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## Childhood dairy consumption is associated with lower age of menarche in a national representative sample of US women

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Additional Declarations: No competing interests reported.

# Abstract Background and aims:

Breast cancer is the most prevalent cancer and leader in cancer-related deaths among women with a variety of established risk factors.

# Methods

Data from a nationally representative sample of 5,574 women who participated in the 2015-2018 NHANES was used to evaluate the correlation of childhood and adolescent dairy milk consumption and age of menarche. Reproductive history was asked of women > 12y. Data regarding dairy consumption between the ages of 5-12 was available for women > 20y. Survey regression models were used to calculate adjusted age of menarche for categories of dairy consumption after adjusting for relevant confounders.

## **Results**

Women who reported never or rarely consuming dairy milk were significantly older at age of menarche compared to those who reported more frequent milk consumption. Age of menarche is affected by consumption of dairy milk in childhood even when controlling for factors which have been consider as possible affecting agents.

## Conclusions

With the known link between the age of menarche and increased risk in breast cancer, guidance regarding childhood milk consumption should be developed.

## BACKGROUND

Breast cancer is the most prevalent cancer and leader in cancer-related deaths among women with many known risk factors (1). Public health officials have identified factors that confer increased risk of breast cancer diagnosis; including early age at menarche (2). A decrease in age of menarche has been found to increase breast cancer risk by a factor of 1.05 for every year younger (2). Age of menarche has declined over 150 years reaching the believed biological limit (3). Early menarche is negatively associated with weight and Body Mass Index (BMI), decreasing age by 13 days for every 1kg of body fat gained (4, 5). Little research addresses nutritional components and age of menarche, though milk intake is associated with rapid early growth rate and BMI in children and adolescents (6, 7).

Previous studies show 'regular' milk consumption before age 9 is associated with increased risk for early menarche (8), few recent studies have evaluated the association between dairy consumption during childhood (age 5–12) and adolescence (age 13–17) and age of menarche. More often, studies have evaluated mechanisms related to menarche, including increased BMI, insulin, and IGF-1 growth hormone factors and how these relate to pubertal time. (8, 9)

This study aims to report the association between childhood milk consumption and age at menarche in a nationally representative sample of US women.

# METHODS Subjects and Data

This study includes data from the National Health and Nutrition Examination Survey (NHANES), a continuously conducted cross-sectional survey designed to evaluate the health and nutritional status of US residents using a complex multi-stage cluster probability design and is nationally representative of the US population. (10) Data from the 2015–2016 and 2017–2018 survey cycles were included in this analysis, representing the current nationally representative data cycles. All subjects signed written informed consent prior to participation. Data collection in the NHANES conforms to all ethical standards and has been approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB – formerly named NCHS IRB) Protocol #2011-17 and Protocol #2018-01.

Data is collected using in-home questionnaires and a comprehensive physical examination in the mobile examination center (MEC). Demographic data regarding race/ethnicity, age, sex, educational attainment, and anthropometric measurements are provided in the NHANES data file. Data on diet behaviors, including milk consumption during childhood, are collected by trained interviewers using the Computer Assisted Personal Interview (CAPI) system during an in-home interview (10). Participants > 20 years were asked to categorize their typical milk consumption habits during childhood (age 5-12y) and adolescence (age 13-17y). Participant responses for milk consumption included one of the following categories: never/rarely (less than once a week), sometimes (once a week or more, but less than once a day), and often (once a day or more).

Questions assessing age of menarche were conducted within the Reproductive Health section of NHANES survey and were asked of female participants 12 years and older. Questions covered menstrual history, pregnancy history, hormone replacement therapy use and other related reproductive conditions and were asked by trained interviewers using the CAPI system at the mobile examination center. Age of menarche was categorized into early (< 11 years old), normal (12-14y), and late (> 15y).

The initial sample included women > 20 and answered reproductive history questions pertaining to age at menarche. Of those, 5,574 women had data regarding childhood milk consumption, representing the final analytic sample size. Women who were pregnant at the time of exam (n = 106) were included in the analytic sample, but excluded from BMI calculations.

## **Statistical Analysis**

The primary outcome measure was adjusted age at menarche for each category of milk consumption. Data was analyzed using SAS 9.4 (SAS Institute, Cary, NC) using survey procedures to address the complex sample design of the NHANES. A Taylor Series Linearization was used to approximate all standard errors (SE) for all estimates reported, and statistical comparisons of milk consumption were evaluated using a univariate t statistic. Because of the influence of body weight on menarche, initial analysis evaluated the association of early menarche with body weight status. Compared to normal weight women, women who are overweight or obese had nearly twice the odds of having early menarche, defined as menarche before age 12 (OR 1.9, 95% CI 1.4–2.4, p = 0.01). As such, modeling was conducted with and without stratifying by weight status (BMI > 25.0 vs BMI < 25.0). All results presented as least-square means adjusted for age at exam, race/ethnicity, educational attainment, poverty:income ratio, and body weight status.

### RESULTS

When evaluating demographic characteristics of the population, it was found that most women in this sample were Non-Hispanic White (63%, n = 1029) with a BMI between 18.5–24.9 kg/m2 (70%, n = 2107). Table 1 shows population characteristics related to consumption of dairy milk and age at menarche.

	Ν	Population %						
Frequency of Milk Intake During Childhood (5-12y) <sup>1</sup>								
Never / Rarely	243	6.2						
Sometimes	490	15.6						
Often	2235	78.2						
Frequency of Milk Intake During Adolescence (13-17y) <sup>2</sup>								
Never / Rarely	436	12.7						
Sometimes	901	32.3						
Often	1625	55.1						
Age at First Menarche <sup>2</sup>								
< 10 years	287	8.5						
10-12 years	1238	45.9						
13-15 years	1255	43.9						
16 or older	56	1.7						

Table 1 Dietary behaviors and age at menarche in a nationally representative sample of US women

Approximately 90% of women were between the ages of 10-15 years at first menarche, with a small proportion reaching menarche prior to 10y of age (n = 287, 9%). When evaluating milk consumption habits, it was noted that 78% of women reported drinking milk 'often' during childhood (between age 5-12y), and 55% of women re-ported drinking milk 'often' during adolescence.

Table 2 shows age at menarche by milk consumption category. Milk consumption during childhood was associated with age at menarche: women who reported drinking milk 'often' during childhood were younger at menarche than women who reported drinking milk rarely or never 13.2 vs. 12.8, p = 0.03. When stratifying by body weight status, the association between milk consumption and age at menarche was stronger for overweight women 13.1 vs. 12.6 years, p = 0.001, but no association was found between milk consumption and age at menarche in women who were not overweight. Milk consumption during adolescence was not associated with age at menarche (data not shown), as most participants had reached menarche by the time of adolescence.

Table 2 Milk Consumption in Childhood and Age at Menarche.

Adjusted Age at Menarche by Childhood (5-12y) Milk Consumption										
Milk Consumption Frequency	Adult Women Overall		Normal Weight Women		Overweight Women					
	Mean	SE	p- value	Mean	SE	p- value	LS Mean	SE	p- value	
Never / Rarely	13.2	0.18	0.03	13	0.4	0.97	13.1	0.2	0.001	
Sometimes	12.9	0.02	0.66	13.2	0.3	0.75	12.6	0.1	0.81	
Often	12.8	0.07	ref	13.1	0.2	ref	12.6	0.1	ref	

## DISCUSSION

The results indicate that age of menarche is affected by consumption of dairy milk in childhood even after controlling for additional factors considered as possible affecting agents. Age of menarche decreases with an increase in consumption of dairy milk between the ages of 5 and 12 years old, but age at menarche is not associated with milk consumption in adolescence, supporting previous research (8, 11, 12).

The relationship between early menarche and increased breast cancer risk has been well established by previous research.(13) The age of menarche in US women has been on a documented decline (3), and further research is necessary to broaden the breadth of knowledge surrounding underlying factors for this decline.

Current dietary guidelines regularly recommended by pediatricians suggest introducing cow's milk at 12 months of age and up to 2–3 cups by 24 months (14). With the known link between the age of menarche and increased risk in breast cancer, nutritional guidelines should be adjusted to limit dairy in the diet of children before reproductive age for maximum risk reduction.

Using data from NHANES is a strength of this study allowing the results to be nationally representative of the US population and a reflection of the general population. An additional strength of using NHANES data is the continual collection allowing research to be conducted and examined to compare historical data with current. Future work may be done to examine the impact of dairy consumption in the years prior to age 5.

## CONCLUSIONS

Given the supporting evidence of increased milk intake leading to a decrease in the age of menarche and the known link between the age of menarche and increased risk in breast cancer, guidance regarding childhood milk consumption should be reexamined.

### Declarations

CONSENT TO PUBLISH: Not applicable.

**ETHICS:** All subjects signed written informed consent prior to participation. Data collection in the NHANES conforms to all ethical standards and has been approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB – formerly named NCHS IRB) Protocol #2011-17 and Protocol #2018-01.

DATA AVAILABITY: Data availability: www.cdc.gov/nchs/nhanes

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CONFLICT OF INTEREST: The authors declare no conflict of interest

**AUTHOR CONTRIBUTIONS:** Conceptualization, J.V.; methodology, J.V. S.S..; formal analysis, J.V., S.S..; writing—original draft preparation, SS, JV.; writing—review and editing, JV; supervision, J.V.; All authors have read and agreed to the published version of the manuscript.

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