescent Questionnaire	No significant association was found between dairy product consumption, calcium intake and overweight; however, there was a significant inverse association between calcium intake, low-fat dairy product consumption and waist-to-hip ratio in white males
(Carruth & Skinner, 2001)	53 white children aged 2-96 months	Using in-home interviews and trained interviewers, 18 days of dietary data and measured height and weight of each child at 6 month intervals were collected; body composition was determined by dual energy X-ray absorptiometry	Higher longitudinal intakes of calcium, monounsaturated fat, and servings of dairy products were associated with lower body fat.
(Choi, Willett, Stampfer, Rimm, & Hu, 2005)	41,254 male participants in the Health Professionals Follow-Up Study	A semiquantitative FFQ that inquired about the average use of approximately 130 foods and beverages during the previous year was used to assess dietary intake	Dietary patterns characterized by higher dairy intake, especially low-fat dairy intake, may lower the risk of type 2 diabetes in men.
(Crichton, Elias, Dore, & Robbins, 2012)	972 participants aged 23-98y from the Maine-Syracuse Longitudinal	Participants completed the Centre for Epidemiologic Studies	Participants who consumed dairy products at least once per day had significantly higher scores on

	Study	Depression Scale (CES-D), the Nurses' Health Study Activity Questionnaire, and the Nutrition and Health Questionnaire within two weeks prior to their laboratory visit; the cognitive tests used were the following: Visual-Spatial Memory and Organization composite, Scanning and Tracking composite, Verbal Episodic Memory composite, Working Memory composite, Executive Function composite, Global composite and the following individual tests: Similarities, a measure of abstract reasoning, and the MMSE (Mini-Mental State Examination)	multiple domains of cognitive function compared with those who never or rarely consumed dairy foods; frequent dairy food intake is associated with better cognitive performance (underlying causal mechanisms are still to be determined).
(Crichton, Murphy, Howe, Buckley, & Bryan, 2012)	Overweight adults with habitually low dairy intakes (< 2 servings/day) were recruited; 38 participants who completed the trial	Study design was a 12 month crossover dietary intervention trial and randomized to a high (4 servings/day) or low (1 serving/day) intake of reduced fat dairy, crossing	Spatial working memory performance was marginally better following 6 months of the high dairy diet compared with the low dairy diet; increasing the dairy intake of habitually low dairy consumers may have the potential to improve

	(average age = 52 ± 2 years; BMI = 31.5 ± 0.8 kg/m^2);	over to the alternate diet after 6 months; participants were tested at the end of each 6 month diet period on multiple measures of cognitive performance, including memory, information processing speed, executive function, attention and abstract reasoning	working memory.
(Crichton, Howe, Buckley, Coates, & Murphy, 2012)	61 overweight or obese adults	Participants were randomly assigned to a high dairy diet (HD, 4 servings of reduced fat dairy/day) or a low dairy control diet (LD, ≤1 serving/day) for 6 months then crossed over to the alternate diet for a further 6 months; anthropometric and cardiometabolic parameters including body composition, metabolic rate, blood lipids, blood pressure and arterial compliance were assessed at the end of each diet phase	There were no significant differences between HD and LD in absolute measures of waist circumference, body weight, fat mass or any other cardiometabolic parameter.
(dos Santos, Cintra, Fisberg, & Martini, 2008)	96 post-pubertal Brazilian adolescents with mean age 16.6	Body composition was assessed by dual-energy X-ray absorptiometry;	There was a negative relationship between calcium intake and body fat and insulin resistance, mainly in

	years	dietary intake was evaluated using a 3-day dietary record	obese girls.
(Drapeau, et al., 2004)	248 volunteers of the Québec Family Study	Body weight, percentage body fat, subcutaneous skinfold thicknesses, and WC measurements as well as 3-d dietary and physical activity records were obtained at each visit; at visit 2, all participants filled out a food-based questionnaire examining changes in the consumption of 10 food categories.	Increased consumption of whole fruit as well as skimmed milk and partly skimmed milk were the 2 food patterns that negatively correlated with the changes of each body weight–related indicator.
(Drouillet et al., 2007)	4,372 adult participants from the DESIR cohort	Data for parameters relating to IRS were recorded, including glucose, serum insulin, TG, HDL-C, WC and blood pressure; total energy, calcium and alcohol intake were estimated using a FFQ	There was a beneficial association between dietary calcium and arterial blood pressure, insulin, and HDL-C levels in women, whereas in men there was only a beneficial association with DBP.
(Elwood, Pickering, & Fehily, 2007)	Representative sample of 2,512 men aged 45–59y in the UK	Data on fasting blood glucose and plasma insulin, TG, and HDL-C, BMI, and blood pressure were used to define MetS; dietary intake data was assessed using data from both a semiquantitative	The consumption of milk and dairy products was associated with a reduced prevalence of MetS.

		FFQ and a 7-day weighed intake record	
(Elwood et al., 2008)	Meta-analysis.	Prospective cohort studies of vascular disease and diabetes with baseline data on milk or dairy consumption and a relevant disease outcome were identified by searching MEDLINE and meta-analyses were conducted	From meta-analysis of 15 studies the relative risk of stroke and/or heart disease in subjects with high milk or dairy consumption was 0.84 (95% CI 0.76, 0.93) and 0.79 (0.75, 0.82) respectively; overall, the consumption of milk and dairy foods provides a survival advantage to individuals living in the UK.
(Ferland et al., 2011)	543 Inuit participants	Dairy product intake and calcium intake were evaluated using a food frequency questionnaire; physiological (lipid profile, fasting glucose, and insulin) and anthropometrical measurements were also obtained	Higher dairy product intake in Nunavik Inuit is not related to protective effects on body weight and CVD; the consumption of dairy products in Nunavik Inuit is probably not sufficient to withdraw beneficial effects on body weight or CVD risk factors, as observed in other North American populations.
(Fluegel et al., 2010)	71 subjects approx. 20y of age	Subjects were randomized to consume either 28 g per day unmodified whey protein concentrate 80 (WPC80) (30 M, 8 F) or 28 g per day hydrolyzed WPC80 (32 M, 6 F) in a 10 oz fruit flavored whey protein drink once a day; blood pressure measurements and blood	In young adults with elevated DBP and SBP, whey beverage consumption significantly decreased SBP, DBP, and MAP; whey beverages also significantly decreased total and low-density lipoprotein cholesterol concentrations.

		draws were also taken.	
(Fumeron et al., 2011)	3,435 French men and women aged 30-65y (DESIR cohort)	Dietary data was collected using a FFQ at baseline and after 3 years; clinical and biological evaluations were conducted every 3 years	Higher consumption of dairy products and calcium was associated with a lower 9-year incidence of MetS and IFG/T2D. Higher dietary calcium density was negatively associated with WC, TG, and SBP.
(Ghayour-Mobarhan et al., 2009)	96 overweight and obese Indian children aged 12-18y	Children were randomized to receive a calorie restricted diet providing a 500 kcal/d deficit from total energy expenditure and 2 (n = 40), 3 (n = 40) or 4 (n = 40) servings of dairy products/day. Anthropometric measurements in addition to serum hs-CRP and lipid profile were measured at baseline and after 12 weeks.	Significant reductions in overall BMI, BMI z-score, weight, total body fat percentage and total body fat mass were observed, however, these reductions were not significantly affected by increasing dairy intake
(Gunther et al., 2005)	155 young (aged 18–30y), healthy, normal weight women with intake of dietary calcium < 800 mg/d and energy intake ≤ 2200 kcal/d	Women were randomly assigned to 1 of 3 groups: *1*) control: continue established dietary intake; *2*) medium dairy: substitute dairy products to achieve intake of calcium of ≈1000–1100 mg/d and maintain isocaloric intake; *3*) high dairy: substitute dairy products to achieve intake	Increased intake of dairy products does not alter body weight or fat mass in young, healthy women over 1y.

		of calcium of 1300–1400 mg/d and maintain isocaloric intake	
(Halkjær, Tjønneland, Overvad, & Sørensen, 2009)	22,570 womenand 20,126 men aged 50-64y at baseline from the Danish Diet, Cancer, and Health Study	Selected participants had complete baseline and follow-up WC, baseline diet (192-item FFQ), BMI, and selected potential confounders	For women, 5-y difference in WC was inversely related to intake from red meat, vegetables, fruit, butter, and high-fat dairy products; intake from potatoes, processed meat, poultry, and snack foods was positively associated. In men, red meat and fruit intakes were inversely associated with 5-y difference in WC, whereas snack foods intake was positively associated.
(Hanks et al., 2010)	315 European American (n =122), African American (n = 107) and Hispanic American (n = 86) children aged 7-12y	Data collected included REE, body composition, and dietary calcium were assessed by indirect calorimetry, dual-energy x-ray absorptiometry, and 24-hour recalls	REE was associated with calcium intake and mediated a relationship between calcium intake and total body fat; calcium intake may play a role in fat accumulation and energy balance through its effects on REE, especially in boys.
(Harvey-Berino, Gold, Lauber, & Starinski, 2005)	Fifty-four subjects (BMI 30 ±2.5 kg/m^2, 45±6.6 years, 4 men)	Subjects were randomly assigned to calorie-restricted (-500 kcal/d) low-dairy calcium (*n* = 29; ~1 serving dairy/d, 500 mg/d calcium) or high-dairy calcium (*n* = 25; 3 to 4 servings dairy/d, 1200 to 1400 mg/d calcium) diets for 12 months	There were no significant differences between groups at baseline; at 12 months, weight and body fat loss were not significantly different; high-dairy calcium diet does not substantially improve weight loss beyond what can be achieved in a behavioral intervention.
(Holecki et al., 2008)	40 obese Polish women	Subjects were divided into	Calcium plus vitamin D

		2 groups comparable with body mass index (BMI) and age; Group 1 was provided with calcium carbonate and 1-(OH)-vitamin D supplementation. Group 2 was provided with only a diet; subjects participated in a 3-month weight reduction therapy (balanced diet, modification of life style, and regular physical exercise); blood samples (serum concentration of Ca, phosphorus (P), parathormone (PTH), 25-(OH)-D3) and clinical characteristics (weight, height, BMI, body composition) were taken at baseline and after the 3-month program	supplementation during a 3-month low caloric diet has no additional effect on weight and fat loss in obese women.
(Hong et al., 2012)	406 Korean adults aged 22-78y	MetS defined according to ATPIII criteria; dietary data collected with 24h recall and 3-day record; factor analysis was used to isolate food patterns.	Fruit and dairy dietary pattern was significantly associated with decreased odds of IFG, hypertriglyceridemia, and MetS.
(Huang & McCrory, 2005)	Review	Review	Implausible dietary reporting in observational studies and the lack of compliance monitoring in

			intervention trials may also contribute to inconsistent findings.
(Jacobsen, Lorenzen, Toubro, Krog-Mikkelsen, & Astrup, 2005)	10 subjects aged 18-50y in Denmark	Study was a randomized crossover study of three isocaloric 1-week diets with: low calcium and normal protein (LC/NP: 500mg calcium, 15% of energy (E%) from protein), high calcium and normal protein (HC/NP:1800mg calcium, 15E% protein), and high calcium and high protein (HC/HP: 1800mg calcium, 23E% protein)	The short-term increase in dietary calcium intake, together with a normal protein intake, increased fecal fat and energy excretion by ~350 kJ/day; this observation may help explain why a high-calcium diet produces weight loss.
(Kelishadi et al., 2009)	120 obese prepubescent Iranian children (~5.6 y of age)	The children were randomly assigned to 3 groups. In addition to attending 6 consecutive monthly family-centered education sessions about healthy lifestyle, an isocaloric dairy-rich diet (>800 mg ca/d) was recommended to the children of one group (DR: dairy-rich diet), the second group was placed on a caloric-restricted regimen (ER: energy-restricted), and the third group received no	After the 6-month trial, TG and insulin levels decreased, and HDL-C and HOMA-R increased; in the DR group, the TG, insulin and HOMA-R levels remained significantly lower than baseline until the 12-month follow-up; an isocaloric diet rich in dairy products can be a safe and practical strategy for weight control in young, overweight children.

		additional recommendation (C: controls). The groups were then followed-up twice a year for 3 years	
(Larson et al., 2009)	1,521 Project EAT (Eating Among Teens) participants; mean age at baseline: 15.9y	Data was collected using the Youth and Adolescent Food Frequency Questionnaire and anthropometric measures taken in high school classrooms; participants were resurveyed 5y later for follow-up	Mean daily intakes of calcium decreased into young adulthood in both males and females; intakes were affected by availability, health and nutrition attitudes, peer support for healthful eating, and taste preferences.
(Larsson et al., 2009)	26,556 Finnish male smokers aged 50 to 69y with no history of stroke within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study between 1985 and 1988	A FFQ was administered to collect dietary data	There were no strong associations between intakes of total dairy, low-fat milk, sour milk, cheese, ice cream, or butter and risk of any stroke subtype; however, a positive association between whole milk and intracerebral hemorrhage was observed.
(Liu et al., 2005)	10,066 women aged ≥45 years participating in the Women's Health Study who were free of cardiovascular disease, cancer, or diabetes and who never used postmenopausal hormones	Participants were asked how often on average they had consumed individual foods of commonly used portions during the previous year; nutrient intakes were computed by multiplying the frequency of consumption of each unit of food from the semiquantitative FFQ by	Intakes of calcium and dairy products may be associated with lower prevalence of MetS in middle-aged and older women.

		the nutrient content of the specified portion size	
(Lorenzen, Molgaard, Michaelsen, & Astrup, 2006)	110 girls with mean age 12y in Denmark	Subjects were randomly assigned to receive 500 mg Ca/d as calcium carbonate or placebo for 1 y; 2 groups of girls were selected according to habitual calcium intake from a large group; one group consumed 1000–1304 mg/d (40th–60th percentile; *n* = 60) and the other group consumed <713 mg/d (<20th percentile; *n* = 50); Height, body weight, body fat, and calcium intake were measured at baseline and after 1y	Habitual dietary calcium intake was inversely associated with body fat, but a low-dose calcium supplement had no effect on body weight, height, or body fat over 1 y.
(Louie, Flood, Hector, Rangan, & Gill, 2011)	Systematic Review	Review of prospective cohort studies	The evidence from the selected prospective cohort studies for a protective effect of dairy consumption on risk of overweight and obesity is suggestive, but inconsistent across studies.
(Lutsey, Steffen, & Stevens, 2008)	9514 participants aged 45-64y enrolled in the Atherosclerosis Risk in Communities (ARIC) study	Dietary intake was assessed at baseline via a 66-item food frequency questionnaire	The Western dietary pattern, meat, and fried foods intake promotes the incidence of MetS, whereas dairy consumption provides some protection.
(Marques-Vidal, Goncalves, & Dias, 2006)	17,771 men and 19,742 women aged ≥18y in	Average daily milk intake was calculated by a	Increased calcium intake is negatively related to BMI in men and

	Portugal	frequency questionnaire that also assessed the average volume of one serving	premenopausal women.
(Mirmiran, Esmaillzadeh, & Azizi, 2005)	462 Iranian subjects aged ≥ 16y	Dietary data were collected by means of a food frequency questionnaire for 1-y and two 24-h dietary recalls; physical activity was assessed by the Lipid Research Clinic (LRC) questionnaire	There was an inverse relationship between dairy consumption and BMI.
(Moore, Bradlee, Gao, & Singer, 2006)	99 families enrolled in the Framingham Children's study with a child aged 6y at baseline	Dairy intake for these analyses was derived from a mean of 15 days of diet records per subject collected before age 6; a trained examiner took two measurements each year of height, weight, and triceps, subscapular, suprailiac, and abdominal skinfolds	Suboptimal dairy intakes during preschool were associated with greater gains in body fat throughout childhood.
(Moore, Singer, Qureshi, & Bradlee, 2008)	Children (5–11 years) and adolescents (12–16 years) were included who had data on diet, anthropometry measures of body fat, and relevant potential confounders (children: n = 3,864 and 2,231; adolescents: n =	Daily dairy intake from 24-hour recalls was classified as low, moderate or high; for girls and boys, respectively: low intake: <1 and <2 servings; moderate intake: 1–<3 and 2–<4 servings; and high intake: ≥3 and	Among children, there was no consistent association between dairy intake and anthropometric indices of body fat; smong adolescents, the lowest dairy intake group (< 1 serving per day for girls and < 2 per day for boys) had higher estimated levels of body fat than those in the highest dairy group.

	1,884 and 2,636 in NHANES III and NHANES 1999–2002, respectively).	≥4 servings per day.	
(Murakami, Okubo, & Sasaki, 2006)	1905 female Japanese dietetic students aged 18 to 20y	Dietary intake was assessed over a 1-month period with a validated, self-administered diet history questionnaire	Intakes of calcium and dairy products were not significantly associated with BMI (were young Japanese women who were relatively lean and had a relatively low intake of calcium and dairy products)
(Newby, et al., 2004)	1,345 children age 2 to 5 years participating in the North Dakota Special Supplemental Nutrition Program for Women, Infants, and Children	Dietary data were collected using a semiquantitative FFQ; anthropometrics were measured by trained personnel.	Weight change was not significantly related to intakes (per ounce) of fruit juice, fruit drinks, milk, soda, or diet soda.
(Novotny, Daida, Acharya, Grove, & Vogt, 2004)	323 girls aged 9-14y from Kaiser Permanente database Hawaii	3-d dietary record that included 2 weekdays (Thursday and Friday) and 1 weekend day (Saturday) was completed by the girls with their parents' assistance	Consumption of dairy and calcium-rich foods and nutrients was associated with decreased iliac skinfold thickness among Asian adolescents, whereas consumption of soda was associated with increased weight.
(Pabjan, Wqdolowska, Slowinska, Czlapka-Matyasik, & Niedzwiedzka, 2010)	277 mother-daughter family pairs aged 43.7±5.5 and 17.1±2.3y, respectively	Dairy products and usual calcium intake from dairy products and from daily diets were assessed using the validated ADOS-Ca questionnaire; respondents' body composition was	Higher dairy and calcium intake by mothers was related to a greater consumption of those products by daughters and, as a result, to a lower fat tissue content in women and to some extent in girls

		evaluated with anthropometric methods	
(Pereira et al., 2002)	General community sample from 4 US metropolitan areas of 3157 black and white adults aged 18-30y who were followed up from 1985-1986 to 1995-1996	Standard questionnaires were used to maintain consistency in the assessment of demographic (age, sex, race, educational level) and behavioral (physical activity and cigarette smoking) information across CARDIA examination visits; CARDIA Diet History was used to obtain a quantitative food frequency of the past 28 days.	Dairy consumption was inversely associated with the incidence of all IRS components among individuals who were overweight (body mass index $\geq$25 kg/m^2) at baseline but not among leaner individuals (body mass index <25 kg/m^2).
(Poddar et al., 2009)	76 college students (mean age 19.2y)	Participants completed 7-day food records; body height (cm), weight (kg), and waist circumference (cm) measurements were taken twice (September 2004 and April 2005); percentage of truncal fat and percentage of total body fat were measured by dual-energy x-ray absorptiometry	Subjects who consumed a higher amount of low-fat dairy products had better diet quality, gained less body weight, and had reductions in WC, percentage truncal fat, and percentage total body fat compared to those with lower intake; low-fat dairy intake may be associated with better diet quality and weight management in college students.
(Rajpathak, Rimm, Rosner, Willet, & Hu, 2006)	Data from the Health Professionals Follow-up Study, a	Data on lifestyle factors and diet were updated biennially with self-	Baseline or change in intake of total calcium was not significantly associated with weight change; there

	prospective cohort of men aged 40–75y in 1986 was used for this study	administered questionnaires; participants reported their body weight in 1986 and in 1998.	was also no association with dietary, dairy, or supplemental calcium intake when evaluated separately; men with the largest increase in total dairy intake gained slightly more weight than men who decreased dairy intake the most.
(Ranganathan, Nicklas, Yang, & Berenson, 2005)	1,266 adults (61% women, 39% men; 74% white, 26% African American) in Bogalusa, LA	Youth/adolescent questionnaire was used to assess dietary intakes and food consumption patterns of subjects	Dairy product consumption by adults has a major influence on their vitamin and mineral intakes; the higher intakes of saturated fat, total energy, and animal protein and lower intake of fiber suggest that it may be useful to consume lower-fat dairy products and/or modify eating patterns to optimize the nutritional contributions of dairy products.
(Ruidavets et al., 2007)	Sample of 912 men aged 45–64y randomly selected from the French population	Questionnaires on risk factors and a three consecutive day food diary were completed; height, weight, WC, and blood pressure were measured; a fasting blood sample was analyzed for lipid and glucose measurements; NCEP-ATP-III definition was used to assess IRS	High consumption of dairy products, fish, or cereal grains is associated with a lower probability of IRS.
(Shahar, Abel, Elhayany, Vardi, & Fraser, 2007)	259 diabetic patients with BMI > 31 kg/m^2 (mean age 55y)	6-month randomized clinical trial that assessed the effect of 3 isocaloric diets in patients with T2D;	Diet rich in dairy calcium increased weight reduction in the patients with T2D.

		dietary intake, weight, CVD risk factors, and diabetes indexes were measured at baseline and at 6 months	
(Shalileh, Shidfar, Haghani, Eghtesadi, & Heydari, 2010)	40 adults with Body Mass Index > 25kg/m^2	Subjects were maintained for 24 weeks on a balanced deficit diet (-500 kcal/d deficit) and randomly assigned into 2 groups with 1000 mg ca/d as calcium carbonate or placebo	24 weeks of supplementation with 1000 mg ca/d did not have any effect on weight, body composition, insulin resistance and blood pressure beyond what can be achieved in an energy restricted diet in obese adults
(Snijder et al., 2007)	2,064 men and women aged 50–75y who participated in the Hoorn Study	MetS was defined according to the NCEP Expert Panel; dairy consumption was assessed by using a semiquantitative FFQ	Higher dairy consumption was not associated with lower weight or more favorable levels of components of MetS (except for a modest association with lower blood pressure)
(Snijder et al., 2008)	1,124 participants of the Hoorn Study	Baseline dairy intake (servings/day) was assessed by a semi-quantitative food-frequency questionnaire; linear and logistic regression analyses were performed to investigate the association between dairy intake and 6.4-year change in weight, fat distribution, and metabolic risk factors and the incidence of MetS	Baseline dairy consumption was not associated with changes in fasting and post-load glucose concentrations, serum lipid levels (HDL-C, LDL-C, and TG), blood pressure, or with the risk of developing MetS in 6.4 years; in overweight and obese subjects, higher dairy consumption was significantly associated with an increase in BMI, weight, waist, and a decrease in HDL-C.

(Soedamah-Muthu et al., 2011)	PubMed, EMBASE, and SCOPUS were searched for articles published up to February 2010. Of more than 5000 titles evaluated, 17 met the inclusion criteria	Random-effects meta-analyses were performed with summarized dose-response data	Milk intake was not associated with total mortality, but may be inversely associated with overall CVD risk.
(Song et al., 2006)	37,183 women in the Women's Health Study	Dietary intake was assessed using a validated SFFQ that inquired about the averageuse of 131 foods and beverages during the previous year	Greater consumption of low-fat dairy products may lower the risk of type 2 diabetes in middle-aged or older women.
(Stancliffe, Thorpe, & Zemel, 2011)	40 overweight and obese adults with MetS	Participants were randomly assigned to receive adequate dairy (3.5 daily servings) or low dairy (<0.5 daily servings) weight-maintenance diets for 12 wk; oxidative and inflammatory biomarkers were assessed at 0, 1, 4, and 12 wk as primary outcomes; body weight and composition were measured at 0, 4, and 12 wk as secondary outcomes	Increased dairy intake attenuated oxidative and inflammatory stress in MetS
(Steijns, 2008)	Review	Goal was to review to what extent current dietary recommendations on intake of preferably low-fat or even skimmed dairy alternatives are	Different types of dairy products have different effects on risk markers of cardiovascular disease (role of fat and type of fat is debatable).

		justified.	
(Striegel-Moore, et al., 2006)	1,210 black and 1,161white girls who participated in the National Heart, Lung, and Blood Institute Growth and Health Study	3-day food diaries were recorded during annual visits beginning at ages 9 or 10y until age 19y	For all girls, milk consumption decreased while soda consumption increased with time; of all beverages, increasing soda consumption predicted the greatest increase of BMI and the lowest increase in calcium intake.
(Tam, Garnett, Cowell, Campbell, Cabrera, & Baur, 2006)	268 children (136 males) with mean age 7.7y were recruited from western Sydney, Australia in 1996-1997	Height and weight were measured at baseline and follow-up; overweight and obesity defined using the International Obesity Task Force criteria; beverage consumption was calculated from a 3-day food record at baseline	No association was observed between dairy intake and weight gain over time; intakes of soft drink in mid-childhood, but not fruit juice/fruit drink and milk, were associated with excess weight gain in early adolescence.
(Tholstrup, 2006)	Review	Summarizes observational and human intervention trial findings on dairy products and CVD	There is no strong evidence that dairy products increase the risk of CHD in healthy men of all ages or young and middle-aged healthy women.
(Torres, Francischetti, Genelhu, & Sanjuliani, 2010)	50 obese subjects aged 22–55y with stable body weight and a low calcium intake (39 participants completed the study)	Participants were randomised into the following outpatient dietary regimens: (i) a low-calcium diet (LCD; < 500 mg/day) or (ii) a HCD [1200–1300 mg/day, supplemented with non-fat powdered milk (60 g/day)]; both groups followed an energy-	Increased calcium intake may enhance the beneficial effects of energy restriction on abdominal obesity and blood pressure.

		restricted diet (−800 kcal/day) throughout the study (16 weeks)	
(Varenna, Binelli, Casari, Zucchi, & Sinigaglia, 2007)	1771 healthy, early postmenopausal women in Italy	Weekly frequency of dairy food consumption was used to estimate the relative intake of dietary calcium	BMI and prevalence of overweight showed significant inverse trends with increasing dairy intake.
(Velde et al., 2011)	374 Dutch participants aged 13 to 36y	Dairy intake was measured periodically using computer-based questions and face-to-face interviews with dietitians.	The longitudinal results of this study did not conclude that greater dairy consumption is protective against overweight or MetS risk factors.
(Wennersberg et al., 2009)	121 middle-aged overweight subjects with traits of the metabolic syndrome were recruited in Finland, Norway, and Sweden	Participants were randomly assigned into milk or control groups. The milk group was instructed to consume 3–5 portions of dairy products daily. The control group maintained their habitual diet. Clinical investigations were conducted on admission and after 6 mo.	There were no significant differences between changes in body weight or body composition, blood pressure, markers of inflammation, endothelial function, adiponectin, or oxidative stress in the milk and the control groups; among participants with a low calcium intake at baseline, there was a significant treatment effect for waist circumference and sagittal abdominal diameter. Overall, this study gives no clear support to the hypothesis that a moderately increasing dairy intake beneficially affects aspects of MetS.
(Wiley, 2010)	U.S. representative sample of children aged 2–4 y (*n* = 1,493) and 5–10 y (*n* = 2,526)	NHANES 1999-2004 survey data was used	Milk was positively associated with BMI (more so than dairy products); associations were strongest among children aged 2–4y

(Yannakoulia et al., 2008)	220 Greek women aged 18-84y	Blood samples were taken, and adiponectin concentrations were measured; food intake was evaluated by 3-day food diaries; PCA was used for the identification of the dietary patterns.	The dietary pattern characterized by a high consumption of whole-grain cereals and low-fat dairy products was modestly positively associated with adiponectin concentrations.
(Yanovski et al., 2009)	340 overweight and obese adults with mean age 38.8y	Randomized, placebo-controlled trial; randomization was computer-generated, and allocation was assigned by pharmacy personnel who prepared intervention and placebo capsules	Dietary supplementation with elemental calcium, 1500 mg/d, for 2 years had no statistically or clinically significant effects on weight in overweight and obese adults.
(Zemel, Thompson, Milstead, Morris, & Campbell, 2004)	27 obese adults ~49y of age	Patients were maintained for 24 weeks on balanced deficit diets (500 kcal/d deficit) and randomized to a standard diet (400 to 500 mg of dietary calcium/d supplemented with placebo), a high-calcium diet (standard diet supplemented with 800 mg of calcium/d), or high-dairy diet (1200 to 1300mg of dietary calcium/d supplemented with placebo)	Increasing dietary calcium significantly augmented weight and fat loss secondary to caloric restriction and increased the percentage of fat lost from the trunk region, whereas dairy products exerted a substantially greater effect.
(Zemel, Sun, Sobhani, &	Twenty subjects (10	Blinded, randomized,	An increase in dairy food intake

Wilson, 2010)	obese, 10 overweight)	crossover study of dairy- compared with soy-supplemented eucaloric diets. Two 28-day dietary periods were separated by a 28-day washout period. Inflammatory and oxidative stress biomarkers were measured on days 0, 7, and 28 of each dietary period.	produces significant and substantial suppression of the oxidative and inflammatory stress associated with overweight and obesity; soy supplementation exerted no significant effects on inflammation and oxidative stress markers.

Abbreviations: y, years; MetS, metabolic syndrome; IFG, impaired fasting glucose; ATP III, Adult Treatment Panel III; DESIR, Data from the Epidemiological study on Insulin Resistance Syndrome; FFQ, food frequency questionnaire; T2D, type 2 diabetes; CVD, cardiovascular disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; TG, fasting serum triglycerides; HDL-C, high-density lipoprotein cholesterol; HOMA-R, homeostasis model assessment of insulin resistance; IRS, insulin resistance syndrome; CHD, coronary heart disease.

APPENDIX D: ADDITIONAL DATA FROM CHAPTER 2 ANALYSES

Table 14. Other relative risk models for individual and combined factors of MetS according to dairy intake in young Mexican adults (18-25 years).

	Model 4†			Model 5‡			Model 6§		
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***
Consumption of < 7 Whole Milk Servings per week									
WC ≥80 cm (F); ≥90 cm (M)	1.1	0.9, 1.4	0.48	1.1	0.9, 1.4	0.45	1.1	0.9, 1.4	0.40
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	1.2	0.5, 2.9	0.77	1.2	0.5, 3.1	0.64	1.1	0.5, 2.9	0.77
Glucose > 100 mg/dL	1.2	0.7, 2.2	0.57	1.1	0.6, 2.1	0.70	1.2	0.7, 2.2	0.51
Triglycerides ≥ 150 mg/dL	1.0	0.6, 1.6	0.99	1.0	0.6, 1.6	0.98	1.0	0.7, 1.6	0.93
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.0	0.8, 1.2	0.79	1.0	0.8, 1.2	0.76	1.0	0.8, 1.2	0.74
MetS (presence of 3 or more risk factors)	1.5	0.7, 3.0	0.29	1.4	0.7, 3.0	0.32	1.5	0.7, 3.1	0.25
Consumption of < 7 Cheese Servings per week									
WC ≥80 cm (F); ≥90 cm (M)	1.0	0.8, 1.3	0.95	1.0	0.8, 1.3	0.94	1.0	0.8, 1.3	0.88
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	1.7	0.5, 5.7	0.38	1.8	0.6, 5.7	0.34	1.7	0.5, 5.7	0.38
Glucose > 100 mg/dL	1.6	0.8, 3.6	0.20	1.7	0.8, 3.6	0.20	1.7	0.8, 3.6	0.18
Triglycerides ≥ 150 mg/dL	1.1	0.7, 1.9	0.69	1.1	0.7, 1.9	0.69	1.1	0.7, 1.9	0.65
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.2	0.9, 1.5	0.30	1.1	0.9, 1.5	0.30	1.1	0.9, 1.5	0.31
MetS (presence of 3 or more risk factors)	1.5	0.6, 3.4	0.36	1.5	0.6, 3.4	0.37	1.5	0.6, 3.5	0.34
Not Meeting Dairy Requirements									
WC ≥80 cm (F); ≥90 cm (M)	1.2	0.9, 1.7	0.17	1.3	0.9, 1.7	0.16	1.3	0.9, 1.7	0.15
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	0.9	0.4, 2.4	0.86	1.0	0.4, 2.7	0.97	0.9	0.4, 2.4	0.86
Glucose > 100 mg/dL	1.0	0.5, 2.0	0.94	1.0	0.5, 1.9	0.90	1.1	0.6, 2.0	0.87
Triglycerides ≥ 150 mg/dL	1.2	0.7, 2.1	0.45	1.2	0.7, 2.2	0.46	1.3	0.7, 2.2	0.41
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.1	0.8, 1.4	0.55	1.1	0.8, 1.4	0.57	1.1	0.8, 1.4	0.57
MetS (presence of 3 or more risk factors)	2.4	0.9, 6.5	0.09	2.3	0.8, 6.3	0.10	2.4	0.9, 6.6	0.08

Table 14 (cont.)

	Model 7[£]			Model 8[€]			Model 9[¥]		
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***
Consumption of < 7 Whole Milk Servings per week									
WC ≥80 cm (F); ≥90 cm (M)	1.1	0.9, 1.4	0.45	1.1	0.9, 1.5	0.31	1.2	0.9, 1.5	0.28
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	1.2	0.5, 3.1	0.64	1.5	0.6, 3.8	0.43	1.3	0.5, 3.4	0.55
Glucose > 100 mg/dL	1.1	0.6, 2.1	0.70	1.1	0.6, 2.0	0.82	1.1	0.6, 2.2	0.67
Triglycerides ≥ 150 mg/dL	1.0	0.6, 1.6	0.98	1.1	0.7, 1.7	0.75	1.1	0.7, 1.8	0.68
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.0	0.8, 1.2	0.76	1.0	0.8, 1.2	0.74	1.0	0.8, 1.2	0.73
MetS (presence of 3 or more risk factors)	1.4	0.7, 3.0	0.32	1.6	0.8, 3.4	0.22	1.7	0.8, 3.6	0.18
Consumption of < 7 Cheese Servings per week									
WC ≥80 cm (F); ≥90 cm (M)	1.0	0.8, 1.3	0.94	1.1	0.8, 1.4	0.72	1.1	0.8, 1.4	0.68
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	1.8	0.6, 5.7	0.34	2.4	0.9, 6.8	0.09	2.3	0.8, 6.3	0.11
Glucose > 100 mg/dL	1.7	0.8, 3.6	0.20	1.6	0.7, 3.6	0.25	1.6	0.7, 3.6	0.27
Triglycerides ≥ 150 mg/dL	1.1	0.7, 1.9	0.69	1.3	0.7, 2.2	0.42	1.3	0.7, 2.3	0.40
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.1	0.9, 1.5	0.30	1.2	0.9, 1.5	0.29	1.2	0.9, 1.5	0.29
MetS (presence of 3 or more risk factors)	1.5	0.6, 3.4	0.37	1.7	0.7, 4.0	0.23	1.8	0.7, 4.2	0.21
Not Meeting Dairy Requirements									
WC ≥80 cm (F); ≥90 cm (M)	1.3	0.9, 1.7	0.16	1.4	1.0, 1.9	0.06	1.4	1.0, 1.9	0.07
Elevated BP (SBP ≥130 and/or DBP ≥ 85 mmHg)	1.0	0.4, 2.7	0.97	1.3	0.4, 3.9	0.63	1.2	0.4, 3.3	0.77
Glucose > 100 mg/dL	1.0	0.5, 1.9	0.90	0.9	0.4, 1.8	0.70	0.9	0.4, 1.9	0.84
Triglycerides ≥ 150 mg/dL	1.2	0.7, 2.2	0.46	1.5	0.8, 2.7	0.22	1.5	0.8, 2.7	0.20
HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.1	0.8, 1.4	0.57	1.1	0.8, 1.4	0.56	1.1	0.8, 1.4	0.55
MetS (presence of 3 or more risk factors)	2.3	0.8, 6.3	0.10	2.9	1.0, 8.4	0.05*	3.1	1.1, 8.9	0.04*

Relative risk ratios were estimated using a modified Poisson logistic regression.
Abbreviations: MetS, metabolic syndrome; WC, waist circumference; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, fasting serum triglycerides; HDL-C, fasting serum HDL-cholesterol.
† Model 4, adjusted for age, age^2, and sex.
‡ Model 5, adjusted for age, age^2, sex, and family history of cardiovascular disease.

[§] Model 6, adjusted for age, age^2,sex, and family history of type 2 diabetes.
[£] Model 7, adjusted for age, age^2,sex, and family history of cardiovascular disease and type 2 diabetes.
[€] Model 8, adjusted for age, age^2,sex, calories, and family history of cardiovascular disease.
[¥] Model 9, adjusted for age, age^2,sex, calories, and family history of type 2 diabetes.
[*] $p \leq 0.05$

Table 15. Relative risk models for combined increased waist circumference and low HDL-C according to dairy intake in young Mexican adults (18-25 years).

	Model 1†			Model 2‡			Model 3§		
	RR	95% CI	*p*	RR	95% CI	*p*	RR	95% CI	*p*
Consumption of < 7 Whole Milk Servings per week WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.0	0.7, 1.4	0.96	1.0	0.7, 1.4	0.96	1.0	0.8, 1.4	0.87
Consumption of < 7 Cheese Servings per week WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.1	0.8, 1.6	0.48	1.1	0.8, 1.6	0.49	1.2	0.8, 1.7	0.36
Not Meeting Dairy Requirements WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.3	0.9, 1.9	0.19	1.3	0.9, 1.9	0.19	1.4	0.9, 2.0	0.12

	Model 4£			Model 5€			Model 6¥		
	RR	95% CI	*p*	RR	95% CI	*p*	RR	95% CI	*p*
Consumption of < 7 Whole Milk Servings per week WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.0	0.7, 1.4	0.95	1.0	0.7, 1.4	0.95	1.0	0.7, 1.4	0.95
Consumption of < 7 Cheese Servings per week WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.1	0.8, 1.6	0.49	1.1	0.8, 1.6	0.49	1.1	0.8, 1.6	0.49
Not Meeting Dairy Requirements WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.3	0.9, 1.9	0.19	1.3	0.9, 1.9	0.20	1.3	0.9, 1.9	0.19

Table 15 (cont.)

	Model 7[¤]			Model 8[¦]			Model 9[*]		
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***
Consumption of < 7 Whole Milk Servings per week									
WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.0	0.8, 1.4	0.84	1.0	0.7, 1.4	0.88	1.0	0.8, 1.4	0.86
Consumption of < 7 Cheese Servings per week									
WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.2	0.8, 1.7	0.34	1.2	0.8, 1.7	0.36	1.2	0.8, 1.7	0.36
Not Meeting Dairy Requirements									
WC ≥80 cm (F); ≥90 cm (M) **and** HDL-C < 50 mg/dL (F); < 40 mg/dL (M)	1.4	0.9, 2.1	0.11	1.4	0.9, 2.1	0.13	1.4	0.9, 2.1	0.11

Relative risk ratios were estimated using a modified Poisson logistic regression.
Abbreviations: WC, waist circumference; HDL-C, fasting serum HDL-cholesterol.
[†] Model 1, adjusted for age and sex.
[‡] Model 2, adjusted for age, age^2, and sex.
[§] Model 3, adjusted for age, sex, and calories.
[£] Model 4, adjusted for age, age^2, sex and family history of cardiovascular disease.
[€] Model 5, adjusted for age, age^2, sex, and family history of type 2 diabetes.
[¥] Model 6, adjusted for age, age^2,sex, and family history of cardiovascular disease and type 2 diabetes.
[¤] Model 7, adjusted for age, age^2,sex, calories, and family history of cardiovascular disease.
[¦] Model 8, adjusted for age, age^2,sex, calories, and family history of type 2 diabetes.
[*] Model 9, adjusted for age, age^2,sex, calories, family history of cardiovascular disease and type 2 diabetes, and physical activity.

APPENDIX E: ADDITIONAL DATA FROM CHAPTER 3 ANALYSES

Table 16. Other relative risk models for blood lipid parameters according to papaya consumption in young Mexican adults (18-25 years).

Consumption of < 3 Papaya Servings per week		**Model 3†**			**Model 4‡**	
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***
Males						
Triglycerides ≥ 150 mg/dL	1.2	0.4, 3.3	0.71	1.2	0.4, 3.3	0.71
HDL-C < 40 mg/dL	0.8	0.5, 1.3	0.37	0.8	0.5, 1.3	0.37
LDL-C > 130 mg/dL	0.9	0.6, 1.4	0.69	0.9	0.6, 1.4	0.70
Total Cholesterol > 200 mg/dL	0.8	0.3, 2.1	0.72	0.8	0.3, 2.1	0.71
Females						
Triglycerides ≥ 150 mg/dL	1.9	0.7, 5.3	0.25	1.8	0.7, 5.2	0.24
HDL-C < 50 mg/dL	1.5	1.0, 2.3	0.07	1.5	1.0, 2.3	0.07
LDL-C > 130 mg/dL	1.4	0.9, 2.4	0.18	1.4	0.9, 2.4	0.18
Total Cholesterol > 200 mg/dL	0.7	0.4, 1.3	0.25	0.7	0.4, 1.3	0.25

Consumption of < 3 Papaya Servings per week		**Model 5§**			**Model 6£**	
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***
Males						
Triglycerides ≥ 150 mg/dL	1.1	0.4, 2.9	0.82	1.2	0.4, 3.2	0.73
HDL-C < 40 mg/dL	0.8	0.5, 1.2	0.27	0.8	0.5, 1.2	0.33
LDL-C > 130 mg/dL	0.9	0.6, 1.3	0.54	0.9	0.6, 1.4	0.71
Total Cholesterol > 200 mg/dL	0.9	0.4, 2.1	0.75	0.8	0.3, 2.1	0.72
Females						
Triglycerides ≥ 150 mg/dL	1.6	0.6, 4.2	0.30	1.8	0.7, 5.0	0.25
HDL-C < 50 mg/dL	1.5	1.0, 2.3	0.06	1.5	1.0, 2.3	0.07
LDL-C > 130 mg/dL	1.4	0.9, 2.4	0.15	1.4	0.9, 2.4	0.18
Total Cholesterol > 200 mg/dL	0.7	0.4, 1.3	0.26	0.7	0.4, 1.3	0.24

Table 16 (cont.)

Consumption of < 3 Papaya Servings per week		Model 7[€]			Model 8[¥]	
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***
Males						
Triglycerides ≥ 150 mg/dL	1.1	0.4, 2.9	0.80	1.2	0.4, 3.3	0.71
HDL-C < 40 mg/dL	0.8	0.5, 1.2	0.31	0.8	0.5, 1.3	0.37
LDL-C > 130 mg/dL	0.9	0.6, 1.3	0.53	0.9	0.6, 1.4	0.70
Total Cholesterol > 200 mg/dL	0.9	0.4, 2.1	0.73	0.8	0.3, 2.1	0.71
Females						
Triglycerides ≥ 150 mg/dL	1.7	0.6, 4.3	0.30	1.8	0.7, 5.2	0.24
HDL-C < 50 mg/dL	1.5	1.0, 2.3	0.05*	1.5	1.0, 2.3	0.07
LDL-C > 130 mg/dL	1.4	0.9, 2.4	0.15	1.4	0.9, 2.4	0.18
Total Cholesterol > 200 mg/dL	0.7	0.4, 1.3	0.26	0.7	0.4, 1.3	0.25

Consumption of < 3 Papaya Servings per week		Model 9[¤]			Model 10[¦]	
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***
Males						
Triglycerides ≥ 150 mg/dL	1.2	0.4, 3.2	0.76	1.2	0.4, 3.5	0.68
HDL-C < 40 mg/dL	0.8	0.5, 1.3	0.38	0.8	0.5, 1.3	0.43
LDL-C > 130 mg/dL	0.9	0.6, 1.4	0.67	1.0	0.6, 1.5	0.83
Total Cholesterol > 200 mg/dL	0.9	0.4, 2.3	0.86	0.9	0.4, 2.2	0.81
Females						
Triglycerides ≥ 150 mg/dL	1.7	0.7, 4.5	0.28	1.9	0.7, 5.4	0.22
HDL-C < 50 mg/dL	1.5	1.0, 2.3	0.06	1.5	1.0, 2.3	0.07
LDL-C > 130 mg/dL	1.5	0.9, 2.4	0.14	1.4	0.9, 2.4	0.17
Total Cholesterol > 200 mg/dL	0.7	0.4, 1.3	0.29	0.7	0.4, 1.3	0.29

Table 16 (cont.)

Consumption of < 3 Papaya Servings per week	Model 11*			Model 12Δ		
	RR	95% CI	*p*	RR	95% CI	*p*
Males						
Triglycerides ≥ 150 mg/dL	1.2	0.4, 3.5	0.68	1.3	0.5, 3.9	0.60
HDL-C < 40 mg/dL	0.8	0.5, 1.3	0.43	0.8	0.5, 1.4	0.47
LDL-C > 130 mg/dL	1.0	0.6, 1.5	0.83	1.0	0.6, 1.6	0.95
Total Cholesterol > 200 mg/dL	0.9	0.4, 2.2	0.81	1.0	0.4, 2.3	0.96
Females						
Triglycerides ≥ 150 mg/dL	1.9	0.7, 5.3	0.22	2.1	0.8, 5.8	0.15
HDL-C < 50 mg/dL	1.5	1.0, 2.3	0.07	1.5	1.0, 2.3	0.07
LDL-C > 130 mg/dL	1.4	0.9, 2.4	0.16	1.4	0.9, 2.4	0.17
Total Cholesterol > 200 mg/dL	0.7	0.4, 1.3	0.28	0.7	0.4, 1.5	0.37

Consumption of < 3 Papaya Servings per week	Model 13∞			Model 14Ω		
	RR	95% CI	*p*	RR	95% CI	*p*
Males						
Triglycerides ≥ 150 mg/dL	1.2	0.4, 3.2	0.79	1.2	0.4, 3.1	0.77
HDL-C < 40 mg/dL	0.8	0.5, 1.4	0.46	0.8	0.5, 1.4	0.49
LDL-C > 130 mg/dL	1.0	0.6, 1.6	0.96	1.0	0.6, 1.6	0.97
Total Cholesterol > 200 mg/dL	1.0	0.4, 2.3	0.94	1.0	0.4, 2.3	0.94
Females						
Triglycerides ≥ 150 mg/dL	2.2	0.8, 6.0	0.12	2.2	0.8, 6.1	0.12
HDL-C < 50 mg/dL	1.5	1.0, 2.3	0.07	1.5	1.0, 2.4	0.06
LDL-C > 130 mg/dL	1.4	0.9, 2.4	0.16	1.4	0.9, 2.4	0.17
Total Cholesterol > 200 mg/dL	0.7	0.4, 1.3	0.38	0.7	0.4, 1.5	0.40

Relative risk ratios were estimated using a modified Poisson logistic regression.

Abbreviations: TG, fasting serum TG; HDL-C, fasting serum HDL cholesterol; LDL-C, fasting serum LDL cholesterol.
[†] Model 3 adjusted for age and calories.
[‡] Model 4 adjusted for age, calories, and family history of cardiovascular disease.
[§] Model 5, adjusted for age and family history of type 2 diabetes.
[£] Model 6, adjusted for age, calories, and family history of type 2 diabetes.
[€] Model 7, adjusted for age and family history of cardiovascular disease and type 2 diabetes.
[¥] Model 8, adjusted for age, calories, and family history of cardiovascular disease and type 2 diabetes.
[¤] Model 9, adjusted for age and physical activity.
[¦] Model 10, adjusted for age, calories, and physical activity.
[*] Model 11, adjusted for age, calories, family history of cardiovascular disease and type 2 diabetes, and physical activity.
[Δ] Model 12, adjusted for age, calories, family history of cardiovascular disease and type 2 diabetes, physical activity, and daily carotenoid intake.
[∞] Model 13, adjusted for age, calories, family history of cardiovascular disease and type 2 diabetes, physical activity, daily carotenoid intake, and daily alcohol consumption.
[Ω] Model 14, adjusted for age, calories, family history of cardiovascular disease and type 2 diabetes, physical activity, daily carotenoid intake, daily alcohol consumption, and smoking status.