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*El contenido de grasa determina la asociación entre el consumo de leche y las enfermedades cardiovasculares: análisis de la NHANES de 2003 a 2018*

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## **ABSTRACT**

**Background:** the relationship between milk fat content and cardiovascular disease (CVD) remains controversial. This research aimed to examine the relationship between whole (3.5 % fat), reduced-fat (2 % fat), low-fat (1 % fat), and skimmed milk (< 0.5 % fat) and various CVDs.

**Methods:** this cross-sectional analysis was based on data gathered from the 2003–2018 National Health and Nutrition Examination Survey (NHANES), which enrolled 18,282 participants (9,017 men and

9,265 women). Participants were organized into four groups based on the type of milk consumed, as reported in the Diet Behavior and Nutrition Questionnaire. Coronary heart disease (CHD), heart failure (HF), and stroke were assessed via standard questionnaires. Weighted logistic regression models with multivariable adjustment were used to assess the association between varying levels of milk fat content and CVD, adjusting for a range of covariates, including dietary data from two 24-hour dietary recalls. Additionally, interaction, subgroup, and sensitivity analyses were conducted to assess effect modification and test result robustness.

**Results:** after adjusting for confounders, the consumption of whole milk was linked to a reduced prevalence of CHD (odds ratio [OR] = 0.582, 95 % confidence interval [CI] = 0.418-0.810,  $p = 0.002$ ) than skimmed milk. Furthermore, whole milk consumption was not associated with HF (OR = 1.518, 95 % CI = 0.939-2.455,  $p = 0.09$ ); however, it was associated with an increased prevalence of stroke (OR = 1.586, 95 % CI = 1.023-2.457,  $p = 0.039$ ). Subgroup and sensitivity analyses confirmed the reproducibility of our findings.

**Conclusions:** our results suggest that consuming whole milk may be linked to reduced CHD but elevated stroke prevalence compared to skimmed milk.

**Keywords:** Milk types. Cardiovascular disease. NHANES. Coronary heart disease. Stroke.

## RESUMEN

**Antecedentes:** la relación entre el contenido de grasa de la leche y las enfermedades cardiovasculares (ECV) sigue siendo controvertida. Esta investigación tuvo como objetivo examinar la relación entre la leche entera (3,5 % de grasa), la leche reducida en grasa (2 % de

grasa), la leche semidescremada (1 % de grasa) y la leche desnatada (< 0,5 % de grasa) y diversas ECV.

**Métodos:** este análisis transversal se basó en datos recopilados de la Encuesta Nacional de Examen de Salud y Nutrición (NHANES) 2003-2018, en la que participaron 18.282 personas (9017 hombres y 9265 mujeres). Los participantes se organizaron en cuatro grupos según el tipo de leche consumida, según lo indicado en el Cuestionario de Comportamiento Dietético y Nutricional. La enfermedad coronaria (EC), la insuficiencia cardíaca (IC) y el accidente cerebrovascular se evaluaron mediante cuestionarios estándar. Se utilizaron modelos de regresión logística ponderada con ajuste multivariable para evaluar la asociación entre los diferentes niveles de grasa láctea y la ECV, ajustando diversas covariables, incluyendo datos dietéticos de dos recordatorios dietéticos de 24 horas. Además, se realizaron análisis de interacción, de subgrupos y de sensibilidad para evaluar la modificación del efecto y la robustez de los resultados de las pruebas.

**Resultados:** tras ajustar por factores de confusión, el consumo de leche entera se relacionó con una menor prevalencia de EC (odds ratio [OR] = 0,582; intervalo de confianza [IC] del 95 % = 0,418-0,810;  $p = 0,002$ ) en comparación con la leche desnatada. Además, el consumo de leche entera no se asoció con la insuficiencia cardíaca (OR = 1,518; IC del 95 % = 0,939-2,455;  $p = 0,09$ ). Sin embargo, se asoció con una mayor prevalencia de ictus (OR = 1,586; IC del 95 % = 1,023-2,457;  $p = 0,039$ ). Los análisis de subgrupos y de sensibilidad confirmaron la reproducibilidad de nuestros hallazgos.

**Conclusiones:** nuestros resultados sugieren que el consumo de leche entera podría estar relacionado con una reducción de la enfermedad coronaria, pero con una mayor prevalencia de ictus, en comparación con la leche desnatada.

**Palabras clave:** Tipos de leche. Enfermedad cardiovascular. NHANES. Enfermedad coronaria. Accidente cerebrovascular.

## **INTRODUCTION**

Cardiovascular disease (CVD) continues to be the leading cause of mortality (1) and poses significant social and economic burdens (2). According to recent data from the United States (US), approximately 28.6 million (9.9 %) adults aged over 20 years are affected by coronary heart disease (CHD), heart failure (HF), and stroke, which are prominent contributors to mortality in the US (3). Therefore, the prevention of CVD requires further in-depth investigation.

Milk is nutritious and is a staple of Western diets and is classified as whole (3.5 %), reduced-fat (2 %), low-fat (1 %), and skimmed milk (< 0.5 %) depending on its fat content in the US (4). Whole milk has a higher fat concentration than low-fat, reduced-fat, and skimmed milk, due to its higher saturated fat content, which is thought to elevate low-density lipoprotein cholesterol levels upon consumption (5). Thus, whole dairy product consumption, including whole milk, is frequently considered a risk factor for CVDs (6).

Dietary guidelines from organizations such as the U.S. Department of Agriculture, the UK Department of Public Health, and the Singapore Health Promotion Board all recommend low-fat or fat-free dairy products to help mitigate the risk of CVD (7-9). Similarly, the Dietary Approaches to Stop Hypertension diet, developed by the National Institutes of Health, advocates low-fat or nonfat dairy products over full-fat alternatives (10). However, some studies have reported contrasting findings. For example, a prospective urban-rural epidemiology study found that a higher consumption of full-fat dairy was associated with a lower prevalence of CVD and decreased mortality rates (11). Similarly, another study based on the Observation of Cardiovascular Risk Factors in Luxembourg survey found that increased intake of full-fat dairy was positively associated

with a reduced risk of CVD (12). Meta-analyses and reviews have yet to reach a consensus on which type of milk is the better choice for patients with CVD (13).

Based on recent observational findings suggesting that whole-fat dairy products may be associated with cardiovascular benefits, we cautiously hypothesized that whole milk might confer benefits for patients with CVD. To test this hypothesis, we analyzed data derived from the comprehensive National Health and Nutrition Examination Survey (NHANES). Our study aimed to investigate the potential association between milk consumption, categorized by fat content, and the prevalence of various CVDs. By elucidating these associations, we sought to provide new insights into CVD prevention and contribute to the refinement of dietary guidelines and public health strategies.

## **METHODS**

### **Study population**

The NHANES is a biennial survey designed to evaluate the health and nutritional status of individuals in the US (14). For this study, we analyzed data collected over eight consecutive biennial cycles (2003-2018). All participants were over 20 years of age. Individuals with missing data on milk type, CVDs, demographics, or other covariates, as well as those who reported consuming more than one of the four milk types, were excluded from the analysis.

### **Definition of CVDs**

The outcomes of our study included CHD, HF, and stroke. These outcomes were assessed through a standardized questionnaire that inquired whether participants had been diagnosed with these conditions by a healthcare professional. Participants diagnosed with CHD, angina, or myocardial infarction were classified into the CHD



group, while those diagnosed with HF and stroke were categorized into the HF and stroke groups, respectively.

### **Assessment of the type of milk consumed**

In the NHANES, standardized questionnaires were used to assess the type of milk consumed. Participants were asked, “What type of milk was it? Was it usually . . . (What type of milk do you usually drink?)” Respondents indicating “whole or regular” were categorized into the whole milk group; those who answered “2 % fat or reduced-fat milk” were categorized into the reduced-fat milk group; those who answered “1 % fat or low-fat milk” were categorized into the low-fat milk group; and those who answered “skim, nonfat, or 0.5 % fat milk” were categorized into the skimmed milk group.

### **Covariates**

The covariates included sex, age, race/ethnicity, educational level, marital status, household income, smoking and drinking status, body mass index (BMI), leisure activity, hypertension (HT), diabetes mellitus (DM), chronic kidney disease (CKD), the estimated glomerular filtration rate (eGFR), and the dietary data. The categories for race/ethnicity included non-Hispanic White, non-Hispanic Black, Mexican American, and other races. Educational levels consisted of three groups: higher education, less than high school, high school. Marital status was divided into unmarried, married/cohabiting, and divorced/separated/widowed. Household income was represented by the ratio of household income to poverty (PIR) and categorized as low ( $PIR < 1.3$ ), medium ( $1.3 \leq PIR < 3.5$ ), and high ( $PIR \geq 3.5$ ). Smoking status was categorized as never smokers (individuals who smoked  $\leq 100$  cigarettes in their lifetime), former smokers (those who smoked  $>100$  cigarettes and are no longer smoking), and current smokers (those who smoked  $\geq$



100 cigarettes and are still smoking). Alcohol consumption was categorized into three levels: excessive intake, defined as more than three drinks per day for women and more than four for men; moderate intake, defined as two drinks daily for women and three for men; and light consumption, which included any intake below these limits. BMI categories were defined as follows: normal weight,  $< 25 \text{ kg/m}^2$ ; overweight,  $25.0\text{-}29.9 \text{ kg/m}^2$ ; and obese,  $\geq 30.0 \text{ kg/m}^2$ . Leisure activity was classified into low, moderate, and vigorous exercise. HT was defined as a systolic blood pressure  $\geq 140 \text{ mmHg}$  or diastolic blood pressure  $\geq 90 \text{ mmHg}$ , a previous diagnosis of HT, or the use of antihypertensive medication (15). DM was defined according to the following criteria: 1) current use of glucose-lowering medication or insulin; 2) a previous diagnosis of DM; 3) glycosylated hemoglobin level  $\geq 6.5 \%$ ; 4) fasting plasma glucose  $\geq 7.0 \text{ mmol/L}$ ; or 5) 2-hour postprandial glucose  $\geq 11.1 \text{ mmol/L}$ . CKD was defined as  $\text{eGFR} < 60 \text{ mL/min/1.73 m}^2$  or urine albumin-to-creatinine ratio  $> 30 \text{ mg/g}$  (16). The eGFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration equation (17). Dietary intake, assessed by calculating the average of two independent 24-hour dietary recalls, included the total energy intake and energy-adjusted intake of fatty acids (saturated, monounsaturated, and polyunsaturated), protein, and carbohydrates. Additionally, it encompassed the intake of fruits, vegetables, and red and processed meats. To avoid dose interference, we also adjusted for the quantity of milk intake. Furthermore, we adjusted for the intakes of yogurt and butter as covariates to account for potential confounding from other dairy products. All detailed measurement procedures for covariates are available on the official NHANES website (18).

## **Statistical analyses**

In this study, we applied the dietary two-day sample weight (WTDR2D) and recalculated the multi-year sample weights ( $1/8 * WTDR2D$ ), weighting all analyses as recommended by the National Center for Health Statistics. Percentages ( %) are used to represent categorical variables, whereas continuous variables are expressed as means with standard deviations. To assess differences between groups, normally distributed data were analyzed using analysis of variance, and categorical variables were tested using chi-square tests. The CVD association across different levels of milk fat content was estimated using multivariable-adjusted logistic regression. Model 1 represented an unadjusted model. In Model 2, adjustments were made for sex, age, race/ethnicity, education level, marital status, household income, smoking and drinking status, BMI, and leisure activity. Model 3 included further adjustments for eGFR, DM, HT, CKD, and other CVDs in addition to the variables from Model 2. Finally, Model 4 was additionally adjusted for dietary data, including total energy intake; energy-adjusted intakes of fatty acids, protein, and carbohydrates; and the intakes of fruits, vegetables, red and processed meats, yogurt, butter, and milk. We performed subgroup analyses by sex, age, and BMI and tested for interaction effects using a design-adjusted Wald test in survey-weighted logistic regression. To avoid confounding, 291 participants who consumed soy or other types of milk were excluded, and the data were reanalyzed to assess the robustness of the findings. Data were analyzed using R software (version 4.2.2).

## **RESULTS**

### **Basic characteristics**

After screening, 18,282 individuals from the NHANES were finally included in this study (Fig. 1). Supplementary table I shows the basic characteristics of the participants stratified by the type of milk consumed. Whole milk consumption was more prevalent among

younger individuals, males, and non-Hispanic Whites. Participants who consumed whole milk were more likely to have lower household income, lower educational attainment, and greater tobacco and alcohol use.

### **Associations between the type of milk consumed and cardiovascular diseases**

The results of the weighted logistic regression analysis of the four types of milk and their association with CHD are presented in table I. Participants who consumed whole milk (odds ratio [OR] = 0.582, 95 % confidence interval [CI] = 0.418-0.810,  $p = 0.002$ ) and reduced-fat milk (OR = 0.668, 95 % CI = 0.502-0.890,  $p = 0.006$ ) had a significantly lower OR of CHD compared to those in the skimmed milk group in Model 4. However, no significant correlation was observed for low-fat milk (OR = 0.776, 95 % CI = 0.538-1.118,  $p = 0.17$ ). Supplementary table II outlines the association between the four types of milk and HF. Whole milk (OR = 1.518, 95 % CI = 0.939-2.455,  $p = 0.09$ ), reduced-fat milk (OR = 1.356, 95 % CI = 0.895-2.055,  $p = 0.15$ ), and low-fat milk (OR = 1.030, 95 % CI = 0.594-1.785,  $p = 0.92$ ) were not significantly associated with HF compared to skimmed milk. As shown in table II, whole milk consumption was associated with a significantly higher prevalence of stroke compared to skimmed milk (OR = 1.586, 95 % CI = 1.023-2.457,  $p = 0.039$ ) in Model 4. However, reduced-fat milk (OR = 1.151, 95 % CI = 0.799-1.660,  $p = 0.44$ ) and low-fat milk (OR = 1.238, 95 % CI = 0.813-1.886,  $p = 0.31$ ) were not significantly associated with stroke.

### **Stratified and sensitivity analyses**

Analyses across subgroups defined by sex, age (< 65 and  $\geq$  65 years), and BMI showed no significant interactions in most subgroups (Fig. 2). The beneficial correlation between whole milk and CHD was significantly influenced by age as an interaction factor, with

the protective relationship being more pronounced among individuals aged 65 years or older. The beneficial association of whole milk with CHD and the adverse association with stroke remained robust in additional weighted logistic regression analyses after excluding individuals who consumed soy or other types of milk (Suppl. Tables III and IV).

## **DISCUSSION**

Consistent with our hypothesis, consuming whole milk was linked to a lower prevalence of CHD compared to skimmed milk. However, contrary to our hypothesis, a higher prevalence of stroke was observed in individuals consuming whole milk. Sensitivity analyses further confirmed the robustness of these findings.

Some studies have yielded different results from ours, particularly in research design and analytical focus. For example, a comparative study of the dietary habits of 210 patients with and without CHD indicated that consuming skimmed milk was associated with a decreased risk of CHD (19). However, it focused on overall dietary patterns as well as identifying differences in the consumption of meat, vegetables, and fruits between the two groups. Consequently, conclusions cannot be drawn solely based on the milk type. In contrast, our study focused on the consumption of milk with different fat contents, adjusting for other dietary factors to minimize confounding effects. Additionally, another prospective cohort study involving 1,746 participants revealed that higher low-fat milk intake was significantly linked to the incidence of CHD and CVD, while whole milk did not exhibit a similar effect (20). Nonetheless, that research was conducted with a limited sample size and within the Danish population; therefore, the external validity is limited as dietary patterns and lifestyles can vary across countries.

Our findings are corroborated by several prior studies. For example, Avalos et al. followed-up 1,759 residents of a Southern California

community for nearly 20 years and observed a higher prevalence of CHD in women with higher skimmed milk intake (21). However, the study primarily included white, middle-class residents, which limits its representativeness. In contrast, our study utilized data from a multiracial population across the US, providing a larger and more representative sample. Additionally, by following 5,273 participants, Sounak et al. found that whole milk intake may offer protection against coronary artery calcification and slow its progression (22). However, this study concentrated on the potential benefits of whole milk and did not compare milk with varying fat content. Furthermore, recent Mendelian randomization studies have shown that skimmed milk has an adverse effect on CHD and HT (23), partially aligning with our findings.

Few investigations have addressed the impact of milk type on stroke risk. A meta-analysis indicated a possible connection between whole milk intake and increased total stroke risk, though the conclusion relied on limited evidence (24). Whole milk consumption was linked to an increased risk of cerebral hemorrhage over a 13.6-year follow-up, while no such association was found with low-fat milk (25). Similarly, a prospective cohort study involving 79,618 participants demonstrated that whole milk consumption was positively associated with hemorrhagic stroke risk, but not with ischemic stroke or total stroke (26). These findings suggest that stroke subtype is an important factor when evaluating the relationship between milk fat content and stroke risk. Our study identifies a potential association between whole milk and a higher prevalence of total stroke; however, as stroke subtypes were not distinguished, these findings should be interpreted with caution.

Several meta-analyses have indicated that there are relatively few direct studies on the association between milk types and CVD risk. Furthermore, issues such as inconsistent findings and heterogeneity in some studies complicate the ability to draw definitive conclusions

regarding which type of milk with differing fat content is more beneficial for cardiovascular health (27,28). Our study offers a new perspective on the potential relationship between various milk types and CVD.

Whole milk contains complex and naturally occurring fatty acids. As the total fat content of milk increases, the contents of fatty acids, such as short-chain fatty acids, conjugated linoleic acid, and polar lipids, also rise (29). These components may significantly contribute to the positive association between whole milk and CHD. It is well known that inflammation is an important pathological process in coronary artery atherosclerosis (30). On the one hand, these fatty acids exhibit direct anti-inflammatory effects by down-regulating pro-inflammatory factors and up-regulating anti-inflammatory factors (31). On the other hand, they also indirectly reduce inflammatory responses by improving the intestinal flora (31). Additionally, these fatty acids can exhibit anti-atherosclerotic properties by inhibiting fat absorption and accelerating fat oxidation, reducing cholesterol levels in the body and alleviating obesity (32,33). Venn-Watson et al. (34) found that when mice were fed different doses of C15:0 (an odd-chain saturated fatty acid in milk), supplementation with C15:0 helped lower cholesterol levels and reduce inflammation. The researchers also found that three saturated fatty acids, C14:0, C15:0, and C16:0, had anti-inflammatory effects in a human cell system simulating inflammation and fibrosis. Cécile et al. conducted a randomized, double-blind experiment (35). After a dietary intervention with different levels of milk polar lipids in 58 postmenopausal women, they found that milk polar lipids significantly reduced plasma cholesterol concentrations both during fasting and postprandial periods.

However, this cholesterol-lowering effect could paradoxically increase the risk of hemorrhagic stroke. Evidence from several population-based studies supports this concern (36,37). Lower cholesterol levels have been suggested to increase the fragility of cerebral arterial



endothelial cells, rendering them more susceptible to damage (38). Once injured, these vessels may be more prone to aneurysm formation, thereby further elevating the risk of intracerebral hemorrhage (39). Additionally, cholesterol is crucial for platelet activation and production. Reduced cholesterol levels can impair the formation of platelet lipid rafts, resulting in diminished platelet activation and aggregation (40). Moreover, low cholesterol may indirectly suppress thrombopoietin signaling, inhibiting platelet production (40). Given that stroke subtypes were not differentiated in our analysis, and considering the observed protective association between whole milk and CHD, it is plausible that the adverse association observed for total stroke may be primarily attributable to hemorrhagic stroke.

A notable strength of this research is its utilization of large-scale data that provided enough statistical power to estimate the relationship of milk type and cardiovascular health. Furthermore, we conducted stratification and sensitivity analyses to ensure our results were robust. However, some limitations need to be acknowledged. First, the use of self-reported data for milk consumption and CVDs may have introduced an inevitable recall bias. Second, using two 24-hour dietary recalls to assess intake may not accurately reflect habitual consumption, especially for a chronic condition like CVD. Although this method is widely used in large-scale surveys like NHANES, it is prone to non-differential measurement errors that can introduce bias. Third, the exclusion of missing data may have introduced selection bias. Fourth, our study focused on the different levels of fat content in milk and adjusted for milk intake, but did not explore the potential dose-response relationship between milk with varying levels of fat and CVDs, limiting our ability to make specific recommendations for preventing CVDs. Fifth, the study did not distinguish between the stroke subtypes. Since the associations of whole milk with hemorrhagic and ischemic stroke may be different, further distinction



in future research is warranted. Finally, causality could not be established due to the cross-sectional study design.

## **CONCLUSION**

Whole milk consumption is associated with a lower prevalence of CHD; however, caution should be exercised when making decisions about its consumption, particularly in relation to stroke. Further research is needed to prospectively examine the relationship between milk consumption with varying fat content and different CVDs, as well as to elucidate the mechanisms underlying the observed benefits of whole milk for CHD and its possible unfavorable association with stroke.

Nutrición  
Hospitalaria

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# Nutrición Hospitalaria



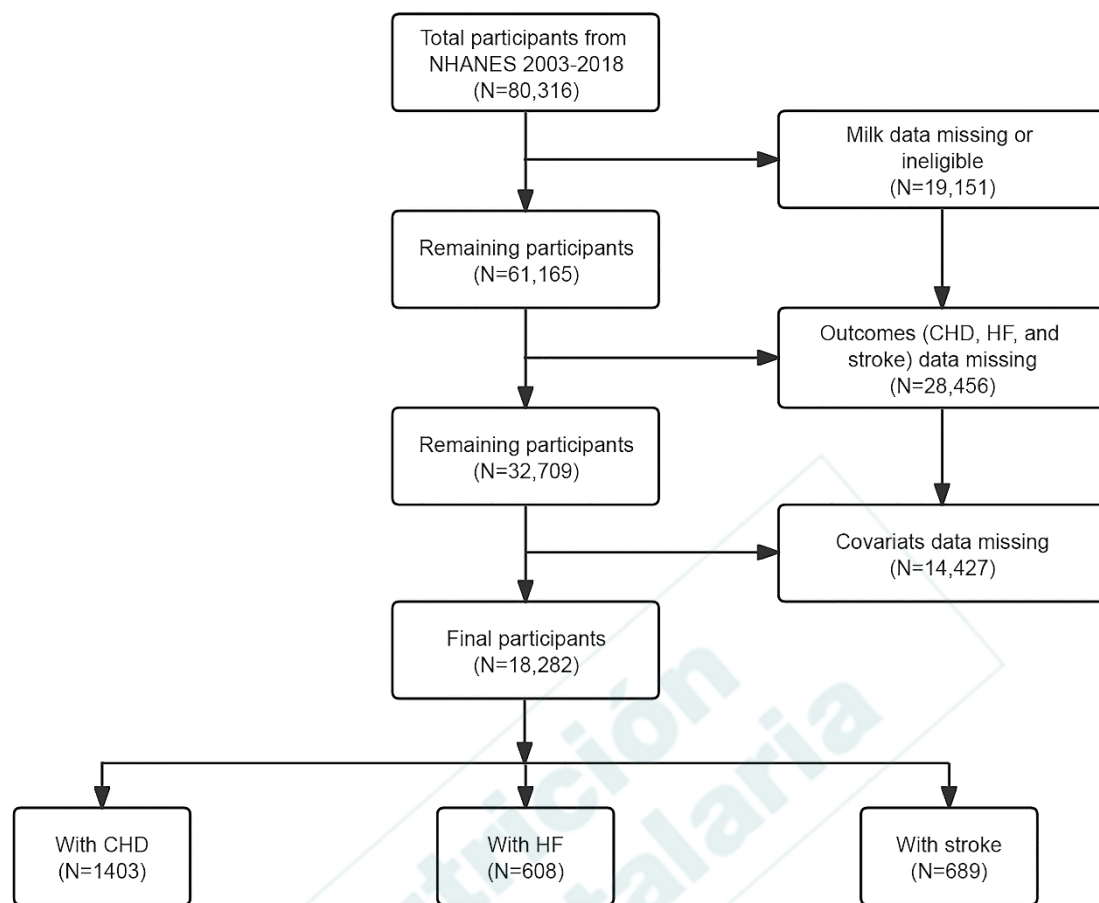
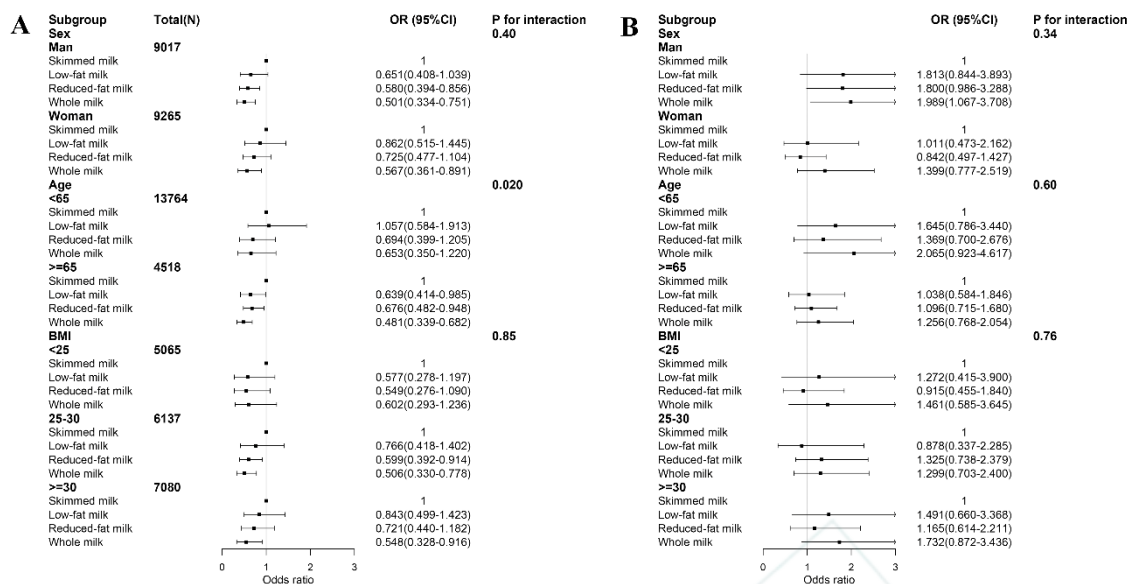


Figure 1. The study's flow diagram. Data from NHANES 2003–2018 for US adults (abbreviations: NHANES: National Health and Nutrition Examination Survey; CHD: coronary heart disease; HF: heart failure).



**Figure 2.** Subgroup analysis of the associations between the four types of milk fat content and CHD (A) and stroke (B). Each analysis adjusted for covariates, including sex, age, race/ethnicity, education level, marital status, household income, smoking and drinking status, BMI, leisure activity, eGFR, DM, HT, CKD, other CVDs, and dietary factors (total energy intake; energy-adjusted intakes of fatty acids, protein, carbohydrates; and intakes of fruits, vegetables, red and processed meats, yogurt, butter, and milk). Statistical significance was set at  $p < 0.05$  (abbreviations: OR: odds ratio; CI: confidence interval; BMI: body mass index; CHD: coronary heart disease).

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Table I. Association between milk consumption with different fat content and CHD

Milk type	Model 1		Model 2		Model 3		Model 4	
	OR (95 % CI)	<i>p</i> value	OR (95 % CI)	<i>p</i> value	OR (95 % CI)	<i>p</i> value	OR (95 % CI)	<i>p</i> value
Skimmed milk	Ref		Ref		Ref		Ref	
Low-fat milk	0.844 (0.605-1.176)	0.31	0.794 (0.567-1.111)	0.18	0.796 (0.553-1.146)	0.22	0.776 (0.538-1.118)	0.17
Reduced-fat milk	0.881 (0.702-1.107)	0.27	0.781 (0.615-0.991)	0.042	0.686 (0.521-0.903)	0.008	0.668 (0.502-0.890)	0.006
Whole milk	0.793 (0.597-1.0523)	0.11	0.685 (0.498-0.942)	0.020	0.601 (0.434-0.833)	0.003	0.582 (0.418-0.810)	0.002
<i>p</i> for trend		0.15		0.026		0.002		0.002

CHD: coronary heart disease; OR: odds ratio; CI: confidence interval; Ref: reference group. Model 1: crude model. Model 2: adjusted for age, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, and other races), marital status (never married, married/living with partner, divorced/separated/widowed), education level (less than high school, high school, and more than high school), household income (low: PIR < 1.3, medium:  $1.3 \leq \text{PIR} < 3.5$ , and high:  $\text{PIR} \geq 3.5$ ), smoking status (never, former, and current), drinking status (light, moderate, and heavy).

and excessive), body mass index (normal weight, overweight, and obese), and leisure activity (low, moderate, and high). Model 3: adjusted for Model 2 + hypertension, diabetes, chronic kidney disease, stroke, heart failure, and estimated glomerular filtration rate. Model 4: adjusted for Model 3 + dietary intake variables, including total energy intake; energy-adjusted intake of fatty acids, protein, and carbohydrates; and the intake of fruits, vegetables, red and processed meats, yogurt, butter, and milk. Statistical significance was set at  $p < 0.05$ .

Table II. Association between milk consumption with different fat content and stroke

Milk type	Model 1		Model 2		Model 3		Model 4	
	OR (95 % CI)	<i>p</i> value	OR (95 % CI)	<i>p</i> value	OR (95 % CI)	<i>p</i> value	OR (95 % CI)	<i>p</i> value
Skimmed milk	Ref		Ref		Ref		Ref	
Low-fat milk	1.214 (0.784-1.881)	0.38	1.153 (0.748-1.776)	0.51	1.254 (0.819-1.918)	0.29	1.238 (0.813-1.886)	0.31
Reduced-fat milk	1.438 (1.003-2.062)	0.048	1.247 (0.866-1.795)	0.23	1.215 (0.838-1.763)	0.30	1.151 (0.799-1.660)	0.44
Whole milk	1.941 (1.294-2.912)	0.002	1.625 (1.055-2.502)	0.028	1.709 (1.108-2.638)	0.016	1.586 (1.023-2.457)	0.039
<i>p</i> for trend		0.001		0.027		0.022		0.06

OR: odds ratio; CI: confidence interval; Ref: reference group. Model 1: crude model. Model 2: adjusted for age, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, and other races), marital status (never married, married/living with partner, divorced/separated/widowed), education level (less than high school, and more than high school), household income (low: PIR < 1.3, medium: 1.3 ≤ PIR < 3.5, and high: PIR ≥ 3.5), smoking status (never, former, and current), drinking status (light, moderate, and excessive), body mass index

(normal weight, overweight, and obese), and leisure activity (low, moderate, and high). Model 3: adjusted for Model 2 + hypertension, diabetes, chronic kidney disease, coronary heart disease, heart failure, and estimated glomerular filtration rate. Model 4: adjusted for Model 3 + dietary intake variables, including total energy intake; adjusted intake of fatty acids, protein, and carbohydrates; and the intake of fruits, vegetables, red and processed meats, yogurt, butter, and milk. Statistical significance was set at  $p < 0.05$ .