Association of cardiovascular diseases with milk intake among general Chinese adults

Xin-Yan Wang[1,2], Fang-Chao Liu[1,2], Xue-Li Yang[1,2], Jian-Xin Li[1,2], Jie Cao[1,2], Xiang-Feng Lu[1,2], Jian-Feng Huang[1,2], Ying Li[1,2], Ji-Chun Chen[1,2], Lian-Cheng Zhao[2], Chong Shen[3], Dong-Sheng Hu[4,5], Ying-Xin Zhao[6], Ling Yu[7], Xiao-Qing Liu[8], Xian-Ping Wu[9], Dong-Feng Gu[1,2,10]

[1]Key Laboratory of Cardiovascular Epidemiology, Chinese Academy of Medical Sciences, Beijing 100037, China;
[2]Department of Epidemiology, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, China;
[3]Department of Epidemiology and Biostatistics, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu 211166, China;
[4]Department of Epidemiology and Health Statistics, College of Public Health, Zhengzhou University, Zhengzhou, Henan 450001, China;
[5]Department of Biostatistics and Epidemiology, School of Public Health, Shenzhen University Health Science Center, Shenzhen, Guangdong 518071, China;
[6]Shandong First Medical University, Jinan, Shandong 271000, China;
[7]Department of Cardiology, Fujian Provincial People's Hospital, Fuzhou, Fujian 350004, China;
[8]Division of Epidemiology, Guangdong Provincial People's Hospital and Cardiovascular Institute, Guangzhou, Guangdong 510080, China;
[9]Sichuan Center for Disease Control and Prevention, Chengdu, Sichuan 610041, China;
[10]School of Medicine, Southern University of Science and Technology, Shenzhen, Guangdong 518055, China.

Abstract

Background: The association of milk intake with cardiovascular disease (CVD) and cause-specific mortality remained controversial and evidence among the Chinese population was limited. We aimed to study the relationship between milk intake and CVDs among general Chinese adults.

Methods: A total of 104,957 participants received questionnaire survey. Results of physical examination such as anthropometric measurements and biochemical tests during 2007 to 2008, demographic data and their information on milk intake were collected through standardized questionnaires. Cox proportional hazard regression models were used to calculate hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) of CVD incidence, cause-specific mortality and all-cause mortality related to milk intake. Restricted cubic splines (RCSs) were applied to examine dose-response associations.

Results: Among the 91,757 participants with a median follow-up period of 5.8 years, we documented 3877 CVD cases and 4091 all-cause deaths. Compared with participants who never consumed milk, the multivariate-adjusted HRs (95% CIs) of CVD incidence for 1 to 150 g/day, 151 to 299 g/day, and ≥300 g/day were 0.94 (0.86–1.03) ($P > 0.05$), 0.77 (0.66–0.89) ($P < 0.05$), and 0.59 (0.40–0.89) ($P < 0.05$), respectively; each 100 g increase of daily milk intake was associated with 11% lower risk of CVD incidence (HR, 0.89; 95% CI: 0.85–0.94; $P < 0.001$), and 11% lower risk of CVD mortality (HR, 0.89; 95% CI: 0.82–0.97; $P = 0.008$) after adjustment for age, sex, residential area, geographic region, education level, family history of CVD, smoking, alcohol drinking, physical activity level, body mass index, and healthy diet status (ideal or not). RCS analyses also showed a linear dose-response relationship with CVD (P for overall significance of the curve <0.001; P for non-linearity = 0.979; P for linearity <0.001) and stroke (P for overall significance of the curve = 0.010; P for non-linearity = 0.998; P for linearity = 0.002) incidence, and CVD mortality (P for overall significance of the curve = 0.045; P for non-linearity = 0.768; P for linearity = 0.014) within the current range of daily milk intake.

Conclusions: Daily milk intake was associated with lower risk of CVD incidence and mortality in a linear inverse relationship. The findings provide new evidence for dietary recommendations in CVD prevention among Chinese adults and people with similar dietary pattern in other countries.

Keywords: Milk; Cardiovascular disease; Incidence; All-cause mortality; Cause-specific mortality; Prospective study; Chinese population

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000000786

Correspondence to: Prof. Dong-Feng Gu, Key Laboratory of Cardiovascular Epidemiology, Chinese Academy of Medical Sciences; Department of Epidemiology, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, 167 Beilishi Road, Beijing 100037, China
E-Mail: gudongfeng@cashq.ac.cn

Copyright © 2020 The Chinese Medical Association, produced by Wolters Kluwer, Inc. under the CC-BY-NC-ND license. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Chinese Medical Journal 2020;133(10)

Received: 21-01-2020 **Edited by:** Pei-Fang Wei

Introduction

Cardiovascular disease (CVD) was responsible for more than 360 million disability-adjusted life years (DALYs) globally and 85 million DALYs in China for the year of 2017.[1] The incidence and mortality rates of CVD tend to fall in the developed world now, but are still on the rise in China and other developing countries along with aging population and modernization of lifestyles.[2] Thus it is crucial to understand potential modifiable risk factors comprehensively and to develop evidence-based and practical primary prevention strategies for reducing both CVD incidence and mortality.

Milk is one of the most consumed beverages worldwide and is an important source of protein, vitamin D, calcium, potassium, and other minerals.[3] Dietary guidelines in different countries all included recommendations on daily intake of dairy products to meet the needs for high-quality nutrients.[4-6] Nevertheless, an overview of previous systematic reviews and meta-analysis showed that there was no association of milk consumption with different health outcomes, and even several minor risks have been found for CVD or stroke.[7] Findings from individual investigations into the associations of milk with CVD incidence, all-cause, and cause-specific mortality remained inconsistent.[8-10] Pooled results stratified by continent also showed high heterogeneity between the western countries and the East Asian countries.[10] Thus, the evidence on health effects of milk derived from the western populations might not be generalizable to the Chinese population due to different genetic backgrounds, different overall dietary patterns across populations as well as different ranges of milk intake.

Though milk consumption used to be at a relatively low level,[11] there has been an increasing trend in recent years along with the shift in lifestyle and dietary patterns in China.[12] However, evidence on the associations of milk with CVD, cause-specific, and all-cause mortality from China was limited and inconsistent.[13-15] One study in Taiwan of China showed favorable effects of milk intake on stroke and mortality,[14] while the association of milk with a composite of mortality or major cardiovascular events reported in the mainland of China was only modest or null.[15]

In this study, we aimed to prospectively evaluate the association of milk intake with CVD and cause-specific mortality based on large-scale prospective cohorts among general Chinese adults, and to provide evidence for the validation and optimization of the dietary recommendations.

Methods

Ethical approval

This study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Institutional Review Board at Fuwai Hospital (No. 2012-399). Informed consent was obtained from each participant prior to data collection.

Study population

This study was based on the project of Prediction for Atherosclerotic Cardiovascular Disease Risk in China (China-PAR), which was a large collaborative study to investigate the epidemic of CVDs and identify the risk factors in the general Chinese population including the China Multi-Center Collaborative Study of Cardiovascular Epidemiology (China MUCA 1992–1994, and China MUCA 1998), the International Collaborative Study of CVD in Asia (InterASIA), and the Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study (CIMIC).[16] The China MUCA 1992–1994 cohort was not included in the current study because the information on milk intake was not collected. The China MUCA 1998 cohort was established in 1998 with cluster random sampling and included about 500 men and 500 women aged 35 to 59 years in each of the 15 clusters.[17] The InterASIA cohort was established from 2000 to 2001, and selected a nationally representative sample of adults aged 35 to 74 years in China using a four-stage stratified sampling method (based on geographic region and urbanization).[18] Participants from the China MUCA 1998 and the InterASIA cohorts were followed twice, from 2007 to 2008, and 2012 to 2015, separately. The CIMIC was a large, community-based cohort that was established from 2007 to 2008 and selected four survey sites from three provinces (Shandong, Henan, and Jiangsu) with different economic development levels in China. In total, 86,428 participants ≥18 years of age completed the baseline study and were invited to participate in the follow-up survey from 2012 to 2015.[16] A total of 104,957 participants attended lifestyle investigations and health examinations during 2007 to 2008, among which 96,048 (follow-up rate: 91.5%) were followed until 2012 to 2015. After further excluding 3782 participants with a history of CVD, cancer or other major chronic diseases and 509 participants without milk intake information from 2007 to 2008, 91,757 (7072 from InterAsia, 6734 from China MUCA-1998, and 77,951 from CIMIC) were included in the current analysis. This process is showed in detail in the flow-chart [Figure 1].

Assessment of milk intake and covariates

We used simplified food frequency questionnaire (FFQ) consisting of closed-end, easy-to-understand questions with appropriate response options. An item on milk intake was included in the FFQ and applied during 2007 to 2008 and 2012 to 2015 for all sub-cohorts. Participants were interviewed by trained and certificated staff face to face and asked to answer whether they drank milk or not, and the amount they drank per day, per week, per month, or per year during the past year. The intake amount was then converted into the intake amount per day. The questionnaire item was described as "milk or yogurt." The serving sizes of whole milk, skim/low fat milk, and yogurt were treated equally. Participants were categorized into four groups according to daily intake level of milk: none, 1 to 150 g/day, 151 to 300 g/day, ≥300 g/day referring to the Dietary Guidelines for Chinese Residents (2016).[6]

Information on demographic characteristics, lifestyle risk factors, and family and personal medical history was also

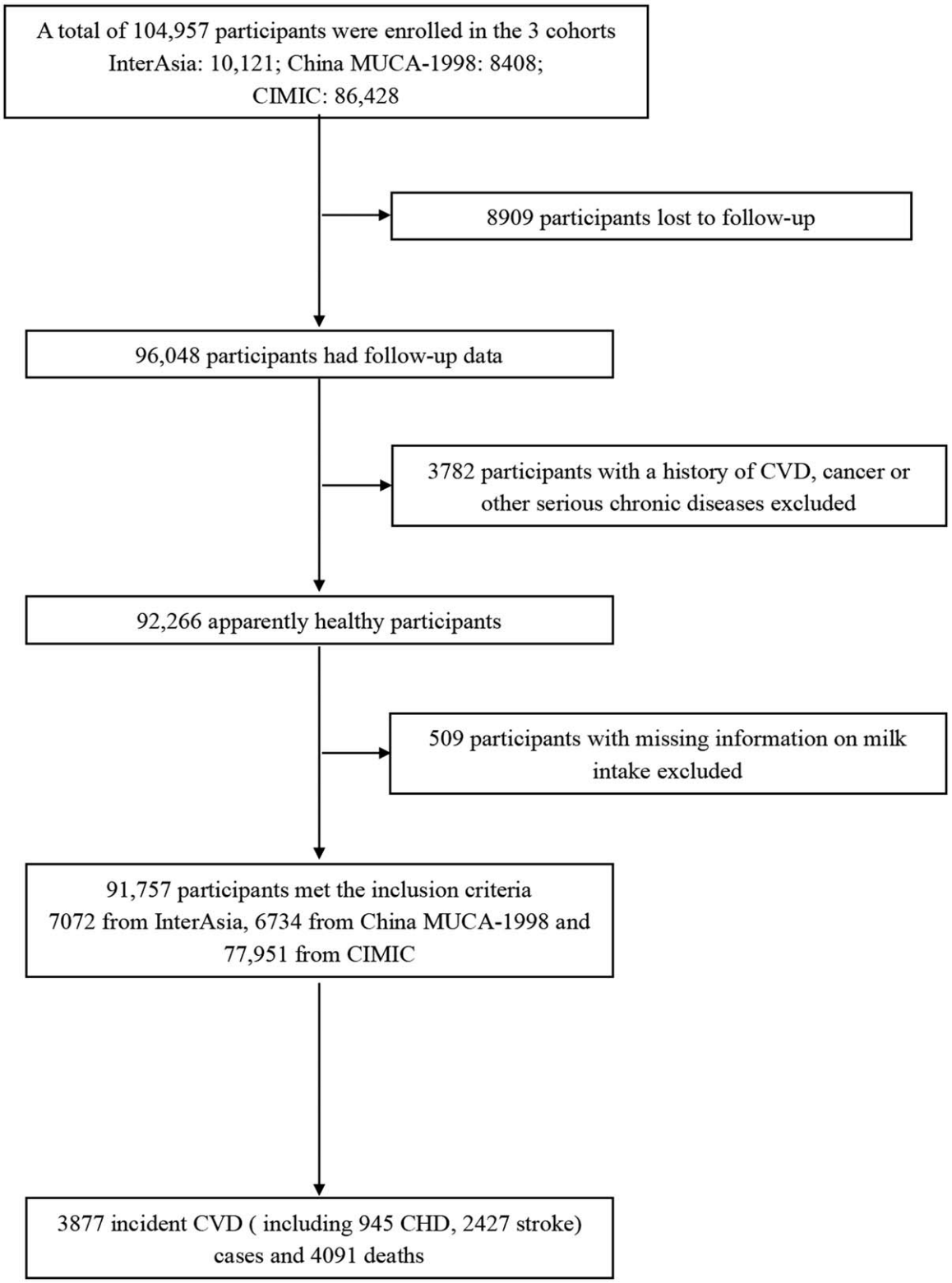

Figure 1: Flowchart of participant inclusion and exclusion. InterASIA: International Collaborative Study of CVD in Asia; China MUCA: China Multi-Center Collaborative Study of Cardiovascular Epidemiology; CIMIC: Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study; CVD: Cardiovascular disease; CHD: Coronary heart disease.

collected via standardized questionnaires. Smoking and drinking status was self-reported and the information on drinking habits was collected over the previous 12 months. Physical activity was assessed by asking time duration spent on rigorous/moderate/light physical activities per day during the previous year including leisure-time physical activity, physical activity from transportation, occupational physical activity, household chores, etc. Ideal physical

activity level was defined as at least 150 min of moderate physical activity or at least 75 min of vigorous physical activity per week according to the WHO's global recommendations on physical activity for health.[19] Habitual dietary intake was collected by asking the frequency of consumption and portion size of those typical food items during the past year using the FFQ. The healthy diet status was defined as ≥2 of ideal selected items including ≥500 g/day, ≤50 g/day, ≥125 g/day, ≥200 g/week, and ≥50 g/month consumption for fresh vegetables and fruits, red meat, soybean products, fish, and tea respectively based on the recommendations of Dietary Guidelines for Chinese Residents (2016)[6] or consistent with our previous study.[20,21] Body weight and height were measured twice only wearing light clothes without shoes and body mass index (BMI) was calculated as the weight in kilograms divided by the square of height in meters. Blood pressure was measured three times after 5 min of rest in a sitting position according to a standard protocol, and the average of three measures was used. Blood samples were drawn after at least 10 h of fasting and were centrifuged immediately to measure serum glucose and lipids. Serum glucose was measured by a modified hexokinase enzymatic method (Hitachi automatic clinical analyzer, model 7060, Hitachi, Ltd., Tokyo, Japan). Total cholesterol, high-density lipoprotein cholesterol (HDL-C), and triglyceride were measured enzymatically with commercial reagents. Low-density lipoprotein cholesterol (LDL-C) was calculated by the following formula: LDL-C = TC–HDL-C–Triglycerides/5.

Outcome measures

Follow-up surveys were conducted during 2012 to 2015 and the same protocols were applied for all three cohorts. An integrated method was applied including performing face-to-face interviews with study participants or their proxies to ascertain disease status, and obtaining hospital records and death certificates.

CVD (International Classification of Diseases, 10th edition, I00-I99) was defined as non-fatal acute myocardial infarction (AMI), unstable angina, heart failure, coronary heart disease (CHD) death, and fatal or non-fatal stroke. CHD (I20–I25) included non-fatal AMI, unstable angina, or CHD death. AMI was identified as a change in biochemical markers of myocardial necrosis accompanied by ischemic symptoms, pathological Q waves, ST-segment elevation or depression, or coronary intervention.[22] Stroke included clinical signs and symptoms of subarachnoid or intra-cerebral hemorrhage or cerebral infarction, which rapidly developed signs of focal (or global) disturbances in cerebral function lasting more than 24 h without an apparent non-vascular cause. According to computed tomography scans, magnetic resonance imaging or autopsy findings, stroke cases were classified as ischemic stroke (IS [I63]) and hemorrhagic stroke (HS, including intra-cerebral hemorrhage [I61], and subarachnoid hemorrhage [I60]).[23] Cases with no records of brain imaging or autopsy for reviewing by the end-point assessment committee were classified as undetermined pathological type. All death cases were recorded, while CVD deaths were defined by ICD-10 and I00-I99.

Statistical analysis

Baseline characteristics were presented according to milk intake categories. Follow-up period was calculated from the survey date during 2007 to 2008 to the date of the outcome, loss to follow-up, or the date of the last follow-up date, whichever came first. Age- and sex-adjusted incidence rates per 100,000 person-years of study outcomes were calculated using Poisson regression.[24] We used Cox regression model stratified by cohort sources to calculate hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs), and the proportional hazards assumption was proved to be met by evaluating the Schoenfeld residuals ($P > 0.05$).[25] Baseline milk intake was included in the models as either a category variable (for HRs of 1–150 g/day, 151–299 g/day, and ≥300 g/day compared with none) or a continuous variable (for HRs per 100 g/day increase). Restricted cubic splines (RCSs) were also employed to explore potential dose-response association. Likelihood ratio test was used to test the non-linearity, comparing the model with only the linear term to the model with the linear and the cubic spline terms.

The following variables were adjusted gradually in multivariable models. Model 1 adjusted age (continuous), sex (men/women), geographic region (north/south), residential area (rural/urban), and education level (≥12 years or not). Model 2 further adjusted for family history of CVD (yes or no), smoking (yes or no), alcohol drinking (yes or no), physical activity level (ideal or not), BMI (continuous), and healthy diet status (ideal or not). Model 3 further adjusted for baseline systolic blood pressure, fasting blood glucose, total cholesterol, and HDL-C.

Stratified analyses were conducted according to baseline demographic characteristics, lifestyle factors, and cardiometabolic risk factors. A cross-product term between the stratification variable and daily milk intake amount (as a continuous variable with the unit of 100 g) was included in the model to investigate the potential effect modifications. Sensitivity analyses were carried out after excluding the cases which occurred during the first 2 years of follow-up to minimize reverse causation. We also analyzed the association of health outcomes with each 100 g/day increase using competing risk models to explore the influence of studying different outcomes together.

Continuous data were presented as mean ± standard deviation. Categorical data were expressed as counts and percentages. Data were analyzed using SAS statistical package (version 9.4, SAS Institute Inc, Cary, NC, USA). All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

Descriptive characteristics of the study population

Milk intake in the China-PAR project was very low, with an average level of 26.2 g/day among all participants and 75.4% (69,222/91,757) of all participants never drank milk from 2007 to 2008. Milk consumers were obviously

Table 1: Characteristics of the study participants in the China-PAR project according to milk intake levels at baseline (2007–2008).

Items	None ($n = 69,222$)	1–150 g/day ($n = 16,081$)	151–299 g/day ($n = 5672$)	≥300 g/day ($n = 782$)	Statistics	*P* value
Milk, g/day	0.00 ± 0.00	43.78 ± 37.32*	229.73 ± 26.10*	530.19 ± 334.17*	131006.00†	<0.001
Age, years	53.6 ± 11.8	49.3 ± 13.3*	53.0 ± 13.4*	53.4 ± 14.1	537.97†	<0.001
Male	26697 (38.57)	6477 (40.28)*	2440 (43.02)*	329 (42.07)*	54.02‡	<0.001
Urban	1567 (2.26)	1378 (8.57)*	1923 (33.90)*	250 (31.97)*	9772.99‡	<0.001
Northern	30501 (44.06)	9527 (59.24)*	3575 (63.03)*	466 (59.59)*	1580.71‡	<0.001
School education ≥12 years	5951 (8.61)	3124 (19.47)*	1996 (35.56)*	271 (34.97)*	4659.42‡	<0.001
Smokers	16771 (24.27)	4111 (25.68)*	1629 (28.82)*	237 (30.38)*	74.92‡	<0.001
Habitual drinkers	13470 (19.46)	2819 (17.53)*	1326 (23.42)*	186 (23.82)*	11.76‡	0.006
Physical active	21111 (30.50)	5892 (36.64)*	2832 (49.94)*	384 (49.10)*	1055.82‡	<0.001
Healthy diet	43459 (62.78)	10954 (68.12)*	3924 (69.18)*	568 (72.63)*	233.88‡	<0.001
BMI, kg/m^2	23.86 ± 3.76	23.76 ± 3.60*	23.92 ± 3.53	23.72 ± 3.49*	4.49†	0.004
SBP, mmHg	130.84 ± 21.66	128.03 ± 21.21*	130.24 ± 20.56	128.02 ± 19.51*	77.11†	<0.001
Fasting blood glucose, mmol/L	5.05 ± 1.49	5.16 ± 1.49*	5.36 ± 1.65*	5.59 ± 1.91*	112.82†	<0.001
Total cholesterol, mmol/L	4.50 ± 0.89	4.50 ± 0.91*	4.77 ± 0.97*	4.69 ± 0.94*	169.60†	<0.001
LDL-C, mmol/L	2.45 ± 0.73	2.48 ± 0.75*	2.70 ± 0.81*	2.61 ± 0.77*	194.83†	<0.001
HDL-C, mmol/L	1.34 ± 0.33	1.32 ± 0.33*	1.35 ± 0.33*	1.35 ± 0.34	22.56†	<0.001

Data were expressed as mean ± standard deviation or *n* (%). * Compared with participants who never drank milk, $P < 0.05$. † *F* value. ‡ χ^2 value. China-PAR: Prediction for Atherosclerotic Cardiovascular Disease Risk in China; BMI: Body mass index; SBP: Systolic blood pressure; LDL-C: Low-density lipoprotein-cholesterol; HDL-C: High-density lipoprotein-cholesterol.

more likely to be male ($\chi^2 = 54.02$, $P<0.001$), smokers ($\chi^2 = 74.92$, $P < 0.001$), urban ($\chi^2 = 9772.99$, $P < 0.001$) and northern residents ($\chi^2 = 1580.71$, $P < 0.001$), have longer years of education ($\chi^2 = 4659.42$, $P < 0.001$), healthy diet status ($\chi^2 = 233.88$, $P < 0.001$), and more physically active ($\chi^2 = 1055.82$, $P < 0.001$). And they also tended to have higher levels of fasting blood glucose ($F = 112.82$, $P < 0.001$), total cholesterol ($F = 169.60$, $P < 0.001$), and LDL-C ($F = 194.83$, $P < 0.001$) [Table 1, Supplementary Tables 1 and 2, http://links.lww.com/CM9/A213].

During the 561,677 person-years (a median of 5.8 years) of follow-up, we documented 3877 CVD events (including 945 CHD and 2427 stroke cases) and 4091 deaths.

Association of milk intake with CVD incidence

Compared with those who never drank milk, the HRs (95% CIs) for CVD incidence were 0.94 (0.86–1.03), 0.77 (0.66–0.89), and 0.59 (0.40–0.89) for those who consumed 1 to 150 g/day, 151 to 299 g/day, and ≥300 g/day of milk, respectively, after adjustment for age, sex, residential area, geographic region, education level, family history of CVD, smoking, alcohol drinking, physical activity level, BMI, and healthy diet status. The corresponding HRs (95% CIs) were 0.82 (0.68–0.98), 0.95 (0.74–1.22), and 0.58 (0.29–1.17) for CHD, and 1.02 (0.91–1.14), 0.78 (0.64–0.94), and 0.72 (0.44–1.17) for stroke, respectively. After further adjustment for blood pressure, blood glucose, and blood lipid levels, the associations were slightly attenuated, and the corresponding HRs (95% CIs) were 0.98 (0.89–1.07), 0.82 (0.71–0.96), and 0.65 (0.43–1.00) for CVD, while similar trends of HRs were shown as 0.85 (0.71–1.02), 1.01 (0.79–1.30), and 0.70 (0.34–1.41) for CHD, 1.05 (0.94–1.17), 0.83 (0.68–1.01), and 0.81 (0.49–1.33) for stroke, respectively. Each 100 g increase of daily intake was associated with 11% (95% CI: 6–15%) risk reduction for CVD ($P < 0.001$), and 9% (95% CI: 3–14%) risk reduction for stroke ($P = 0.006$) after adjustment for age, sex, residential area, geographic region, education level, family history of CVD, smoking, alcohol drinking, physical activity level, BMI, and healthy diet status. After further adjustment for cardiometabolic risk factors, these inverse associations were slightly attenuated but remained statistically significant for CVD incidence (HR, 0.92; 95% CI: 0.87–0.97; $P = 0.002$) and marginally significant for stroke (HR, 0.94; 95% CI: 0.88–1.00; $P = 0.069$). The associations of milk intake with IS or HS subtypes were similar, with HRs (95% CIs) associated with each 100 g/day increase of 0.91 (0.83–0.99) for IS and 0.86 (0.75–0.99) for HS, respectively (model 2) [Table 2]. RCS analyses also showed a linear dose-response relationship with CVD (*P* for overall significance of the curve <0.001; *P* for non-linearity = 0.979; *P* for linearity <0.001) and stroke (*P* for overall significance of the curve = 0.010; *P* for non-linearity = 0.998; *P* for linearity = 0.002) incidence within the current range of daily milk intake [Figure 2].

Association of milk intake with all-cause and cause-specific mortality

Similar inverse association with daily milk intake was also observed for CVD mortality with multivariate-adjusted HRs (95% CIs) of 1.00 (0.87–1.15), 0.81 (0.63–1.02), and 0.52 (0.26–1.04) for participants who consumed 1 to 150 g/day, 151 to 299 g/day, and ≥300 g/day of milk compared with those who never drank milk after adjustment for age, sex, residential area, geographic region, education level, family history of CVD, smoking, alcohol drinking, physical activity level, BMI, and healthy diet status; after further adjustment for cardiometabolic risk factors, the corresponding adjusted HRs (95% CIs) were 1.04 (0.90–1.21), 0.89 (0.70–1.14), and 0.63 (0.31–1.26), respectively. Each 100 g increase of daily intake was associated with 11% (95% CI: 3–18%) risk reduction for CVD mortality ($P = 0.008$) after adjustment for age, sex, residential area, geographic region, education level, family history of CVD, smoking, alcohol drinking,

Table 2: HRs (95% CI) of CVD incidence according to baseline milk intake in the China-PAR project.

Items	None ($n = 69,222$)	1–150 g/day ($n = 16,081$)	151–299 g/day ($n = 5672$)	≥300 g/day ($n = 782$)	HR per 100 g increase	*P* for trend
CVD						
No. of event, *n*/person-years	2989/40,1337	634/92,200	227/31,425	27/4346		
Adjusted incidence (95% CI), No. of event/100,000 person-year*	731 (687–777)	753 (685–828)	712 (610–830)	642 (428–963)		
Model 1	1.00 (Ref)	0.95 (0.86–1.03)	0.76 (0.66–0.89)†	0.59 (0.40–0.89)‡	0.89 (0.84–0.94)	<0.001
Model 2	1.00 (Ref)	0.94 (0.86–1.03)	0.77 (0.66–0.89)†	0.59 (0.40–0.89)‡	0.89 (0.85–0.94)	<0.001
Model 3	1.00 (Ref)	0.98 (0.89–1.07)	0.82 (0.71–0.96)‡	0.65 (0.43–1.00)	0.92 (0.87–0.97)	0.002
CHD						
No. of event, *n*/person-years	697/404,814	150/93,096	90/31,786	8/4394		
Adjusted incidence (95% CI), No. of event/100,000 person-year*	176 (156–200)	174 (143–211)	198 (152–259)	155 (68–353)		
Model 1	1.00 (Ref)	0.83 (0.69–0.99)‡	0.95 (0.75–1.22)	0.58 (0.29–1.18)	0.93 (0.85–1.02)	0.113
Model 2	1.00 (Ref)	0.82 (0.68–0.98)‡	0.95 (0.74–1.22)	0.58 (0.29–1.17)	0.93 (0.85–1.02)	0.104
Model 3	1.00 (Ref)	0.85 (0.71–1.02)	1.01 (0.79–1.30)	0.70 (0.34–1.41)	0.96 (0.88–1.05)	0.357
Stroke						
No. of event, *n*/person-years	1882/40,3072	406/92,624	122/31,694	17/4392		
Adjusted incidence (95% CI), No. of event/100,000 person-year*	453 (420–488)	481 (427–541)	435 (355–533)	432 (267–700)		
Model 1	1.00 (Ref)	1.02 (0.91–1.14)	0.77 (0.63–0.94)†	0.72 (0.44–1.16)	0.91 (0.85–0.97)	0.005
Model 2	1.00 (Ref)	1.02 (0.91–1.14)	0.78 (0.64–0.94)‡	0.72 (0.44–1.17)	0.91 (0.86–0.97)	0.006
Model 3	1.00 (Ref)	1.05 (0.94–1.17)	0.83 (0.68–1.01)	0.81 (0.49–1.33)	0.94 (0.88–1.00)	0.069
Ischemic stroke						
No. of event, *n*/person-years	1012/40,4121	215/92,884	76/31,760	8/4404		
Adjusted incidence (95% CI), No. of event/100,000 person-year*	243 (221–268)	252 (215–295)	271 (209–352)	169 (84–341)		
Model 1	1.00 (Ref)	0.98 (0.84–1.14)	0.88 (0.68–1.12)	0.60 (0.30–1.22)	0.91 (0.83–0.99)	0.035
Model 2	1.00 (Ref)	0.97 (0.84–1.13)	0.88 (0.69–1.13)	0.60 (0.30–1.22)	0.91 (0.83–0.99)	0.037
Model 3	1.00 (Ref)	0.99 (0.85–1.15)	0.91 (0.71–1.17)	0.61 (0.29–1.28)	0.92 (0.84–1.01)	0.083
Hemorrhagic stroke						
No. of event, *n*/person-years	521/405,167	114/93,188	25/31,916	4/4415		
Adjusted incidence (95% CI), No. of event/100,000 person-year*	124 (109–142)	135 (109–167)	94 (61–144)	106 (40–284)		
Model 1	1.00 (Ref)	1.04 (0.84–1.28)	0.58 (0.38–0.89)	0.68 (0.25–1.83)	0.86 (0.75–0.99)	0.034
Model 2	1.00 (Ref)	1.04 (0.85–1.29)	0.59 (0.38–0.90)	0.68 (0.25–1.84)	0.86 (0.75–0.99)	0.037
Model 3	1.00 (Ref)	1.13 (0.91–1.39)	0.68 (0.44–1.03)	0.89 (0.33–2.39)	0.92 (0.80–1.06)	0.235

* Adjusted for age and sex. † Compared with participants who never drank milk, $P < 0.05$. ‡ Compared with participants who never drank milk, $P < 0.01$. Model 1: Adjusted for baseline age, sex, geographic region (north/south), residential area (rural/urban), and education level (≥12 years or not). Model 2: Further adjusted for family history of CVD (yes or no), smoking (yes or no), drinking (yes or no), physical activity level, body mass index, and healthy diet status (ideal or not). Model 3: Further adjusted for systolic blood pressure, fasting blood glucose, total cholesterol, and high-density lipoprotein-cholesterol. HR: Hazard ratio; CI: Confidence interval; CVD: Cardiovascular disease; China-PAR: Prediction for Atherosclerotic Cardiovascular Disease Risk in China; CHD: Coronary heart disease.

physical activity level, BMI, and healthy diet status. After further adjustment for cardiometabolic risk factors, no significant association was observed between milk intake increase and CVD mortality (HR, 0.93; 95% CI: 0.86–1.01; $P = 0.092$) [Table 3]. The RCS analysis indicated a significant dose-response association (*P* for overall significance of the curve = 0.045; *P* for non-linearity = 0.768; *P* for linearity = 0.014) [Figure 3]. However, we did not identify the significant dose-response relationship between milk intake and all-cause mortality (*P* for overall significance of the curve = 0.341; *P* for non-linearity = 0.171; *P* for linearity = 0.599) [Table 3 and Figure 3].

Subgroup and sensitivity analyses

In the subgroup analyses, the inverse associations with CVD incidence, all-cause and cause-specific mortality were similar across strata [Supplementary Tables 3–5, http://links.lww.com/CM9/A213]. For example, the multivariable adjusted HRs (95% CIs) associated with each 100 g/day increase were 0.88 (0.81−0.95) and 0.90 (0.84−0.96) for CVD incidence among women and men, respectively (*P* for interaction = 0.878) [Supplementary Table 3, http://links.lww.com/CM9/A213]. In the sensitivity analyses, the multivariable adjusted HRs (95% CIs) associated with each 100 g/day increase after excluding the cases which occurred during the first 2 years were 0.87 (0.82–0.92) for CVD incidence, 0.89 (0.82–0.98) for CVD mortality and 0.97 (0.92–1.02) for all-cause mortality, respectively, and were similar to the original results [Supplementary Table 6, http://links.lww.com/CM9/A213]. Using competing risk models did not change the observed associations [Supplementary Table 7, http://links.lww.com/CM9/A213].

Discussion

Based on this prospective study involving 91,757 participants, we found higher milk intake would reduce the risk of CVD following an inverse linear relationship among general Chinese adults. Similar favorable effects were also observed for CVD mortality and stroke incidence. Our findings have great public health implications on guiding CVD prevention through lifestyle intervention.

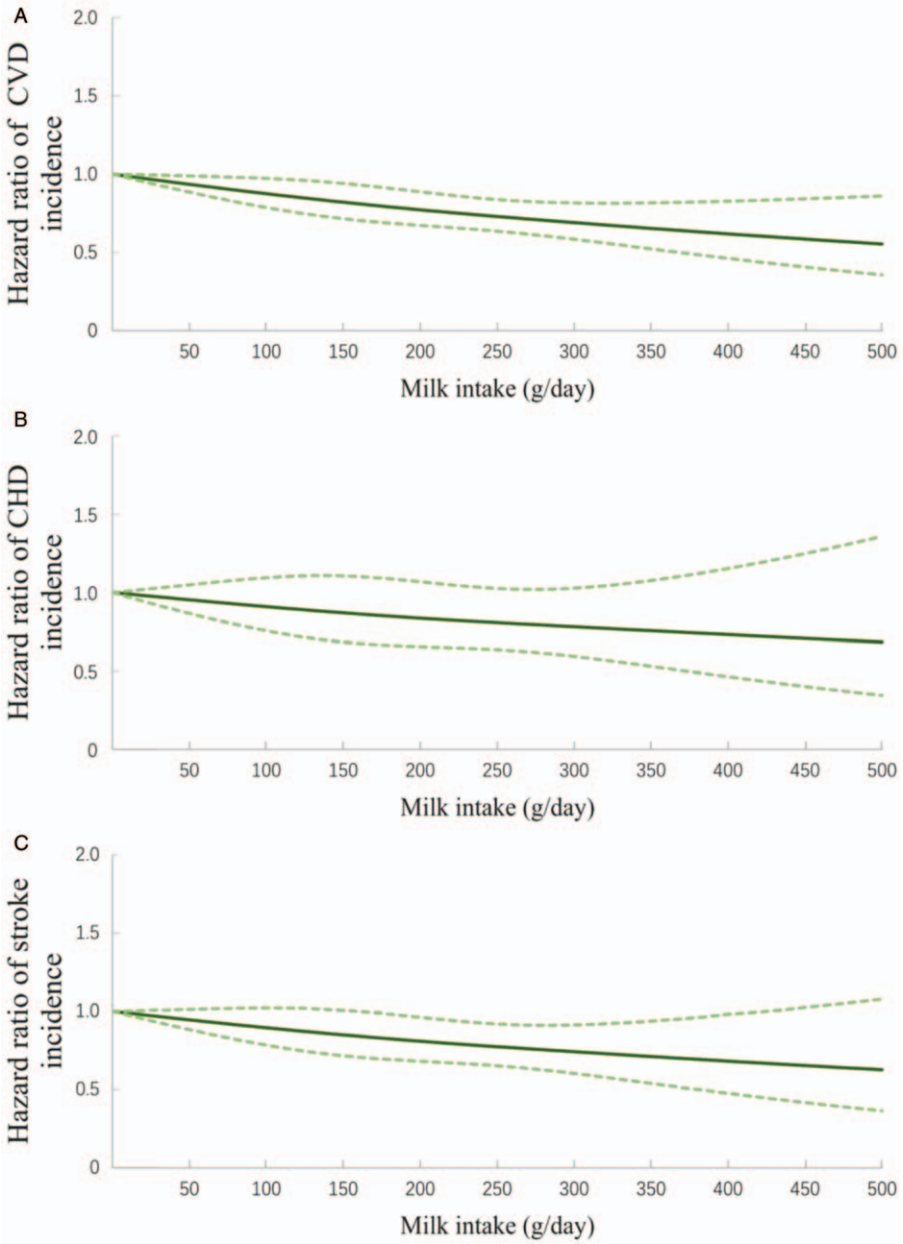

Figure 2: Dose-response associations of baseline milk intake with CVD incidence (A), CHD incidence (B) and stroke incidence (C) in the China-PAR project. The solid lines show the estimations of hazard ratios, and the dashed lines indicate 95% confidence intervals. Adjusted for baseline age, sex, geographic region (north/south), residential area (rural/urban), education level (≥12 years or not), family history of cardiovascular disease (yes or no), smoking (yes or no), alcohol drinking (yes or no), physical activity level (ideal or not), body mass index, and healthy diet status (ideal or not). CVD: Cardiovascular disease; CHD: Coronary heart disease; China-PAR: Prediction for Atherosclerotic Cardiovascular Disease Risk in China.

The associations between dairy intake and CVD have been widely studied in the western populations, with pooled results indicating inverse or null associations.[7-9,26-28] However, the results remained inconsistent. Findings from large cohorts in countries with high levels of dairy intake like the Netherlands and the United States indicated that milk intake would increase the risk of CVD.[29,30] On the contrary, previous studies in East Asian populations have consistently associated higher daily milk intake with lower risk of CVD, especially stroke.[13,14,31-36] In this study, we found that higher daily milk intake was inversely associated with the risks of CVD, CHD, and stroke, and CVD mortality in a population with plant food-based dietary and generally low intake level of dairy products. Of note, we observed statistically significant dose-response relationships between daily milk intake with CVD and stroke, and each 100 g/day increase of milk intake was associated with 11% lower risk of CVD, 9% lower risk of stroke, and 11% lower risk of CVD mortality. Similarly, a pooled analysis of 18 studies with 762,414 individuals and 29,943 stroke events reported that the risk of stroke decreased by 7% in the overall population, and 18% in the East Asian population with an increment of 200 g/day of milk intake.[10]

The potential protective effects of milk intake against CVD could be interpreted as follows. The content of high-quality protein, calcium, and potassium in milk could ameliorate a

Table 3: HRs (95% CI) of cause-specific mortality according to baseline milk intake in the China-PAR project.

Items	None ($n = 69,222$)	1–150 g/day ($n = 16,081$)	151–299 g/day ($n = 5672$)	≥300 g/day ($n = 782$)	HR per 100 g increase	*P* for trend
CVD mortality						
No. of event, *n*/person-years	1184/40,5697	241/93,300	82/31,946	8/4417		
Adjusted incidence (95% CI), No. of event/100,000 person-year*	731 (687–777)	753 (685–828)	712 (610–830)	642 (428–963)		
Model 1	1.00 (Ref)	1.00 (0.87–1.15)	0.79 (0.62–1.01)	0.52 (0.26–1.05)	0.89 (0.82–0.97)	0.007
Model 2	1.00 (Ref)	1.00 (0.87–1.15)	0.81 (0.63–1.02)	0.52 (0.26–1.04)	0.89 (0.82–0.97)	0.008
Model 3	1.00 (Ref)	1.04 (0.90–1.21)	0.89 (0.70–1.14)	0.63 (0.31–1.26)	0.93 (0.86–1.01)	0.092
CHD mortality						
No. of event, *n*/person-years	297/405,697	67/93,300	31/31,946	3/4417		
Adjusted incidence (95% CI), No. of event/100,000 person-year*	73 (60–90)	73 (54–99)	89 (59–136)	71 (22–232)		
Model 1	1.00 (Ref)	0.93 (0.71–1.23)	1.05 (0.70–1.56)	0.67 (0.21–2.11)	0.96 (0.84–1.11)	0.595
Model 2	1.00 (Ref)	0.92 (0.70–1.20)	1.05 (0.70–1.56)	0.65 (0.21–2.04)	0.96 (0.83–1.10)	0.435
Model 3	1.00 (Ref)	0.93 (0.71–1.23)	1.12 (0.75–1.66)	0.75 (0.24–2.36)	0.98 (0.85–1.13)	0.578
Stroke mortality						
No. of event, *n*/person-years	620/405,697	128/93,300	36/31,946	5/4417		
Adjusted incidence (95% CI), No. of event/100,000 person-year*	146 (125–171)	153 (122–191)	142 (99–204)	158 (65–384)		
Model 1	1.00 (Ref)	1.00 (0.82–1.22)	0.66 (0.46–0.94)†	0.64 (0.26–1.55)	0.86 (0.77–0.98)	0.019
Model 2	1.00 (Ref)	1.00 (0.82–1.22)	0.66 (0.46–0.95)†	0.63 (0.26–1.53)	0.87 (0.77–0.98)	0.092
Model 3	1.00 (Ref)	1.06 (0.87–1.29)	0.75 (0.53–1.07)	0.79 (0.32–1.91)	0.91 (0.81–1.03)	0.337
All-cause mortality						
No. of event, *n*/person-years	3218/405,697	614/93,300	217/31,946	42/4417		
Adjusted incidence (95% CI), No. of event/100,000 person-years*	754 (710–800)	792 (722–868)	774 (668–896)	1107 (813–1506)		
Model 1	1.00 (Ref)	1.03 (0.94–1.13)	0.90 (0.78–1.05)	1.16 (0.85–1.57)	0.99 (0.95–1.04)	0.755
Model 2	1.00 (Ref)	1.02 (0.94–1.12)	0.91 (0.78–1.05)	1.14 (0.84–1.56)	0.99 (0.95–1.04)	0.708
Model 3	1.00 (Ref)	1.03 (0.94–1.13)	0.91 (0.78–1.06)	1.14 (0.83–1.58)	0.99 (0.95–1.04)	0.767

* Adjusted for age and sex. † Compared with participants who never drank milk, $P < 0.05$. Model 1: Adjusted for baseline age, sex, geographic region (north/south), residential area (rural/urban), and education level (≥12 years or not). Model 2: Further adjusted for family history of CVD (yes or no), smoking (yes or no), drinking (yes or no), physical activity level (ideal or not), body mass index, and healthy diet status (ideal or not). (ideal or not) Model 3: Further adjusted for systolic blood pressure, fasting blood glucose, total cholesterol, and high-density lipoprotein-cholesterol. HR: Hazard ratio; CI: Confidence interval; China-PAR: Prediction for Atherosclerotic Cardiovascular Disease Risk in China; CVD: Cardiovascular disease; CHD: Coronary heart disease.

cluster of risk factors including dyslipidemia, insulin resistance, increased blood pressure, and abdominal obesity, which together markedly increase the risk of diabetes and CVD.[37] Secondly, saturated fat acids (SFAs) in milk were the main components to blame in some previous studies. However, based on the indigenous reality, the SFA content was much lower among the Chinese population than that among the western populations and the attendant risk of increasing intake of SFAs from moderate milk consumption would not be the uppermost concern.[15] In addition, some types of SFAs might also help increase the concentration of HDL-C, which could reverse the cholesterol transport pathways, inhibit LDL-C oxidation, and prevent inflammatory process.[38]

Milk intake was not associated with the risk of all-cause mortality in our study. While most previous observational studies found no associations between milk and all-cause mortality,[9,39,40] studies in the Sweden and the United States reported that non-fermented or whole milk would increase the risk of all-cause mortality.[30,41] By contrast, milk intake was found to be inversely associated with all-cause mortality in the United Kingdom and in Japan.[42,43] These inconsistencies in the associations of milk intake with health outcomes might due to the differences in the average intake levels and types of dairy products in different populations. The different lifestyle and dietary pattern, genetic backgrounds, and disease profiles might also influence the results.

To our knowledge, this study was the first to investigate the associations of milk intake with CVD incidence, all-cause and cause-specific mortality and to explore the potential dose-response relationships using prospective cohorts among the general Chinese population in the mainland of China. The reliability and credibility of the current results were guaranteed by the rigorous study design and

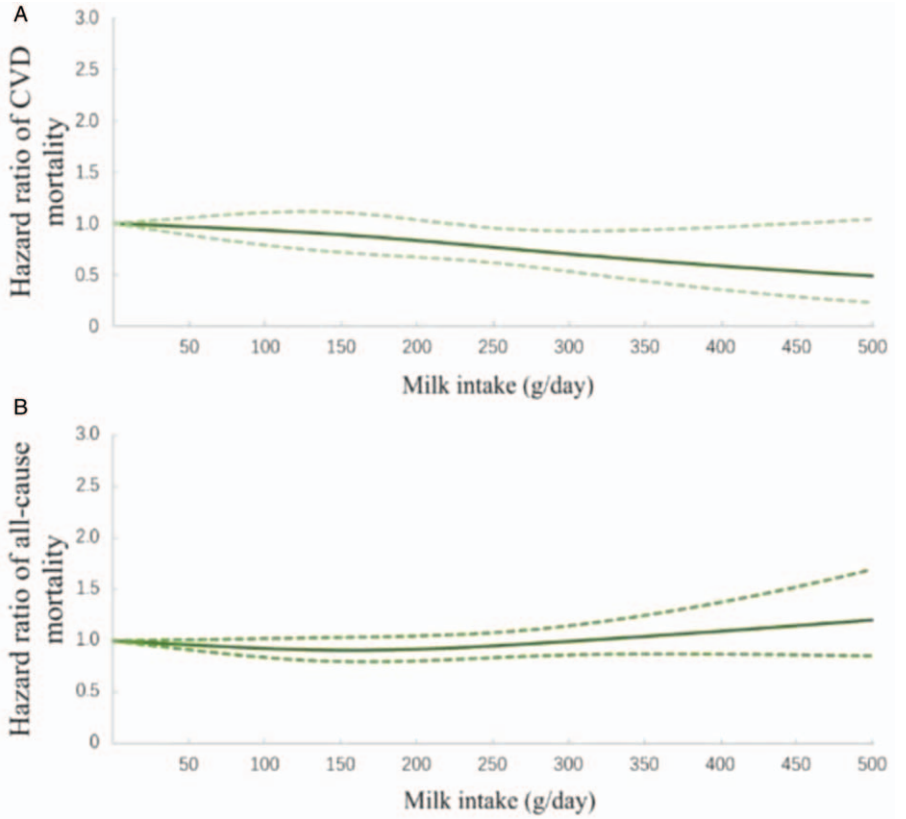

Figure 3: Dose-response associations of baseline milk intake with risks of CVD mortality (A) and all-cause mortality (B) in the China-PAR project. The solid lines show the estimations of hazard ratios, and the dashed lines indicate 95% confidence intervals. Adjusted for baseline age, sex, geographic region (north/south), residential area (rural/urban), education level (≥12 years or not), family history of cardiovascular disease (yes or no), smoking (yes or no), alcohol drinking (yes or no), physical activity level (ideal or not), body mass index, and healthy diet status (ideal or not). CVD: Cardiovascular disease; China-PAR: Prediction for Atherosclerotic Cardiovascular Disease Risk in China.

discipline, face-to-face interviews, trained and certificated staff, and standardized questionnaires. Nevertheless, several limitations should also be considered. Firstly, we did not collect information on fat contents or fermentation types. However, the majority of dairy intake in China was whole milk.[15] So the proportion of missing information would be limited and generally non-differential, and might not have had a large impact on the results. Secondly, information on total energy intake, and other dietary factors including salt and sugar was not collected. However, we adjusted the overall dietary pattern and physical activity level to reduce the influence. Thirdly, it was inevitable that some people with higher milk intake were prone to being well-educated, or engaged in other healthy lifestyle behaviors. However, adjustment of lifestyle factors only slightly attenuated the observed associations in the current study and the stratified results by residential areas, education levels or lifestyle factors did not show major differences or interactive effects. In addition, we only used milk intake information during 2007 to 2008, and the inevitable measurement error due to FFQ and the changes of milk intake over years would influence the results. And the limited number of incident cases of CHD, and limited number of participants within the highest intake category weaken the robustness of the results. With the ongoing follow-ups of the China-PAR population and increasing number of incident cases, we will validate the observed associations from the current study and explore the effects of changes in milk intake. We also call for other further studies to validate our findings.

In conclusion, our results showed that increase of daily milk intake was associated with lower risk of CVD incidence and mortality in a linear inverse relationship. These findings could support the renewal of lifestyle and dietary guidelines in China or populations with similar characteristics. Further studies are still warranted to validate our results.

Acknowledgements

The authors thank the staffs and participants of the China-PAR project for their important participation and contribution.

Funding

This study was supported by grants from the Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences (Nos. 2017-I2M-1-004, 2019-I2M-2-003), National Key R&D Program of China (Nos. 2017YFC0211700 and 2018YFE0115300), and the National Natural Science Foundation of China (No. 91643208).

Conflicts of interest

None.

References

1. GBD Compare Data Visualization. Washington: Institute for Health Metrics and Evaluation, 2019. Available from: https://vizhub.healthdata.org/gbd-compare/. [Accessed December 25, 2019]
2. Chen WW, Gao RL, Liu LS, Zhu ML, Wang W, Wang YJ, *et al*. China cardiovascular diseases report 2015: a summary. J Geriatr Cardiol 2017;14:1–10. doi: 10.11909/j.issn.1671-5411.2017.01.012.
3. Mozaffarian D, Wu JHY. Flavonoids, dairy foods, and cardiovascular and metabolic health: a review of emerging biologic pathways. Circ Res 2018;122:369–384. doi: 10.1161/CIRCRESAHA.117.309008.
4. Dietary Guidelines for Americans 2015–2020. Washington: US Department of Health and Human Services and US Department of Agriculture, 2006. Available from: https://health.gov/dietaryguidelines/2015/. [Accessed December 25, 2019]
5. The Eatwell Guide. London: Public Health England, 2016. Available from: https://www.gov.uk/government/publications/the-eatwell-guide. [Accessed December 25, 2019]
6. The Chinese Nutrition Society. Dietary Guidelines for Chinese Residents (2016). Beijing: People's Medical Publishing House Co., Ltd, 2016.
7. Fontecha J, Calvo MV, Juarez M, Gil A, Martínez-Vizcaino V. Milk and dairy product consumption and cardiovascular diseases: an overview of systematic reviews and meta-analyses. Adv Nutr 2019;10(suppl_2):S164–S189. doi: 10.1093/advances/nmy099.
8. Guo J, Astrup A, Lovegrove JA, Gijsbers L, Givens DI, Soedamah-Muthu SS. Milk and dairy consumption and risk of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. Eur J Epidemiol 2017;32:269–287. doi: 10.1007/s10654-017-0243-1.
9. Soedamah-Muthu SS, Ding EL, Al-Delaimy WK, Hu FB, Engberink MF, Willett WC, *et al*. Milk and dairy consumption and incidence of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. Am J Clin Nutr 2011;93:158–171. doi: 10.3945/ajcn.2010.29866.
10. de Goede J, Soedamah-Muthu SS, Pan A, Gijsbers L, Geleijnse JM. Dairy consumption and risk of stroke: a systematic review and updated dose-response meta-analysis of prospective cohort studies. J Am Heart Assoc 2016;5.pii: e002787. doi: 10.1161/JAHA.115.002787.
11. Gu JF. 2015 report on Chinese resident's chronic disease and nutrition. Acta Nutrimenta Sinica 2016;38:525–529. doi: 10.13325/j.cnki.acta.nutr.sin.2016.06.004.
12. Milk Imports Into China Will Continue To Grow In 2017. Switzerland: Agrochart, 2017. Available from: https://www.agrochart.com/uk/news/5928/milk-imports-into-china-will-continue-to-grow-in-2017.html. [Accessed January 12, 2020].
13. Lin PH, Yeh WT, Svetkey LP, Chuang SY, Chang YC, Wang C, *et al*. Dietary intakes consistent with the DASH dietary pattern reduce blood pressure increase with age and risk for stroke in a Chinese population. Asia Pac J Clin Nutr 2013;22:482–491. doi: 10.6133/apjcn.2013.22.3.05.
14. Huang LY, Wahlqvist ML, Huang YC, Lee MS. Optimal dairy intake is predicated on total, cardiovascular, and stroke mortalities in a Taiwanese cohort. J Am Coll Nutr 2014;33:426–436. doi: 10.1080/07315724.2013.875328.
15. Dehghan M, Mente A, Rangarajan S, Sheridan P, Mohan V, Iqbal R, *et al*. Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. Lancet 2018;392:2288–2297. doi: 10.1016/S0140-6736(18)31812-9.
16. Yang X, Li J, Hu D, Chen J, Li Y, Huang J, *et al*. Predicting the 10-year risks of atherosclerotic cardiovascular disease in Chinese population: The China-PAR Project (Prediction for ASCVD Risk in China). Circulation 2016;134:1430–1440. doi: 10.1161/CIRCULATIONAHA.116.022367.
17. Wu Y. Current status of major cardiovascular risk factors in Chinese populations and their trends in the past two decades (in Chinese). Chin J Cardiol 2001;29:74–79. doi: 10.3760/j:issn:0253-3758.2001.02.004.
18. He J, Neal B, Gu D, Suriyawongpaisal P, Xin X, Reynolds R, *et al*. International collaborative study of cardiovascular disease in Asia: design, rationale, and preliminary results. Ethn Dis 2004;14:260–268.
19. Global Recommendations on Physical Activity for Health. Geneva: World Health Organization, 2010. Available from: https://www.who.int/dietphysicalactivity/factsheet_recommendations/en/. [Accessed December 25, 2019].
20. Han C, Liu F, Yang X, Chen J, Li J, Cao J, *et al*. Ideal cardiovascular health and incidence of atherosclerotic cardiovascular disease among Chinese adults: the China-PAR project. Sci China Life Sci 2018;61:504–514. doi: 10.1007/s11427-018-9281-6.
21. Wang X, Yang X, Li J, Liu F, Chen J, Liu X, *et al*. Impact of healthy lifestyles on cancer risk in the Chinese population. Cancer 2019;125:2099–2106. doi: 10.1002/cncr.31971.
22. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined–a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000;36:959–969. doi: 10.1016/s0735-1097(00)00804-4.
23. Bronner LL, Kanter DS, Manson JE. Primary prevention of stroke. N Engl J Med 1995;333:1392–1400. doi: 10.1056/nejm199511233332106.
24. Zhao D, Anderson N. Poisson regression adjustment of event rates and its macro procedure ADJ_POIS. Available from: https://www.lexjansen.com/cgi-bin/saspapers_xml.php?x=sugi24&c=sugi2. [Accessed December 20, 2020]
25. Schoenfeld D. Partial residuals for the proportional hazards regression model. Biometrika 1982;69:239–241. doi: 10.1093/biomet/69.1.239.
26. Larsson SC, Crippa A, Orsini N, Wolk A, Michaëlsson K. Milk consumption and mortality from all causes, cardiovascular disease, and cancer: a systematic review and meta-analysis. Nutrients 2015;7:7749–7763. doi: 10.3390/nu7095363.
27. Alexander DD, Bylsma LC, Vargas AJ, Cohen SS, Doucette A, Mohamed M, *et al*. Dairy consumption and CVD: a systematic review and meta-analysis. Br J Nutr 2016;115:737–750. doi: 10.1017/S0007114515005000.
28. Elwood PC, Pickering JE, Givens DI, Gallacher JE. The consumption of milk and dairy foods and the incidence of vascular disease and diabetes: an overview of the evidence. Lipids 2010;45:925–939. doi: 10.1007/s11745-010-3412-5.
29. Goldbohm RA, Chorus AM, Galindo Garre F, Schouten LJ, van den Brandt PA. Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in The Netherlands. Am J Clin Nutr 2011;93:615–627. doi: 10.3945/ajcn.110.000430.
30. Ding M, Li J, Qi L, Ellervik C, Zhang X, Manson JE, *et al*. Associations of dairy intake with risk of mortality in women and men: three prospective cohort studies. BMJ 2019;367:l6204. doi: 10.1136/bmj.l6204.
31. Umesawa M, Iso H, Ishihara J, Saito I, Kokubo Y, Inoue M, *et al*. Dietary calcium intake and risks of stroke, its subtypes, and coronary heart disease in Japanese: the JPHC Study Cohort I. Stroke 2008;39:2449–2456. doi: 10.1161/STROKEAHA.107.512236.
32. Kondo I, Ojima T, Nakamura M, Hayasaka S, Hozawa A, Saitoh S, *et al*. Consumption of dairy products and death from cardiovascular disease in the Japanese general population: the NIPPON DATA80. J Epidemiol 2013;23:47–54. doi: 10.2188/jea.je20120054.
33. Ozawa M, Yoshida D, Hata J, Ohara T, Mukai N, Shibata M, *et al*. Dietary protein intake and stroke risk in a general Japanese population: the Hisayama study. Stroke 2017;48:1478–1486. doi: 10.1161/STROKEAHA.116.016059.
34. Eguchi E, Iso H, Tanabe N, Wada Y, Yatsuya H, Kikuchi S, *et al*. Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study. Eur Heart J 2012;33:467–477. doi: 10.1093/eurheartj/ehr429.
35. Sauvaget C, Nagano J, Allen N, Grant EJ, Beral V. Intake of animal products and stroke mortality in the Hiroshima/Nagasaki life span study. Int J Epidemiol 2003;32:536–543. doi: 10.1093/ije/dyg151.
36. Talaei M, Koh WP, Yuan JM, Pan A. The association between dairy product intake and cardiovascular disease mortality in Chinese adults. Eur J Nutr 2017;56:2343–2352. doi: 10.1007/s00394-016-1274-1.
37. Astrup A. Yogurt and dairy product consumption to prevent cardiometabolic diseases: epidemiologic and experimental studies.

Am J Clin Nutr 2014;99:1235S–1242S. doi: 10.3945/ajcn.113.073015.
38. Samara A, Herbeth B, Ndiaye NC, Fumeron F, Billod S, Siest G, *et al*. Dairy product consumption, calcium intakes, and metabolic syndrome-related factors over 5 years in the STANISLAS study. Nutrition 2013;29:519–524. doi: 10.1016/j.nut.2012.08.013.
39. Mullie P, Pizot C, Autier P. Daily milk consumption and all-cause mortality, coronary heart disease and stroke: a systematic review and meta-analysis of observational cohort studies. BMC Public Health 2016;16:1236. doi: 10.1186/s12889-016-3889-9.
40. Pala V, Sieri S, Chiodini P, Masala G, Palli D, Mattiello A, *et al*. Associations of dairy product consumption with mortality in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Italy cohort. Am J Clin Nutr 2019;110:1220–1230. doi: 10.1093/ajcn/nqz183.
41. Tognon G, Nilsson LM, Shungin D, Lissner L, Jansson JH, Renström F, *et al*. Nonfermented milk and other dairy products: associations with all-cause mortality. Am J Clin Nutr 2017;105:1502–1511. doi: 10.3945/ajcn.116.140798.
42. Wang C, Yatsuya H, Tamakoshi K, Iso H, Tamakoshi A. Milk drinking and mortality: findings from the Japan collaborative cohort study. J Epidemiol 2015;25:66–73. doi: 10.2188/jea.JE20140081.
43. Stasinopoulos LC, Zhou A, Hyppönen E. Association of supplemental calcium and dairy milk intake with all-cause and cause-specific mortality in the UK Biobank: a prospective cohort study. Br J Nutr 2020;123:574–582. doi: 10.1017/S0007114519003076.

How to cite this article: Wang XY, Liu FC, Yang XL, Li JX, Cao J, Lu XF, Huang JF, Li Y, Chen JC, Zhao LC, Shen C, Hu DS, Zhao YX, Yu L, Liu XQ, Wu XP, Gu DF. Association of cardiovascular diseases with milk intake among general Chinese adults. Chin Med J 2020;133:1144–1154. doi: 10.1097/CM9.0000000000000786