THE ASSOCIATION BETWEEN MILK CONSUMPTION DURING CHILDHOOD AND PRECOCIOUS MENARCHE

by

Younjung Choi

A thesis submitted to the faculty of
The University of North Carolina at Charlotte
in Partial Fulfillment of the requirements
for the degree of Master of Public Health

Charlotte

2018

Approved By:

____
Dr. Larissa R. Brunner Huber

____
Dr. Jan Warren-Findlow

____
Dr. Sarah B. Laditka

ABSTRACT

YOUNJUNG CHOI. The association between milk consumption between ages 5 and 12 and precocious menarche. (Under the direction of DR. LARISSA R. BRUNNER HUBER)

Menarche, the last stage of the normal pubertal development in girls, is one of the most significant events in a woman's life as it signifies that a girl is capable of becoming pregnant from then on. Furthermore, menarche also means that a girl has already faced various physiological and emotional changes that are attributable to secondary sex characteristics. In this regard, the timing of menarche is considered a factor that affects a woman's health in her later life. Specifically, precocious menarche is known to be associated with various adverse health outcomes in adulthood such as obesity, breast and endometrial cancers, type 2 diabetes, and cardiovascular disease (CVD). Furthermore, with the decrease in the average age of menarche in girls residing in the United States, it is even more imperative to identify risk factors of precocious menarche. Although many studies have identified various factors that promote early onset of menarche, some factors still remain unclear. One such factor is milk consumption during childhood. Few studies have examined the association between milk intake during childhood and precocious menarche, and the results of studies that have examined this potential relationship have been inconsistent.

Accordingly, the primary purpose of this study was to determine whether more frequent milk intake between ages 5 and 12 was associated with increased odds of precocious menarche. Self-reported data collected from 4,740 females ages 20 to 49 who participated in the 2005-2014 National Health and Nutrition Examination Survey (NHANES) were used. Weighted multivariate logistic regression was used to compute

odds ratios (ORs) and 95% confidence intervals (CIs). In the unadjusted model, women who consumed milk daily and sometimes/varied between the ages of 5 and 12 had decreased odds of precocious menarche as compared to those who never/rarely consumed milk during the same period (daily: OR=0.83, 95% CI: 0.55-1.25 and sometimes/varied: OR=0.81, 95% CI: 0.45-1.47); however, this result was not statistically significant. The result remained relatively unchanged and not statistically significant after adjustment for race/ethnicity, birth cohort, country of birth, and adult body mass index (BMI) (daily: OR=0.82, 95% CI: 0.53-1.27 and sometimes/varied: OR=0.77, 95% CI: 0.42-1.43). Further studies on this topic are needed given that findings have been inconsistent. Specifically, studies with improved measurement of milk consumption by type of milk, i.e., fat level, organic/non-organic product, hormone-treated/non-hormone-treated product, and cow milk/non-cow milk, are desired to better examine the association between milk and precocious menarche.

ACKNOWLEDGEMENTS

First, I would like to thank God for giving me the strength required to pursue my MPH degree as a mother of two kids. I would like to express my deep gratitude to Dr. Larissa Huber, my wonderful academic advisor and the committee chair, for her guidance and supports. I also thank Dr. Jan Warren-Findlow and Dr. Sarah Laditka for being on my committee and providing valuable feedback. Finally, I must express my gratitude to my husband, parents, parents-in-law, and sister for prayers, encouragement, and endless love for me.

TABLE OF CONTENTS

LIST OF TABLES viii

CHAPTER 1: INTRODUCTION 1

CHAPTER 2: LITERATURE REVIEW 6

2.1 Overview of Precocious Menarche and Secular Trend. 6

2.2 Adverse Health Outcomes of Precocious Menarche 7

2.3 Determinants of Precocious Menarche 7

2.4 Milk Consumption 8

2.5 Studies about Milk Intake and Onset of Menarche 9

2.6 Possible Biological Mechanisms 15

2.7 Summary and Concluding Remarks 16

CHAPTER 3: HYPOTHESIS 18

CHAPTER 4: METHODS 19

4.1 Study Design and Population 19

4.2 Measurement of Variables 22

4.2.1 Exposure Variable 22

4.2.2 Outcome Variable 22

4.3 Covariates 23

4.4 Data Analysis 23

4.5 Sample Size and Power 24

CHAPTER 5: RESULTS 25

5.1 Univariate Analysis 25

5.2 Bivariate Analysis 26

5.3 Multivariate Analysis 27

CHAPTER 6: DISCUSSION 28

6.1 Summary of Main Findings 28

6.2 Strengths and Limitations 29

6.2.1 Nondifferential Misclassification 29

6.2.2 Selection Bias 29

6.2.3 Information Bias 30

6.2.4 Temporal Bias 30

6.2.5 Confounding 30

6.2.6 Generalizability 31

6.3 Implications and Future Research 31

REFERENCES 34

APPENDIX: TABLES 43

LIST OF TABLES

TABLE 1: Characteristics of the milk consumption-age at menarche study. sample by childhood milk consumption frequency, NHANES 2005-2014 43

TABLE 2: Unadjusted odd ratios (OR) and 95% confidence intervals (CI) of the association between select characteristics and precocious menarche, NHANES 2005-2014 45

TABLE 3: Adjusted odd ratio (OR^3) and 95% confidence interval (CI) of the association between frequency of milk consumption between ages 5 and 12 and precocious menarche, NHANES 2005-2014 46

CHAPTER 1. INTRODUCTION

Puberty is the period when various physical changes and sexual maturity take place (Pinyerd & Zipf, 2005). Typical pubertal stages in a girl progress in the order of breast development, pubic hair growth, and menarche, i.e., the first occurrence of menstruation (U.S. National Library of Medicine, 2016). Menstruation is normal monthly discharge of blood and tissues that occurs as part of a menstrual cycle when the ovulated egg is not fertilized (National Institute of Child Health and Human Development, n.d.b.). While breast development is the result of a relatively simple estrogenic action, menarche results from maturation events that consist of a more complex sequence (Parent et al., 2003). Menarche is considered a significant milestone in one's life since it means not only that a girl has the reproductive ability to become pregnant, but also that she has started to experience physiological and emotional changes that can affect her physical and mental health in her later life (Cesario & Hughes, 2007; Greif & Ulman, 1982; Stubbs, 2008).

The normal age ranges of pubertal development are between 8 and 13 years in girls and between 9 and 14 years in boys (National Institute of Child Health and Human Development, n.d.a.). Pubertal development that occurs before those age ranges is referred to as precocious puberty (Partsch & Sippell, 2001). With a secular trend toward earlier puberty timing being reported in the United States, precocious puberty, which has greater impacts on girls than on boys, has emerged as a public health issue (Parent et al., 2003). Reported ages of onset of breast development based on large scaled data have declined from 12.8 years for girls born in the 1960s to 10 years for girls born in 2006 (Biro, Greenspan, & Galvez, 2012). A similar trend in age at menarche among girls living in the United States also has been reported. The mean age at menarche was 14.7 years in 1877 but declined to 12.5 years in 2001 (Karapanou & Papadimitriou, 2010; Wyshak & Frisch, 1982).

The decrease in the average age of menarche in girls living in the United States has significant implications for public health. Since menarche is a relatively late marker of pubertal development in girls, it is reasonable to assume that a girl who has experienced the onset of menarche is likely to have already started to show physical differences that are attributable to secondary sex characteristics. Accordingly, how different a girl's age at menarche is from the average or that of her peers can have an impact on her health, particularly as it relates to psychological and social/behavioral problems (Mendle, Turkheimer, & Emery, 2007). Precocious menarche, in particular, has been shown to be associated with increased likelihood of life-time drunkenness episodes, early sexual intercourse, teen pregnancy, and overweight or obesity (Deardorff, Gonzales, Christopher, Roosa, & Millsap, 2005; Gaudineau et al., 2010). In addition, precocious menarche in girls is associated with a broad range of adverse health outcomes in adulthood including increased adult body mass index, breast and endometrial cancers, type 2 diabetes, cardiovascular disease (CVD), and premature or early natural menopause (F. R. Day et al., 2017; Farahmand, Tehrani, Dovom, & Azizi, 2017; R. Lakshman et al., 2009a; Mishra et al., 2017; Prentice & Viner, 2013).

The onset of menarche is determined by a combination of various factors that interrelate together such as genetic, environmental, and lifestyle (Karapanou & Papadimitriou, 2010). Many studies have been conducted to identify determinants and risk factors of precocious menarche. One of the risk factors identified is childhood overweight/obesity as defined by body mass index. Elevated body mass index in childhood is associated with earlier age at menarche (Ahmed, Ong, & Dunger, 2009; Bralic et al., 2012; Freedman et al., 2002). As a genetic factor, heritability of maternal age at menarche is known to be possible (Kaprio et al., 1995). Studies have also demonstrated that childhood family structure factors such as the number of siblings and birth order may influence age at menarche (Morris, Jones, Schoemaker, Ashworth, & Swerdlow, 2010). Another study indicated that childhood socioeconomic status including family income, paternal occupation, and education also had an influence on age at menarche (James-Todd, Tehranifar, Rich-Edwards, Titievsky, & Terry, 2010). Other factors considered to have effects on precocious menarche include physical activity, nutritional habits, and exposure to endocrine disrupting chemicals (Buttke, Sircar, & Martin, 2012; Merzenich, Boeing, & Wahrendorf, 1993; Rogers et al., 2010).

Despite neurobiological mechanisms of the onset of menarche, it remains unclear how the macro factors mentioned above influence timing of menarche. Although many studies have examined the associations between various factors and precocious menarche, only a few factors (e.g., maternal age at menarche, childhood obesity, and level of physical activity) have been well established as associated factors of precocious menarche (Bralic et al., 2012; Kaprio et al., 1995; Merzenich et al., 1993; Yermachenko & Dvornyk, 2014). Due to inconsistent study results, the role of other factors on the timing of menarche remains controversial. One factor that has inconsistent effects on the timing of menarche is nutritional habits. Different nutrients, including both macro and micro nutrients such as protein, fat, calcium, vitamins D, and dietary fiber, were examined by various studies, and higher intake of animal protein was one of the nutritional habits that showed inconsistent effects on the timing of menarche. Although various studies have shown that higher intake of animal protein during childhood is associated with accelerated onset of menarche, results are inconsistent depending on the study design used and the source of animal protein studied (Berkey, Gardner, Frazier, & Colditz, 2000; Rogers et al., 2010). For example, while higher red meat intake was associated with earlier menarcheal age in a study, milk consumption did not demonstrate an effect on earlier menarcheal age in another study (Carwile et al., 2015; Jansen, Marin, Mora-Plazas, & Villamor, 2016). Inconsistent results attributable to differences in study design were also observed among studies that investigated milk intake and early menarche (<12 years) (Ramezani Tehrani et al., 2013; Wiley, 2011). In a cross-sectional study, the researcher suggested that girls aged 9-12 years who consumed up to 244g of milk per day had a lower risk of early menarche than girls who did not consume milk (Wiley, 2011). In contrast, a prospective cohort study reported that girls aged 4-12 years who consumed milk more than 34g of milk per day had an increased risk of early menarche than girls who consumed less milk (Ramezani Tehrani et al., 2013).

As milk is known to be a good source of protein and other nutrients, the Dietary Guidelines for Americans recommend regular consumption of milk and dairy products (DeSalvo, Olson, & Casavale, 2016; Fogli-Cawley et al., 2006; Quann, Fulgoni, & Auestad, 2015). In particular, regular milk consumption during childhood is strongly recommended due to its importance in bone health and optimal growth (Greer, Krebs, & American Academy of Pediatrics Committee on, 2006). Accordingly, milk has been regularly consumed by the majority of children and adolescents: approximately 92% of girls and 85% of boys who participated in the 2007-2008 NHANES reported consumption of milk on a daily or a weekly basis (Kit, Carroll, & Ogden, 2011). Although regular milk consumption has nutritional benefits, some studies suggest that regular milk consumption is associated with precocious menarche due to its animal protein components and Insulin-like Growth Factor-1 (IGF-1) (Wiley, 2012). However, the association between milk consumption and increased likelihood of earlier age at menarche is still controversial due to inconsistency of study results (Carwile et al., 2015; Wiley, 2011). Therefore, this study examined the association between frequency of milk intake between ages 5 and 12 and precocious menarche based on National Health and Nutrition Examination Survey (NHANES) data collected from representative samples of the United States female population.

CHAPTER 2. LITERATURE REVIEW

2.1 Overview of Precocious Menarche and Secular Trend

Menarche refers to the onset of the first menstrual cycle (U.S. National Library of Medicine, n.d.). Menstruation refers to normal monthly excretion of blood and tissue from the lining of the uterus through the vagina when ovulation did not lead to fertilization and menarche refers to occurrence of the first menstruation (NICHD, n.d.b.). There is no definitive age limit that distinguishes normal and precocious menarche. However, precocious menarche has been generally defined in many studies as onset of menarche before the age of 12 (Gaudineau et al., 2010; Ibitoye, Choi, Tai, Lee, & Sommer, 2017).

Between the mid-19th and the mid-20th century, a significant decrease in menarcheal age was observed in the United States and countries in Western Europe (Parent et al., 2003). Specifically, the average menarcheal age was 17 years in the mid-19th century and dropped to below 14 years in the mid-20th century (Parent et al., 2003). A study that analyzed 1999-2004 NHANES data found a birth cohort-related declining trend observed in the ages at menarche of 6,788 females (McDowell, Brody, & Hughes, 2007). In the study, the mean age at menarche of women born before 1920 was 13.3 years (95% CI: 13.1, 13.5) and that of later birth cohorts continued to show a decreasing trend and reached 12.4 years (95% CI: 12.2, 12.6) in the birth cohort group of 1980 to 1984 (McDowell et al., 2007). This decline was consistently observed in all racial/ethnic groups (McDowell et al., 2007). Other studies have also observed this decline in the mean age of menarche (Herman-Giddens et al., 1997; MacMahon, 1972; Parent et al., 2003; Tanner & Davies, 1985).

2.2 Adverse Health Outcomes of Precocious Menarche

The declining trend in menarcheal age is considered a public health issue since girls who experience precocious menarche are at higher risk for various negative health outcomes in their adulthood (Day, Elks, Murray, Ong, & Perry, 2015). Studies have continued to add evidence supporting associations between younger age at menarche and higher risks for adulthood obesity, type 2 diabetes, CVD, and breast and endometrial cancers (F. R. Day et al., 2017; Elks et al., 2013; Farahmand et al., 2017; R. Lakshman et al., 2009b; Prentice & Viner, 2013). In studies, precocious menarche appeared to be associated with approximately twice the odds of adult obesity and 1.7 to 3.6 times the risk of type 2 diabetes (Elks et al., 2013; Farahmand et al., 2017; Prentice & Viner, 2013). The odds of CVD incidence among women who had menarche before 12 years of age was 28% greater than that of those women who did not have menarche before 12 years (Rajalakshmi Lakshman et al., 2009). Regarding breast and endometrial cancers, a large-scale genomic study demonstrated that the increase in age at menarche by one year was associated with decreased odds of breast and endometrial cancers by 6.5% and by 22% respectively (Felix R. Day et al., 2017).

2.3 Determinants of Precocious Menarche

Much research conducted to identify determinants of pubertal development timing has revealed that age at menarche is not determined by a single factor, but by the complex interaction of numerous factors (Karapanou & Papadimitriou, 2010). Based on studies, the factors that are thought to play a role in determining the onset of menarche include both genetic and non-genetic factors (Karapanou & Papadimitriou, 2010). Regarding genetic effects, a study suggested that genetic factors accounted for approximately half of impact on determining age at menarche independent of shared environments, and this finding was consistent with many previous studies (Towne et al., 2005).

With regards to non-genetic factors associated with age at menarche, many studies report that childhood obesity and nutrition are correlated with age at menarche (Karapanou & Papadimitriou, 2010). Childhood obesity is a well-known risk factor that has shown a consistent link with precocious menarche although causality has not been explicitly proven (Ahmed et al., 2009). A large-scale study demonstrated that girls with a BMI at the 75th percentile were at approximately 1.8 times greater risk of onset of menarche before the age of 11 than were girls with a BMI of the 25th percentile (Freedman et al., 2002).

Effects of nutritional or dietary habits on age at menarche have been investigated by many researchers as another potential influence on onset of menarche. Numerous studies suggest that higher intake of animal foods during childhood is related to earlier onset of menarche and higher animal protein was considered to be an important contributing factor (Berkey et al., 2000; Cheng et al., 2012; Gunther, Karaolis-Danckert, Kroke, Remer, & Buyken, 2010; Villamor & Jansen, 2016). A study reported that higher meat intake in childhood was strongly associated with promoting onset of menarche (Rogers et al., 2010). The study especially indicated that an increased protein intake and meat consumption at age 7 elevated the odds of onset of menarche at age 12.7 years by 14% and 57%, respectively (Rogers et al., 2010).

2.4 Milk Consumption

Milk is a well-known food source of protein as well as other essential nutrients and has been widely consumed as part of routine dietary components, especially by children (Rozenberg et al., 2016; Wiley, 2012). According to the 2003-2006 NHANES, milk served as the most important dietary source for children's total energy (7%) and protein (13.2%) (Keast, Fulgoni, Nicklas, & O'Neil, 2013). The wide consumption of milk among children may be largely attributable to the government's recommendation on milk intake through Dietary Guidelines for Americans (DGA). Since 1980, the Department of Health and Human Services (HHS) and the Department of Agriculture (USDA) have officially recommended regular milk consumption through DGA due to its benefits such as adequate growth and bone health (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 1980, 1985, 1990, 1995, 2000, 2005, 2010, 2015). Since 1990, the HHS and USDA suggested a specified recommended amount of milk intake, ranging from 2 to 3 cups of fat-free or low-fat milk per day.

2.5 Studies about Milk Intake and Onset of Menarche

Despite the benefits of milk intake, milk has been suggested to contribute to onset of menarche at an earlier age (Kato, Tominaga, & Suzuki, 1988; Ramezani Tehrani et al., 2013; Wiley, 2011). A limited number of studies have been conducted to assess the association between milk consumption and age at menarche; many of these studies have been conducted with participants in countries other than the United States (Carwile et al., 2015; Gaskins et al., 2017; Kato et al., 1988; Ramezani Tehrani et al., 2013; Wiley, 2011; Zhu et al., 2006). Results vary vastly across or within the study, and thus, the association between milk consumption and precocious menarche still remains unclear.

A baseline survey for a population-based cohort study in Japan obtained information regarding factors related to late menopause and early menarche (Kato et al., 1988). The study collected relevant data from 17,790 women aged 40 or more. The women were categorized into three groups of early (mean 12.5 years), average (mean 14.6 years), and late (mean 17.2 years) menarche according to the age distribution. In this study, daily intake of milk was positively associated with early menarche (standardized partial regression coefficient of daily milk intake=0.039, $p<0.01$). However, it should be noted that current milk intake was used as a proxy for past milk intake. Thus, the exposure may be misclassified. Additionally, generalizability may be limited since the study participants were Japanese women who lived in two selected regions. In addition, the study was published approximately 30 years ago and thus, the results may not be applicable to more recent cohorts.

A 2-year school milk intervention study assigned 698 Chinese girls aged 10 years into three groups that received calcium-fortified milk, calcium and Vitamin D-fortified milk, or nothing and followed them for three years. The researchers found no significant difference in mean age at menarche among the three groups (12.2 years, 12.1 years, and 12.2 years for the calcium-fortified milk group, the calcium and vitamin D-fortified milk group, and the control group respectively, $p=0.6$) (Zhu et al., 2006). It is important to note that the control group was told to continue their usual dietary habits. Thus, the lack of significant results could be due to the fact that the control really resembled one of the milk groups studied. Also, since the milk intake-age at menarche association was not the main focus of the study, the authors did not control for any potential confounding factors.

Furthermore, this study may not be generalizable to other populations since the study was conducted in nine schools in China.

A study analyzed 1999-2004 NHANES data in multiple ways to investigate the association between milk and age at menarche by using two samples of females (2,657 females ages 20-49 years and 1,008 girls ages 9-12 years) (Wiley, 2011). To analyze the adult female data, the researchers grouped the women into three categories (daily, sometimes/varied, and never/rarely) based on their milk consumption frequency at ages 5-12 years. By conducting a multivariate linear regression, the study found a weak negative association between milk consumption and age at menarche after controlling for ethnicity and country of birth (β=–0.317 years, p<0.095 for the “daily” group and β=–0.378 years, p<0.061 for the “sometimes/varied” group, each compared to the “never/rarely” group) (Wiley, 2011). In addition, Cox regression did not find any difference in the risk of early menarche (<12 years) between the compared groups: “daily” vs. “never/rarely (Hazard Ratio [HR]=1.25, p<0.23) and “sometimes/varied” vs. “never/rarely” (HR=1.20, p<0.42) (Wiley, 2011). Similarly, when the researchers considered the younger girls (ages 9-12 years) who participated in NHANES they found no association between frequency of milk consumption in the past 30 days and early menarche (<12 years) after adjusting for birth weight, ethnicity, and overweight status (daily vs. never/rarely/sometimes/varied [HR=0.9, 95% CI: 0.6, 1.6]) (Wiley, 2011). However, among the young girl sample, an association between quantity of milk consumed in the past 24 hours and early menarche was observed, Specifically, girls who consumed milk up to 244g in the past 24 hours had a lower risk of early menarche (HR=0.6, 95% CI: 0.4, 0.9, p<0.02) than did girls who consumed milk 245g or more after adjusting for birth weight, ethnicity, overweight status, height, total calcium intake, and dairy fat intake (Wiley, 2011).

In sum, despite the multipronged approach used to investigate the association between milk consumption and age at menarche in the NHANE dataset, the study yielded inconsistent results and has some factors that hampered comparability and usability of the results. In the study, age at menarche was predicted by linear regression, which is used when the dependent variable is a continuous variable (Alexopoulos, 2010). However, the dependent variable, age at menarche of the adult women who participated in the NHANES, was collected as a whole number rather than as a continuous variable (Centers for Disease Control and Prevention, n.d.d.). The way age was measured may have weakened the study's finding. Furthermore, although this study limited the age range of the sample included in the analysis to 20-49 years to prevent a cohort effect, i.e., a period-related effect that may affect age groups differently, it is still possible that a cohort effect had an impact on the result (Keyes, Utz, Robinson, & Li, 2010). In addition, since onset of menarche is determined by both genetic and non-genetic factors, not only country of birth but also length of time participants have lived in the United States prior to menarche may be important to include as covariates (Karapanou & Papadimitriou, 2010).

A prospective cohort study that enrolled 134 representative Iranian girls aged between 4 and 12 years provided evidence that milk consumption at pre-pubertal ages has a role on the odds of menarche at or under the age of 12 years (Ramezani Tehrani et al., 2013). Milk intake was measured two times, approximately 10 days apart, by expert dietitians and converted into grams. Age at menarche was collected in the form of a whole number by asking participants an open-ended question: "At what age did you have your first menstrual period?" To assure better accuracy of the data, participants were asked the probing question "Do you remember what grade you were when your menstruation began?" In the study, total energy intake, protein intake, age interval between study initiation and onset of menarche, maternal age at menarche, and BMI were adjusted for in different regression models (Ramezani Tehrani et al., 2013). After adjustment, girls who consumed more than 34 grams of milk a day had over twice the odds of onset of menarche at age 12 or younger compared to girls who consumed milk less than 34 grams a day (OR=2.34, 95% CI: 1.05, 5.18, p=0.04) (Ramezani Tehrani et al., 2013). However, this study included a relatively small sample size and the results may not be applicable to the United States population due to possible differences in milk consumption patterns and other dietary habits.

A prospective cohort study that followed 5,583 premenarcheal girls aged 9 to 14 years from the United States from 1996 through 2001 investigated the association between milk consumption and age at menarche (Carwile et al., 2015). Participants were asked to complete questionnaires annually. For milk consumption frequency, participants were asked to answer on average, how frequently they consumed 1 glass of milk. The accumulated data on frequency of milk intake before menarche were averaged for analysis. To measure age at menarche, participants were asked if their menstrual cycles had begun and if so, their age and the calendar month at menarche. The factors that served as covariates included total energy intake, maternal age at menarche, race/ethnicity, physical activity, inactivity, birthweight, sugar-sweetened beverage consumption, household composition (no father or stepfather, father, and stepfather), frequency of family dinner, BMI, and height. In the model that adjusted for all factors except BMI and height, girls who consumed more than 3 glasses of milk per day did not show an increased risk of attaining menarche in the next month compared to those girls who consumed 1.1-4 glasses of milk per week (HR=0.93, 95% CI: 0.83, 1.04). After BMI and height were controlled for, girls who consumed more milk had a decreased risk of attaining menarche in the next month compared to the referent group (HR=0.87, 95% CI: 0.77, 0.97). With the assumption that BMI or height may be on the causal pathway between milk consumption and age at menarche, the study intentionally differentiated the models with or without BMI and height to avoid overadjustment. Overall, the study found that regular milk consumption after the age of 9 years does not affect onset of menarche (Carwile et al., 2015). The findings of this study may not be generalizable to other populations since the participants are children of registered nurses in 15 states who were enrolled in Nurse's Health Study II (Curhan, Willett, Knight, & Stampfer, 2004; Rockett, Berkey, Field, & Colditz, 2001).

A prospective study conducted in Chile also did not find a clear association between milk consumption and onset of menarche (Gaskins et al., 2017). The study followed 324 girls aged 3 and 4 years for 10 years starting in 2006 to assess the association between dairy product intake and pubertal development. Data on dietary intake and date of menarche were collected every 6 months. The results of this study showed inconsistent findings regarding the role of milk intake on onset of menarche. Total milk intake did not appear to have a role in early onset of menarche after adjustment for total energy intake, sugar-sweetened beverage intake, television watching after school, maternal age at menarche, maternal education level, BMI, and height

(HR=0.85, 95% CI: 0.60, 1.22, p-trend=0.55). However, low fat milk was associated with decreased risks of menarche in the next month by 28% to 43% (HR=0.57, 95% CI: 0.40, 0.82 for low fat milk consumption 1-125g/d and HR=0.72, 95% CI: 0.48, 1.07 for low fat milk consumption more than 125g/day, each compared to the group that did not consume low fat milk). This study result cannot be generalized to other populations because the participants were Chilean girls with low-middle socioeconomic status (Gaskins et al., 2017). In addition, the study had a relatively small sample size.

2.6 Possible Biological Mechanisms

Given that milk serves as a primary source of energy and various macronutrients like many other foods, it is important to focus on components that distinguishably exist in milk when evaluating its role on the onset of menarche (Wiley, 2012). Insulin-like growth factor I (IGF-I), part of protein fraction in milk, is one of the components that has been researched extensively (Wiley, 2012). According to a study of Danish children, increased milk intake at 2.5-year-old was associated with increased levels of circulating IGF-I in children (Hoppe et al., 2004). An elevated IGF-I level has been shown to stimulate the release of Gonadotrophin-releasing hormone (GnRH), which regulates timing of puberty (Daftary & Gore, 2005). GnRH is well known to play a critical role in activating reproductive maturation (Ebling, 2005). These mechanisms are also supported by another study that reported higher levels of IGF-I at age 8 were associated with earlier age at menarche (Thankamony et al., 2012). Taken together, milk may have a role in accelerating the onset of menarche by increasing the level of circulating IGF-I, which enhances GnRH secretion, and consequently, activates pubertal development and contributes to earlier age at menarche.

2.7 Summary and Concluding Remarks

Age at menarche has shown a remarkable decrease over time (Karapanou & Papadimitriou, 2010; Wyshak & Frisch, 1982). Consequently, precocious menarche has emerged as an important public health issue due to its association with various negative health outcomes in adulthood (F. R. Day et al., 2017; Farahmand et al., 2017; R. Lakshman et al., 2009a; Mishra et al., 2017; Prentice & Viner, 2013). Since the onset of menarche results from the complex interactions of various factors involved, the independent effects of each factor on age at menarche are still largely unclear. Postnatal factors that have been reported to have an association with earlier age at menarche include childhood obesity, physical activity, and nutritional habits, in particular, higher intake of animal protein (Ahmed et al., 2009; Cheng et al., 2012; Gunther et al., 2010; Jansen et al., 2016; Karapanou & Papadimitriou, 2010).

Milk is one of the most common sources of animal protein. Given that the United States Department of Agriculture encourages regular milk consumption through Dietary Guidelines for Americans, drinking milk has become a common dietary habit in the United States (Wiley, 2012). Despite various benefits of milk consumption such as it being a good source of energy and other macronutrients, it is possible that milk intake plays a role in earlier age at menarche. However, evidence of the role of milk in onset of menarche is sparse and inconsistent. Many of the key studies enrolled relatively small number of samples (Gaskins et al., 2017; Ramezani Tehrani et al., 2013; Zhu et al., 2006) or had incomplete control of confounding (Wiley, 2011; Zhu et al., 2006). In addition, many studies were conducted outside the United States (Gaskins et al., 2017; Kato et al., 1988; Ramezani Tehrani et al., 2013; Zhu et al., 2006). However, findings from the studies may not be applicable to other populations due to the lack of racial/ethnic diversity in their study samples. Therefore, if a study that utilizes a representative sample of United States population is conducted, findings from the study may be more useful since the study population will be more diverse with respect to ethnicity/race. Although the study based on the 1999-2004 NHANES used a nationally representative sample, there is an opportunity to extend that work (Wiley, 2011). The current study analyzed childhood milk consumption patterns of over 4,700 females and their age at menarche using the 2005-2014 NHANES and additionally controlled for birth cohort and adult BMI as a proxy for childhood BMI (Serdula et al., 1993). This study aimed to provide additional evidence regarding the role of milk intake in the onset of menarche that can be generalized to the United States population.

CHAPTER 3. HYPOTHESIS

This cross-sectional study examined the association between frequency of milk intake between ages 5 and 12 and reported age at menarche among females aged between 20 and 49 years who participated in the National Health and Nutrition Examination Survey (NHANES) from 2005 through 2014. The specific hypothesis was:

- There is a dose-response relationship between consumption of milk and odds of precocious menarche. Females who consumed milk daily or sometimes/varied between the ages of 5 and 12 will have increased odds of precocious menarche compared to those females who never or rarely consumed milk between the same age period.

CHAPTER 4. METHODS

4.1 Study Design and Population

My research used data from the 2005-2014 National Health and Nutrition Examination Survey (NHANES). NHANES, a cross-sectional survey designed by the National Center for Health Statistics (NCHS) that was first initiated in the early 1960s, is designed to collect data focusing on different target populations or health topics (Centers for Disease Control and Prevention, 2017). In 1999, NHANES became a continuous biennial survey that assesses the health and nutritional status of adults and children residing in the United States (CDC, 2017). Unlike the other programs governed by NCHS, NHANES uses a combination of interviews, physical examinations, and laboratory tests to assess the health and nutritional status of United States residents (CDC, 2017).

Since 1999, NHANES has covered a variety of items associated with respondents' health and nutrition as well as items related to demographics (CDC, 2017). NHANES data provide basic information that describes national standards for measured components such as height, weight, and blood pressure (CDC, 2017). NHANES data also serve as the basis for assessing the nutritional status of the population, determining the prevalence of major diseases, and identifying risk factors for diseases (CDC, 2017). Ultimately, the data are used in epidemiological studies, and research findings contribute to public health policy development, health intervention planning, and health knowledge dissemination (CDC, 2017).

NHANES employs a complex probability sampling method that selects participants through multiple stages to extract a representative sample of the non-institutionalized United States civilian population of all ages (Centers for Disease Control and Prevention, 2013a). Selection of participants is conducted in four stages, which include selecting primary sampling units (PSUs), segments, households, and individuals respectively (Centers for Disease Control and Prevention, 2013a, 2016). In the first stage, all the counties in the United States are divided into 15 groups. Mostly, a single county is selected from each group, and accordingly, 15 counties participate in the NHANES surveys. These counties serve as PSUs. In the second stage, segments, which are generally city blocks, are formed within each PSU and 20 to 24 segments are selected from each PSU. In the next stage, households in each segment are identified and a random sample of 30 households is drawn from each segment. In the last stage, some, all, or none of the household members are randomly selected by a computer algorithm (Centers for Disease Control and Prevention, 2013a, 2016). To assure reliability and precision, NHANES oversamples certain population subgroups of specific public health interest (CDC, 2013a). Mexican Americans, low-income White Americans, persons age 60 and older, and adolescents aged 12-19 years are examples of subgroups oversampled in the past (Centers for Disease Control and Prevention, n.d.a.).

The NHANES program uses several different modes of data collection for enhanced efficiency, quality, and accuracy of data (Centers for Disease Control and Prevention, 2013b). Trained interviewers, including bilingual interviewers, use Computer-Assisted Personal Interview (CAPI) technology to conduct initial in-person interviews that take place in participants' homes (Centers for Disease Control and Prevention, n.d.b.). Participants who complete the initial interview may participate in physical examinations and laboratory tests. Both physical examinations and laboratory tests that are performed by physicians and/or other required special technicians take place in standardized Medical Examination Centers (MECs) (CDC, n.d.b.). The standardized environments of MECs allow the examination and laboratory teams to minimize site-specific errors by using systemized equipment and specimen collection (CDC, n.d.b.). Additional health interviews, including the dietary interview and private health interview were conducted in the MEC (Zipf et al., 2013). In these interviews, CAPI and Audio Computer-Assisted Self-Interviewing system (ACASI) were used (Zipf et al., 2013). The duration of an individual examination varies by age and gender and was between 40 minutes and 4 hours (Zipf et al., 2013).

Among all participants of the NHANES, females who participated in the NHANES between 2005 and 2014, were aged between 20 and 49 at the time of participation, and provided complete information on the exposure and outcome were included in this study. Annually, approximately 5,000 individuals are interviewed and examined through NHANES (CDC, 2017). In the five consecutive NHANES cycles encompassing 2005 through 2014, a total of 66,840 individuals were screened. Among the screened individuals, there were a total of 33,593 females. Of the screened females, 9,883 were aged between 20 and 49. The response rate of the female participants in the age group was 77.5% (7,656 persons) for completion of the health interview and 75.3% (7,438 persons) for completion of all components of the study (Centers for Disease Control and Prevention, n.d.c.).

4.2 Measurement of Variables

4.2.1 Exposure Variable

The main exposure in this study is frequency of milk intake between the ages of 5 and 12 years old. This information was collected during the diet behavior and nutrition interview. During the interview, participants were asked how often they had drunk any type of milk, including milk added to cereal, when they were a child between the ages of 5 and 12 years old. They were given predetermined response options, which were never, rarely (less than once a week), sometimes (once a week or more, but less than once a day), often (once a day or more), and varied. These response options were collapsed into three categories. If the respondent answered "never" or "rarely - less than once a week", she was considered unexposed. Respondents who answered "sometimes - once a week or more, but less than once a day" or "varied" were considered sometimes/varied consumers of milk while respondents who indicated "often – once a day or more" were categorized as daily consumers of milk. Women who responded with "refused" or "don't know" were not included in the analyses. This categorization has been used in a prior study that evaluated the association between milk consumption and age at menarche (Wiley, 2011).

4.2.2 Outcome Variable

The outcome of interest is precocious menarche. Based on the mean age at menarche in girls living in the United States and definitions of precocious menarche in various studies, this study considers precocious menarche as onset of menarche before the age of 12 (Gaudineau et al., 2010; Ibitoye et al., 2017). Precocious menarche was assessed based on the reproductive health data. Participants were asked their age at menarche during the reproductive health interview session. The exact question the participants were asked was “How old were you when you had your first menstrual period?” If the reported age at menarche was under 12 years, the participant was considered to have the outcome. If the response was 12 and above or “not yet started”, the participant was not considered to have the outcome. The analyses excluded responses of “refused” or “don’t know”.

4.3 Covariates

Information on demographic characteristics collected on the NHANES questionnaires was considered as potential confounding factors. The considered confounding factors were based on the literature and other factors that are not believed to be on the causal pathway between exposure and outcome. The potential confounders that were assessed included birth cohort (birth year before 1960, birth year between 1961 and 1970, birth year between 1971and 1980, and birth year between 1981 and 1993), race/ethnicity, country of birth, length of time in the United States prior to menarche, and BMI (Wiley, 2011). Adult BMI was used as a proxy for childhood BMI since childhood BMI data were not collected from participants and adult BMI is known to be highly correlated with childhood BMI (Serdula et al., 1993).

4.4 Data Analysis

The frequencies and percentages of demographic characteristics, milk consumption during childhood, and age at menarche were calculated to summarize the characteristics of the participants in the study. By using logistic regression, unadjusted odds ratios and 95% confidence intervals were calculated to assess the crude association between milk intake frequency between the ages of 5 and 12 and precocious menarche. In addition, associations between each of the covariates and precocious menarche were examined to identify other risk factors. Multivariate logistic regression was used to calculate adjusted odds ratios and 95% confidence intervals to determine the association between milk intake frequency between the ages of 5 and 12 and precocious menarche. To identify which factors to adjust for in the final model, a backward elimination approach was used. In addition to the exposure, potential confounders that had a p-value <0.20 were retained in the final model (Budtz-Jorgensen, Keiding, Grandjean, & Weihe, 2007). SAS 9.4 was used to analyze the data. Due to the complex probability sampling method employed by NHANES, weighted analyses were performed using PROC SURVEY procedures in SAS.

4.5 Sample Size and Power

A total of 4,740 females aged between 20 and 49 were included in this analysis. Considering those who never or rarely consumed milk between ages 5 and 12 as the unexposed and experiencing menarche before the age of 12 as the outcome of interest, the ratio of unexposed:exposed was approximately 0.04:1 and the frequency of the outcome among the unexposed was approximately 24.4%. With the confidence level set at 95%, power at 80%, the ratio of unexposed to exposed at 0.04:1, and the frequency of the outcome among those who never or rarely consumed milk between ages of 5 and 12 of 24.4%, the smallest detectable OR was 1.63.

CHAPTER 5: RESULTS

5.1 Univariate Analysis

A total of 7,438 females aged between 20 and 49 years participated in the 2005-2014 NHANES. Females were excluded if they did not provide information about menarcheal age (n=1,040) or if they answered that they had not yet reached menarche (n=3). Females were also excluded if they did not answer the question on milk consumption frequency between the ages of 5 and 12 years (n=1,655). After excluding those females, 4,740 females were available for analysis.

The majority of females were non-Hispanic White (64.3%), followed by Hispanic (16.4%), non-Hispanic Black (12.1%), and others (7.1%; Table 1). The majority of females (85.4%) responded that they had consumed milk daily between the ages of 5 and 12 while those who consumed milk sometimes/varied and never/rarely consumed milk during the same period accounted for 10.8% and 3.8% respectively. Over three quarters of respondents reported that they reached menarche at the age of 12 years or above (78.8%). Respondents with precocious menarche, menarche reached before the age of 12 years, accounted for 21.2% of the sample.

Among those women who consumed milk daily or sometimes/varied during childhood, 65.2% were non-Hispanic White while among those who never/rarely consumed milk during childhood, non-Hispanic White females accounted for only 41.6%. Only 6.8% of the study participants were born prior to 1961. The remaining women were fairly evenly distributed across the remaining birth cohorts (birth cohort 1961-1970: 32%, birth cohort 1971-1980: 31.4%, and birth cohort 1981-1993: 29.8%). The majority of respondents were born in the United States (82.1%), and in turn, most women spent 6 years or more in the United States before menarche (85.8%). Among females who responded that they had never/rarely consumed milk during childhood, those who were born in the United States accounted for slightly more than half (56.5%). However, among females who consumed milk daily or sometimes/varied during childhood, the majority were born in the United States (84.0% for females who consumed milk daily and 76.3% for females who consumed milk sometimes/varied).

5.2 Bivariate Analysis

Females who consumed milk daily or sometimes/varied between the ages of 5 and 12 had approximately 20% decreased odds of precocious menarche as compared to those females who never or rarely consumed milk between the same age period (sometimes/varied: OR=0.81; 95% CI: 0.45-1.47 and daily: OR=0.83; 95% CI: 0.55-1.25; Table 2); however, these findings were not statistically significant.

Non-Hispanic Black and Hispanic females had over 1.5 times increased odds of precocious menarche compared to Non-Hispanic White females (non-Hispanic Black: OR=1.55; 95% CI: 1.27-1.88 and Hispanic: OR=1.60; 95% CI: 1.30-1.97). Females of other races had slightly increased odds of precocious menarche compared to Non-Hispanic White females; however, the odds ratio was not statistically significant (Others: OR=1.16; 95% CI: 0.86-1.57).

Compared to females who were born before 1961, females who were born after 1970 had greater odds of precocious menarche (females born between 1971 and 1980: OR=1.15; 95% CI: 0.77-1.70 and females born between 1981 and 1993: OR=1.24; 95% CI: 0.85-1.81). In contrast, females born between 1961 and 1970 had 12% decreased odds of precocious menarche compared to those born before 1961 (OR= 0.88; 95% CI: 0.57-1.35). However, the results were not statistically significant.

Females born in the United States had a nearly 10% increased odds of precocious menarche compared to those born in countries other than the United States and the result was not statistically significant (OR=1.11; 95% CI: 0.90-1.37). Compared to females with adult BMI classified as underweight or normal weight, females with higher adult BMI had greater odds of precocious menarche. Specifically, females who were classified as being obese in adulthood had over twice the odds of precocious menarche compared to females with adult BMI of under/normal weight, and the result was statistically significant (OR=2.26, 95% CI: 1.85-2.77). Females who were classified as being overweight as adults, however, had 20% increased odds of precocious menarche compared to those with underweight/normal adult BMIs, but the result was not statistically significant (OR=1.20; 95% CI: 0.94-1.52).

5.3 Multivariate Analysis

After adjustment for race/ethnicity, birth cohort, country of birth, and BMI, the magnitude of the association between milk consumption between the ages of 5 and 12 years and precocious menarche remained relatively unchanged, and the results continued to not be statistically significant. Specifically, females who consumed milk sometimes/varied between ages 5 and 12 years had 23% decreased odds of precocious menarche compared to those who never/rarely consumed milk during the same period (OR=0.77; 95% CI: 0.42-1.43). In addition, females who consumed milk daily during the same period also had decreased odds of precocious menarche compared to those who never/rarely consumed milk (OR=0.82; 95% CI: 0.53-1.27).

CHAPTER 6. DISCUSSION

6.1 Summary of Main Findings

This cross-sectional study found that the frequency of milk consumption between the ages 5 and 12 was associated with decreased odds of precocious menarche after adjustment for race/ethnicity, birth cohort, country of birth, and adult BMI. However, these findings were not statistically significant.

Although studies have been conducted to assess the association between milk consumption pattern and age at menarche, findings have been inconsistent. The findings of the current study were consistent with the results of a previous study that also used NHANES data as well as a large scaled prospective study conducted in the United States (Carwile et al., 2015; Wiley, 2011). The findings of the current study were also similar in terms of the direction and magnitude of the association with those of a prospective study that followed Chilean girls aged 3 and 4 years (Gaskins et al., 2017).

In contrast, the results of this study did not support findings of some studies conducted outside the United States. In a cross-sectional study conducted in Japan, Kato et al. found that daily milk consumption was one of the factors positively associated with earlier age at menarche (Kato et al., 1988). Similarly, in the prospective cohort study in Iran in 2013, the researchers found that higher daily milk intake between ages 4 and 12 years played a role in attaining menarche before the age of 12 after adjustment for total energy and protein intake, maternal age at menarche, BMI, and the length of time of participation in the study (Ramezani Tehrani et al., 2013). The inconsistency in results may be attributable to differences in the measurement of the exposure, i.e., consumption frequency or amount of intake, study sample age ranges, sample size, and general milk consumption patterns that vary across countries.

6.2 Strengths and Limitations

Like all research, the present study also has strengths and limitations and they are described in the following passages:

6.2.1 Nondifferential Misclassification

Nondifferential misclassification may have occurred both for the exposure and the outcome. The exposure, frequency of milk consumption between the ages of 5 and 12 years, was self-reported by respondents during the health interview. It is possible that respondents may have incorrectly reported their milk consumption behaviors between the ages of 5 and 12 years especially since they were being asked to recall their diet from at least 8 to 15 years ago. In addition, as the exposure was only measured in terms of intake frequency despite various types of milk depending on fat level, organic/non-organic product, hormone-treated/non-hormone-treated product, and cow milk/non-cow milk, this also can contribute to nondifferential misclassification. If nondifferential misclassification of the exposure occurs the results will be based toward the null value.

Nondifferential misclassification of age at menarche is also possible. The outcome in the current study, the onset of menarche before the age of 12, was obtained through the health interview by asking participants their age at menarche. Given that menarche is a significant event in a woman's life, women may have accurately reported their age at menarche (Must et al., 2002). If nondifferential misclassification of the outcome occurs, it may bias the association toward the null.

6.2.2 Selection Bias

NHANES employs a complex sampling method to select participants for the survey. The average response rate for the women aged 20-49 years was 77.5% for completing the interview. It is possible that women who participated in the study are different from those who did not participate. For example, women who participated may have been more engaged in regular milk consumption as part of healthy diets compared to those who did not participate. However, the extent to which participation in NHANES is related to both the exposure and the outcome is unknown. Given the response rate of 77.5%, selection bias is not likely to meaningfully affect the results. If selection bias did occur, however, the assessed association between the exposure and the outcome would either overestimate or underestimate the true association.

6.2.3 Information Bias

Information bias is unlikely in this study. The trained interviewers were responsible for collecting data and thus, it is unlikely that the interviewers would have acted or spoken differently to participants if he/she was aware of whether or not the participants had reached menarche before the age of 12 years.

6.2.4 Temporal Bias

A cross-sectional study, the study design employed in the current study, is susceptible to temporal bias since exposure and outcome information is collected simultaneously. In the current study, however, the temporal sequence between the exposure and the outcome is relatively clear given that the question for the exposure specified the exact time period. Therefore, temporal bias may be less of a concern in the current study.

6.2.5 Confounding

The potential confounders controlled for in this study were selected from the variables that were available in the NHANES data. This study aimed to assess the association between participants' past dietary behaviors and age at menarche. Given that most information collected by NHANES pertains to current characteristics or status of participants, potential confounders that could be included in the study were somewhat limited. This study controlled for birth cohort, race/ethnicity, country of birth, length of time in the United States before menarche, and BMI (Karapanou & Papadimitriou, 2010; Wiley, 2011). It is not possible to control for other potential confounding factors, including maternal menarcheal age, maternal weight gain during pregnancy, birth weight, childhood obesity, and total energy intake between ages of 5 and 12 years. Additional unknown confounders are also possible. Failure to control for these potential confounders could result in an over- or underestimation of the true association.

6.2.6 Generalizability

The 2005-2014 NHANES employed a complex, multistage probability sampling method to generate a sample that is representative of the non-institutionalized United States civilian population of all ages. In addition, NHANES oversampled underrepresented population subgroups to ensure the representativeness of the sample. Therefore, the results of this study may be generalized to non-institutionalized women ages 20-49 years living in the United States.

6.3 Implications and Future Research

Precocious menarche, a well-known risk factor for breast cancer and other various negative health outcomes, has increased among girls residing in the United States over time and in turn, has emerged as an important public health issue. The onset of menarche is determined not by a single factor, but by a combination of various factors that interrelate together. Studies to identify risk factors of precocious menarche have been conducted by many researchers. Previous studies have identified elevated BMI or childhood obesity as a strong predictor of precocious menarche (Ahmed et al., 2009; Freedman et al., 2002). However, study results on other potential risk factors are inconsistent and the biological mechanisms are still largely unknown (Cesario & Hughes, 2007; Wiley, 2012; Yermachenko & Dvornyk, 2014). Milk consumption before onset of menarche is an example of one such factor. Only a few studies have been conducted to assess the association between milk consumption and precocious menarche and the studies yielded inconsistent results (Carwile et al., 2015; Gaskins et al., 2017; Kato et al., 1988; Ramezani Tehrani et al., 2013; Wiley, 2011, 2012; Zhu et al., 2006). While some studies found an inverse relationship between milk consumption and age at menarche, other studies found no association or even reported that milk intake may delay onset of menarche. Therefore, conclusive evidence for its role in precocious menarche is limited.

Milk consumption is encouraged through Dietary Guidelines for Americans by USDA, and in turn, milk is one of the widely consumed foods among children. However, if excessive or too frequent milk consumption could be a risk factor of early onset of menarche, children need to be more cautious about their milk consumption despite various benefits of regular milk intake as a source of diverse nutrients. Given that the review of past literature found that it is still controversial to draw a conclusion on whether milk plays a critical role in precocious menarche due to inconsistent study results, this study provides additional evidence for milk consumption between the ages 5 and 12 years not affecting onset of menarche. However, the evidence is still insufficient to draw a definitive conclusion on the association between milk and precocious menarche and in turn, further studies are needed. Future studies that examine the role of milk on precocious menarche in a more sophisticated way by controlling possible critical confounding factors such as diet, childhood BMI, and genetic factors such as maternal menarcheal age are necessary. In addition, the assessment of milk consumption should be more fully developed. For example, fat level, organic/non-organic product, and hormone-treated/non-hormone-treated product are all potentially important factors to consider. Furthermore, the exposure assessment can be improved by measuring not only the frequency of consumption, but also the true amount of intake. In addition, by better categorizing milk, i.e., cow milk, soy milk, almond milk, and so forth, it may be possible to better determine if milk consumption plays a role in early menarche. Finally, including additional information on consumption of dairy products other than milk in future research will also help investigate whether or not milk has a critical role on precocious menarche.

REFERENCES

Ahmed, M. L., Ong, K. K., & Dunger, D. B. (2009). Childhood obesity and the timing of puberty. *Trends Endocrinol Metab, 20*(5), 237-242. doi:10.1016/j.tem.2009.02.004

Alexopoulos, E. C. (2010). Introduction to multivariate regression analysis. *Hippokratia, 14*(Suppl 1), 23-28.

Berkey, C. S., Gardner, J. D., Frazier, A. L., & Colditz, G. A. (2000). Relation to childhood diet and body size to menarche and adolescent growth in girls. *Am J Epidemiol, 152*. doi:10.1093/aje/152.5.446

Biro, F. M., Greenspan, L. C., & Galvez, M. P. (2012). Puberty in girls of the 21(st) century. *Journal of pediatric and adolescent gynecology, 25*(5), 289-294. doi:10.1016/j.jpag.2012.05.009

Bralic, I., Tahirovic, H., Matanic, D., Vrdoljak, O., Stojanovic-Spehar, S., Kovacic, V., & Blazekovic-Milakovic, S. (2012). Association of early menarche age and overweight/obesity. *J Pediatr Endocrinol Metab, 25*(1-2), 57-62. doi:10.1515/jpem-2011-0277

Budtz-Jorgensen, E., Keiding, N., Grandjean, P., & Weihe, P. (2007). Confounder selection in environmental epidemiology: assessment of health effects of prenatal mercury exposure. *Ann Epidemiol, 17*(1), 27-35. doi:10.1016/j.annepidem.2006.05.007

Buttke, D. E., Sircar, K., & Martin, C. (2012). Exposures to endocrine-disrupting chemicals and age of menarche in adolescent girls in NHANES (2003-2008). *Environ Health Perspect, 120*(11), 1613-1618. doi:10.1289/ehp.1104748

Carwile, J. L., Willett, W. C., Wang, M., Rich-Edwards, J., Frazier, A. L., & Michels, K. B. (2015). Milk Consumption after Age 9 Years Does Not Predict Age at Menarche. *J Nutr, 145*(8), 1900-1908. doi:10.3945/jn.115.214270

Centers for Disease Control and Prevention. (2013a). Sample Design. Retrieved October 21, 2017, from https://www.cdc.gov/nchs/tutorials/nhanes/surveydesign/SampleDesign/intro.htm

Centers for Disease Control and Prevention. (2013b). Survey Overview. Retrieved October 21, 2017, from https://www.cdc.gov/nchs/tutorials/nhanes/SurveyOrientation/SurveyOverview/intro.htm

Centers for Disease Control and Prevention. (2016). Welcome NHANES Participants. Retrieved Nov 12, 2017, from https://www.cdc.gov/nchs/nhanes/participant.htm

Centers for Disease Control and Prevention. (2017). About the National Health and Nutrition Examination Survey. Retrieved October 21, 2017, from https://www.cdc.gov/nchs/nhanes/about_nhanes.htm

Centers for Disease Control and Prevention. (n.d.a.). Continuous NHANES Web Tutorial: Specifying Sampling Parameters: Key Concepts about NHANES Survey Design. Retrieved October 21, 2017, from https://www.cdc.gov/nchs/tutorials/NHANES/SurveyDesign/SampleDesign/Info1.htm

Centers for Disease Control and Prevention. (n.d.b.). Continuous NHANES Web Tutorial: Survey Overview: Survey Methodology. Retrieved October 21, 2017, from https://www.cdc.gov/nchs/tutorials/NHANES/SurveyOrientation/SurveyOverview/Info2. htm

Centers for Disease Control and Prevention. (n.d.c.). Questionnaires, Datasets, and Related Documentation. Retrieved October 21, 2017, from https://wwwn.cdc.gov/nchs/nhanes/ResponseRates.aspx

Centers for Disease Control and Prevention. (n.d.d.). NHANES Questionnaire Data. Retrieved Nov 17, 2017, from https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Questionnaire

Cesario, S. K., & Hughes, L. A. (2007). Precocious puberty: a comprehensive review of literature. *J Obstet Gynecol Neonatal Nurs, 36*(3), 263-274. doi:10.1111/j.1552-6909.2007.00145.x

Cheng, G., Buyken, A. E., Shi, L., Karaolis-Danckert, N., Kroke, A., Wudy, S. A., . . . Remer, T. (2012). Beyond overweight: nutrition as an important lifestyle factor influencing timing of puberty. *Nutr Rev, 70*(3), 133-152. doi:10.1111/j.1753-4887.2011.00461.x

Curhan, G. C., Willett, W. C., Knight, E. L., & Stampfer, M. J. (2004). Dietary factors and the risk of incident kidney stones in younger women: Nurses' health study ii. *Archives of Internal Medicine, 164*(8), 885-891. doi:10.1001/archinte.164.8.885

Daftary, S. S., & Gore, A. C. (2005). IGF-1 in the brain as a regulator of reproductive neuroendocrine function. *Exp Biol Med (Maywood), 230*(5), 292-306.

Day, F. R., Elks, C. E., Murray, A., Ong, K. K., & Perry, J. R. (2015). Puberty timing associated with diabetes, cardiovascular disease and also diverse health outcomes in men and women: the UK Biobank study. *Sci Rep, 5*, 11208. doi:10.1038/srep11208

Day, F. R., Thompson, D. J., Helgason, H., Chasman, D. I., Finucane, H., Sulem, P., . . . Perry, J. R. B. (2017). Genomic analyses identify hundreds of variants associated with age at menarche and support a role for puberty timing in cancer risk. *Nat Genet, 49*(6), 834-841. doi:10.1038/ng.3841
http://www.nature.com/ng/journal/v49/n6/abs/ng.3841.html#supplementary-information

Day, F. R., Thompson, D. J., Helgason, H., Chasman, D. I., Finucane, H., Sulem, P., . . . Perry, J. R. B. (2017). Genomic analyses identify hundreds of variants associated with age at menarche and support a role for puberty timing in cancer risk. *Nat Genet, 49*(6), 834-841. doi:10.1038/ng.3841

Deardorff, J., Gonzales, N. A., Christopher, F. S., Roosa, M. W., & Millsap, R. E. (2005). Early puberty and adolescent pregnancy: the influence of alcohol use. *Pediatrics, 116*(6), 1451-1456. doi:10.1542/peds.2005-0542

DeSalvo, K. B., Olson, R., & Casavale, K. O. (2016). Dietary Guidelines for Americans. *Jama, 315*(5), 457-458. doi:10.1001/jama.2015.18396

Ebling, F. J. (2005). The neuroendocrine timing of puberty. *Reproduction, 129*(6), 675-683. doi:10.1530/rep.1.00367

Elks, C. E., Ong, K. K., Scott, R. A., van der Schouw, Y. T., Brand, J. S., Wark, P. A., . . . Wareham, N. J. (2013). Age at menarche and type 2 diabetes risk: the EPIC-InterAct study. *Diabetes Care, 36*(11), 3526-3534. doi:10.2337/dc13-0446

Farahmand, M., Tehrani, F. R., Dovom, M. R., & Azizi, F. (2017). Menarcheal Age and Risk of Type 2 Diabetes: A Community-Based Cohort Study. *J Clin Res Pediatr Endocrinol, 9*(2), 156-162. doi:10.4274/jcrpe.3370

Fogli-Cawley, J. J., Dwyer, J. T., Saltzman, E., McCullough, M. L., Troy, L. M., & Jacques, P. F. (2006). The 2005 Dietary Guidelines for Americans Adherence Index: development and application. *J Nutr, 136*(11), 2908-2915.

Freedman, D. S., Khan, L. K., Serdula, M. K., Dietz, W. H., Srinivasan, S. R., & Berenson, G. S. (2002). Relation of age at menarche to race, time period, and anthropometric dimensions: the Bogalusa Heart Study. *Pediatrics, 110*(4), e43.

Gaskins, A. J., Pereira, A., Quintiliano, D., Shepherd, J. A., Uauy, R., Corvalan, C., & Michels, K. B. (2017). Dairy intake in relation to breast and pubertal development in Chilean girls. *Am J Clin Nutr, 105*(5), 1166-1175. doi:10.3945/ajcn.116.150359

Gaudineau, A., Ehlinger, V., Vayssiere, C., Jouret, B., Arnaud, C., & Godeau, E. (2010). Factors associated with early menarche: results from the French Health Behaviour in School-aged Children (HBSC) study. *BMC Public Health, 10*, 175. doi:10.1186/1471-2458-10-175

Greer, F. R., Krebs, N. F., & American Academy of Pediatrics Committee on, N. (2006). Optimizing bone health and calcium intakes of infants, children, and adolescents. *Pediatrics, 117*(2), 578-585. doi:10.1542/peds.2005-2822

Greif, E. B., & Ulman, K. J. (1982). The psychological impact of menarche on early adolescent females: a review of the literature. *Child Dev, 53*(6), 1413-1430.

Gunther, A. L., Karaolis-Danckert, N., Kroke, A., Remer, T., & Buyken, A. E. (2010). Dietary protein intake throughout childhood is associated with the timing of puberty. *J Nutr, 140*(3), 565-571. doi:10.3945/jn.109.114934

Herman-Giddens, M. E., Slora, E. J., Wasserman, R. C., Bourdony, C. J., Bhapkar, M. V., Koch, G. G., & Hasemeier, C. M. (1997). Secondary sexual characteristics and menses in young girls seen in office practice: a study from the Pediatric Research in Office Settings network. *Pediatrics, 99*(4), 505-512.

Hoppe, C., Udam, T. R., Lauritzen, L., Molgaard, C., Juul, A., & Michaelsen, K. F. (2004). Animal protein intake, serum insulin-like growth factor I, and growth in healthy 2.5-y-old Danish children. *Am J Clin Nutr, 80*(2), 447-452.

Ibitoye, M., Choi, C., Tai, H., Lee, G., & Sommer, M. (2017). Early menarche: A systematic review of its effect on sexual and reproductive health in low- and middle-income countries. *PLoS One, 12*(6), e0178884. doi:10.1371/journal.pone.0178884

James-Todd, T., Tehranifar, P., Rich-Edwards, J., Titievsky, L., & Terry, M. B. (2010). The impact of socioeconomic status across early life on age at menarche among a racially diverse population of girls. *Ann Epidemiol, 20*(11), 836-842. doi:10.1016/j.annepidem.2010.08.006

Jansen, E. C., Marin, C., Mora-Plazas, M., & Villamor, E. (2016). Higher Childhood Red Meat Intake Frequency Is Associated with Earlier Age at Menarche. *J Nutr*. doi:10.3945/jn.115.226456

Kaprio, J., Rimpela, A., Winter, T., Viken, R. J., Rimpela, M., & Rose, R. J. (1995). Common genetic influences on BMI and age at menarche. *Hum Biol, 67*(5), 739-753.

Karapanou, O., & Papadimitriou, A. (2010). Determinants of menarche. *Reproductive Biology and Endocrinology, 8*(1), 115. doi:10.1186/1477-7827-8-115

Kato, I., Tominaga, S., & Suzuki, T. (1988). Factors related to late menopause and early menarche as risk factors for breast cancer. *Jpn J Cancer Res, 79*(2), 165-172.

Keast, D. R., Fulgoni, V. L., 3rd, Nicklas, T. A., & O'Neil, C. E. (2013). Food sources of energy and nutrients among children in the United States: National Health and Nutrition Examination Survey 2003-2006. *Nutrients, 5*(1), 283-301. doi:10.3390/nu5010283

Keyes, K. M., Utz, R. L., Robinson, W., & Li, G. (2010). What is a cohort effect? Comparison of three statistical methods for modeling cohort effects in obesity prevalence in the United States, 1971–2006. *Soc Sci Med, 70*(7), 1100-1108. doi:10.1016/j.socscimed.2009.12.018

Kit, B. K., Carroll, M. D., & Ogden, C. L. (2011). Low-fat milk consumption among children and adolescents in the United States, 2007-2008. *NCHS Data Brief*(75), 1-8.

Lakshman, R., Forouhi, N. G., Sharp, S. J., Luben, R., Bingham, S. A., Khaw, K.-T., . . . Ong, K. K. (2009). Early Age at Menarche Associated with Cardiovascular Disease and Mortality. *The Journal of Clinical Endocrinology & Metabolism, 94*(12), 4953-4960. doi:10.1210/jc.2009-1789

Lakshman, R., Forouhi, N. G., Sharp, S. J., Luben, R., Bingham, S. A., Khaw, K. T., . . . Ong, K. K. (2009a). Early age at menarche associated with cardiovascular disease and mortality. *J Clin Endocrinol Metab, 94*(12), 4953-4960. doi:10.1210/jc.2009-1789

Lakshman, R., Forouhi, N. G., Sharp, S. J., Luben, R., Bingham, S. A., Khaw, K. T., . . . Ong, K. K. (2009b). Early age at menarche associated with cardiovascular disease and mortality. *J Clin Endocrinol Metab, 94*. doi:10.1210/jc.2009-1789

MacMahon, B. (1972). Age at menarche, United States. *Vital Health Stat 11*(133), 1-36.

McDowell, M. A., Brody, D. J., & Hughes, J. P. (2007). Has age at menarche changed? Results from the National Health and Nutrition Examination Survey (NHANES) 1999-2004. *J Adolesc Health, 40*(3), 227-231. doi:10.1016/j.jadohealth.2006.10.002

Mendle, J., Turkheimer, E., & Emery, R. E. (2007). Detrimental Psychological Outcomes Associated with Early Pubertal Timing in Adolescent Girls. *Dev Rev, 27*(2), 151-171. doi:10.1016/j.dr.2006.11.001

Merzenich, H., Boeing, H., & Wahrendorf, J. (1993). Dietary fat and sports activity as determinants for age at menarche. *Am J Epidemiol, 138*(4), 217-224.

Mishra, G. D., Pandeya, N., Dobson, A. J., Chung, H. F., Anderson, D., Kuh, D., . . . Weiderpass, E. (2017). Early menarche, nulliparity and the risk for premature and early natural menopause. *Hum Reprod, 32*(3), 679-686. doi:10.1093/humrep/dew350

Morris, D. H., Jones, M. E., Schoemaker, M. J., Ashworth, A., & Swerdlow, A. J. (2010). Determinants of age at menarche in the UK: analyses from the Breakthrough Generations Study. *Br J Cancer, 103*(11), 1760-1764. doi:10.1038/sj.bjc.6605978

Must, A., Phillips, S. M., Naumova, E. N., Blum, M., Harris, S., Dawson-Hughes, B., & Rand, W. M. (2002). Recall of early menstrual history and menarcheal body size: after 30 years, how well do women remember? *Am J Epidemiol, 155*(7), 672-679.

National Institute of Child Health and Human Development. (n.d.a.). Puberty and Precocious Puberty: Condition Information. Retrieved October 21, 2017, from https://www.nichd.nih.gov/health/topics/puberty/conditioninfo/Pages/default.aspx

National Institute of Child Health and Human Development. (n.d.b.). About Menstruation. Retrieved October 19, 2017, from https://www.nichd.nih.gov/health/topics/menstruation/conditioninfo/Pages/default.aspx# menstruation

Parent, A. S., Teilmann, G., Juul, A., Skakkebaek, N. E., Toppari, J., & Bourguignon, J. P. (2003). The timing of normal puberty and the age limits of sexual precocity: variations around the world, secular trends, and changes after migration. *Endocr Rev, 24*(5), 668-693. doi:10.1210/er.2002-0019

Partsch, C. J., & Sippell, W. G. (2001). Pathogenesis and epidemiology of precocious puberty. Effects of exogenous oestrogens. *Hum Reprod Update, 7*(3), 292-302.

Pinyerd, B., & Zipf, W. B. (2005). Puberty-timing is everything! *J Pediatr Nurs, 20*(2), 75-82. doi:10.1016/j.pedn.2004.12.011

Prentice, P., & Viner, R. M. (2013). Pubertal timing and adult obesity and cardiometabolic risk in women and men: a systematic review and meta-analysis. *Int J Obes (Lond), 37*(8), 1036-1043. doi:10.1038/ijo.2012.177

Quann, E. E., Fulgoni, V. L., & Auestad, N. (2015). Consuming the daily recommended amounts of dairy products would reduce the prevalence of inadequate micronutrient intakes in the United States: diet modeling study based on NHANES 2007–2010. *Nutrition Journal, 14*, 90. doi:10.1186/s12937-015-0057-5

Ramezani Tehrani, F., Moslehi, N., Asghari, G., Gholami, R., Mirmiran, P., & Azizi, F. (2013). Intake of dairy products, calcium, magnesium, and phosphorus in childhood and age at menarche in the Tehran Lipid and Glucose Study. *PLoS One, 8*(2), e57696. doi:10.1371/journal.pone.0057696

Rockett, H. R., Berkey, C. S., Field, A. E., & Colditz, G. A. (2001). Cross-sectional measurement of nutrient intake among adolescents in 1996. *Prev Med, 33*(1), 27-37. doi:10.1006/pmed.2001.0850

Rogers, I. S., Northstone, K., Dunger, D. B., Cooper, A. R., Ness, A. R., & Emmett, P. M. (2010). Diet throughout childhood and age at menarche in a contemporary cohort of British girls. *Public Health Nutr, 13*(12), 2052-2063. doi:10.1017/s1368980010001461

Rozenberg, S., Body, J. J., Bruyere, O., Bergmann, P., Brandi, M. L., Cooper, C., . . . Reginster, J. Y. (2016). Effects of Dairy Products Consumption on Health: Benefits and Beliefs--A Commentary from the Belgian Bone Club and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases. *Calcif Tissue Int, 98*(1), 1-17. doi:10.1007/s00223-015-0062-x

Serdula, M. K., Ivery, D., Coates, R. J., Freedman, D. S., Williamson, D. F., & Byers, T. (1993). Do obese children become obese adults? A review of the literature. *Prev Med, 22*(2), 167-177. doi:10.1006/pmed.1993.1014

Stubbs, M. L. (2008). Cultural perceptions and practices around menarche and adolescent menstruation in the United States. *Ann N Y Acad Sci, 1135*, 58-66. doi:10.1196/annals.1429.008

Tanner, J. M., & Davies, P. S. (1985). Clinical longitudinal standards for height and height velocity for North American children. *J Pediatr, 107*(3), 317-329.

Thankamony, A., Ong, K. K., Ahmed, M. L., Ness, A. R., Holly, J. M., & Dunger, D. B. (2012). Higher levels of IGF-I and adrenal androgens at age 8 years are associated with earlier age at menarche in girls. *J Clin Endocrinol Metab, 97*(5), E786-790. doi:10.1210/jc.2011-3261

Towne, B., Czerwinski, S. A., Demerath, E. W., Blangero, J., Roche, A. F., & Siervogel, R. M. (2005). Heritability of age at menarche in girls from the Fels Longitudinal Study. *Am J Phys Anthropol, 128*(1), 210-219. doi:10.1002/ajpa.20106

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (1980). *Nutrition and Your Health, Dietary Guidelines for Americans, 1980*. Retrieved from https://health.gov/dietaryguidelines/1980thin.pdf?_ga=2.230002460.1662249623.1511276029-1645859807.1511276029.

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (1985). *Nutrition and Your Health, Dietary Guidelines for Americans, 1985*. Retrieved from https://health.gov/dietaryguidelines/1985thin.pdf?_ga=2.167191102.1662249623.1511276029-1645859807.1511276029.

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (1990). *Nutrition and Your Health, Dietary Guidelines for Americans, 1990*. Retrieved from https://health.gov/dietaryguidelines/1990thin.pdf?_ga=2.69684624.1662249623.1511276029-1645859807.1511276029.

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (1995). *Nutrition and Your Health, Dietary Guidelines for Americans, 1995*. Retrieved from https://health.gov/dietaryguidelines/dga95/DGAC95.HTM?_ga=2.125274634.1662249623.1511276029-1645859807.1511276029.

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (2000). *Nutrition and Your Health, Dietary Guidelines for Americans, 2000*. Retrieved from https://health.gov/dietaryguidelines/dga2000/dietgd.pdf.

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (2005). *Dietary Guidelines for Americans, 2005. 6th Edition*. Washington, DC: U.S. Government Printing Office, January 2005. Retrieved from https://health.gov/DietaryGuidelines/dga2005/document/default.htm.

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (2010). *Dietary Guidelines for Americans, 2010. 7th Edition*. Washington, DC: U.S. December 2010: Government Printing Office Retrieved from https://health.gov/DietaryGuidelines/dga2005/document/default.htm.

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (2015). *2015–2020 Dietary Guidelines for Americans. 8th Edition*. Retrieved from http://health.gov/dietaryguidelines/2015/guidelines/.

U.S. National Library of Medicine. (2016). Puberty: MedlinePlus. Retrieved October 20, 2017, from https://medlineplus.gov/puberty.html

U.S. National Library of Medicine. (n.d.). Menarche. Retrieved Oct 19, 2017, from https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0030333/

Villamor, E., & Jansen, E. C. (2016). Nutritional Determinants of the Timing of Puberty. *Annu Rev Public Health, 37*, 33-46. doi:10.1146/annurev-publhealth-031914-122606

Wiley, A. S. (2011). Milk intake and total dairy consumption: associations with early menarche in NHANES 1999-2004. *PLoS One, 6*(2), e14685. doi:10.1371/journal.pone.0014685

Wiley, A. S. (2012). Cow milk consumption, insulin-like growth factor-I, and human biology: a life history approach. *Am J Hum Biol, 24*(2), 130-138. doi:10.1002/ajhb.22201

Wyshak, G., & Frisch, R. E. (1982). Evidence for a secular trend in age of menarche. *N Engl J Med, 306*(17), 1033-1035. doi:10.1056/nejm198204293061707

Yermachenko, A., & Dvornyk, V. (2014). Nongenetic determinants of age at menarche: a systematic review. *Biomed Res Int, 2014*, 371583. doi:10.1155/2014/371583

Zhu, K., Zhang, Q., Foo, L. H., Trube, A., Ma, G., Hu, X., . . . Greenfield, H. (2006). Growth, bone mass, and vitamin D status of Chinese adolescent girls 3 y after withdrawal of milk supplementation. *Am J Clin Nutr, 83*(3), 714-721.

Zipf, G., Chiappa, M., Porter, K. S., Ostchega, Y., Lewis, B. G., & Dostal, J. (2013). National health and nutrition examination survey: plan and operations, 1999-2010. *Vital Health Stat 1*(56), 1-37.

APPENDIX: TABLES

Table 1. Characteristics of the milk consumption-age at menarche study sample by childhood milk consumption frequency, NHANES 2005-2014

	Milk Consumption Frequency between 5 and 12 years olds			
	All N (%[1])	Never/Rarely N (%[1])	Sometimes/Varied N (%[1])	Daily N (%[1])
Race/Ethnicity				
Non-Hispanic White	2,021 (64.3)	49 (41.6)	182 (56.5)	1,790 (66.3)
Non-Hispanic Black	929 (12.1)	37 (11.8)	124 (15.1)	768 (11.8)
Hispanic	1,348 (16.4)	116 (31.7)	165 (18.8)	1,067 (15.4)
Others	442 (7.1)	37 (15.0)	68 (9.7)	337 (6.4)
Birth Cohort				
Born before 1961	267 (6.8)	21 (10.9)	27 (6.9)	219 (6.6)
Born between 1961-1970	1,429 (32.0)	77 (31.5)	152 (29.4)	1,200 (32.4)
Born between 1971-1980	1,608 (31.4)	84 (33.9)	168 (27.8)	1,356 (31.7)
Born between 1981-1993	1,436 (29.8)	57 (23.7)	192 (35.9)	1,187 (29.3)
Born in USA				
Yes	3,451 (82.1)	95 (56.5)	353 (76.3)	3,003 (84.0)
No	1,288 (17.9)	144 (43.5)	186 (23.7)	958 (16.0)
Length of Time in US before Menarche				
0-5 years	1,052 (14.2)	133 (41.4)	156 (18.6)	763 (12.4)
≥6 years	3,614 (85.8)	98 (58.6)	376 (81.4)	3,140 (87.6)
Adult BMI[2]				
Under/Normal weight	1,683 (38.6)	81 (38.6)	178 (35.8)	1,424 (39.0)
Overweight	1,292 (26.8)	82 (28.0)	151 (28.1)	1,059 (26.6)
Obese	1,765 (34.6)	76 (33.4)	210 (36.1)	1,479 (34.4)
Age at Menarche				
<12 years	1,083 (21.2)	56 (24.4)	113 (20.8)	914 (21.1)
≥12 years	3,657 (78.8)	183 (75.6)	426 (79.2)	3,048 (78.9)

[1] Weighted percentage

[2] BMI categorization
Under/Normal weight: Body Mass Index below 24.9 kg/m^2
Overweight: Body Mass Index 25.0-29.9 kg/m^2
Obese: Body Mass Index 30.0 kg/m^2 and above

Table 2. Unadjusted odd ratios (OR) and 95% confidence intervals (CI) of the association between select characteristics and precocious menarche, NHANES 2005-2014

	Odds Ratios (OR)	95% Confidence Intervals (CI)
Milk Consumption 5 - 12 yrs		
Never/Rarely	1.00	Referent
Sometimes/Varied	0.81	0.45, 1.47
Daily	0.83	0.55, 1.25
Race/Ethnicity		
Non-Hispanic White	1.00	Referent
Non-Hispanic Black	1.55	1.27, 1.88
Hispanic	1.60	1.30, 1.97
Others	1.16	0.86, 1.57
Birth Cohort		
Born before 1961	1.00	Referent
Born between 1961-1970	0.88	0.57, 1.35
Born between 1971-1980	1.15	0.77, 1.70
Born between 1981-1993	1.24	0.85, 1.81
Born in USA		
Yes	1.11	0.90, 1.37
No	1.00	Referent
Length of Time in US before Menarche		
0-5 years	1.00	Referent
≥6 years	1.17	0.95, 1.44
Adult BMI		
Under/Normal Weight	1.00	Referent
Overweight	1.20	0.94, 1.52
Obese	2.26	1.85, 2.77

Table 3. Adjusted odd ratio (OR[3]) and 95% confidence interval (CI) of the association between frequency of milk consumption between ages 5 and 12 and precocious menarche, NHANES 2005-2014

	Odds Ratio (OR[3])	95% Confidence Interval (CI)
Milk Consumption 5 - 12 yrs		
Never/Rarely	1.00	Referent
Sometimes/Varied	0.77	0.42, 1.43
Daily	0.82	0.53, 1.27

[3] Adjusted for race/ethnicity, birth cohort, country of birth, and adult BMI.