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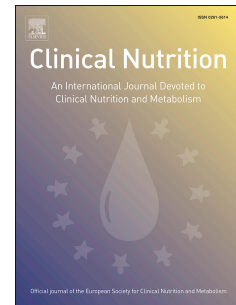
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**Milk consumption and risk of mortality from all-cause, cardiovascular disease  
and cancer in older people**

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## ABSTRACT

**Background:** Milk as a common diet is recommended by many guidelines, but the results on the association of milk consumption with the risk of cardiovascular disease (CVD) or cancer were contradictory. Moreover, evidence regarding milk consumption and mortality risk in Chinese is scarce.

**Objective:** We examined the associations of milk consumption with the risk of all-cause, CVD and cancer mortality in a low milk consumption population using data from the Guangzhou Biobank Cohort Study.

**Design:** 18,214 participants aged 50+ years without CVD history at baseline (2003-6) were included. Causes of death were identified through record linkage. Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

**Results:** Of the 18,214 participants, 12,670 (69.6%) did not consume milk, 2,669 (14.7%) had moderate (1-3 portions/week; 1 portion=250 ml) and 2,875 (15.8%) had high (3+ portions/week) consumption. During an average follow-up of 11.5 (standard deviation=2.3) years, 2,697 deaths occurred, including 917 CVD and 1,029 cancer deaths. Compared with no consumption, the adjusted HR (95% CIs) of all-cause, CVD, ischemic heart disease (IHD) and stroke mortality for moderate milk consumption was 0.92 (0.81-1.04), 0.72 (0.57-0.92), 0.57 (0.38-0.85) and 0.77 (0.63-0.94), respectively. High consumption was associated with a higher risk of total cancer and esophagus cancer mortality, with the adjusted HR (95% CIs) being 1.33

(1.12-1.57) and 3.20 (1.21-8.43) respectively. No significant association of high consumption with lung cancer, liver cancer, gastrointestinal cancer, or colorectal and anal cancer was found.

**Conclusions:** In our sample of Chinese with much lower milk consumption than those in the West, compared with no consumption, moderate milk consumption showed a lower risk of CVD mortality, but high milk consumption showed a higher risk of total cancer mortality. Further studies are warranted to verify the differential effects of milk on CVD and cancer.

**Key Words:** Milk consumption, cardiovascular disease, cancer, ischemic heart disease, stroke, mortality

## Introduction

More than half of the deaths annually in the world are due to cardiovascular disease (CVD) and cancer [1, 2]. Nearly 70% CVD and cancer deaths occur in low- and middle-income countries[1, 2], and they account for more than 65% of deaths in China [3]. Milk as a common diet is recommended by many dietary guidelines and consumed across all ages in the world [4-8]. However, the magnitude of the associations between milk consumption and risks of all-cause, CVD and cancer mortality varied by populations, and within one population, varied across different studies. The results on the association of milk consumption with the risk of CVD or cancer were contradictory [9-19]. As for CVD, some reported positive associations [10, 14, 15, 19], some reporting negative [11-13, 18], and some no association [9, 16, 17]. And for cancer, the results were also mixed, with two studies showing no association [11, 14], two showing positive [15, 19] and another showing negative association [18]. Most of the previous studies were from the West, where dairy products are widely available and consumed. We found only four studies from Asia [11, 12, 17, 18], and three of them showing a negative association of milk consumption and CVD mortality [11, 12, 18]. These discrepancies were notably due to differences in exposure level and genetic factors associated with milk consumption. For example, the prevalence of lactose intolerance is different in different ethnic populations, varying from less than 10% in northern Europe to as high as 50% in Asia [20]. The symptoms from lactose intolerance may lead to low milk intake. In addition,

although milk and dairy products are important foods and ingredients for many western foods in high-income countries, they are relatively expensive and much less frequently used in Chinese dishes or meals in other low- and middle-income countries.

The 2016 Chinese Dietary Guidelines recommend daily intake of a variety of dairy products, equivalent to 300 grams of liquid milk [6]. However, only less than 2% of older Chinese reached the recommended level [21]. In populations with low milk consumption, it is unclear whether milk consumption is associated with the risk of all-cause, CVD and cancer mortality. Moreover, it is unclear whether there is an optimal level of milk intake associated with a lower risk of mortality. Therefore, we conducted a prospective cohort study, using data from the Guangzhou Biobank Cohort Study (GBCS) to examine the associations of milk consumption with the risk of all-cause, CVD and cancer mortality in a low milk consumption population.

## **Subjects and methods**

### **Study design and participants**

The Guangzhou Biobank Cohort Study (GBCS) is an on-going population-based cohort study [22]. Briefly, all participants were recruited from a community social and welfare association, the Guangzhou Health and Happiness Association for the Respectable Elders (GHHARE) from 2003-2008. GHHARE is a large unofficial



organization with ten branches throughout all districts of Guangzhou. Membership of this association is open to Guangzhou residents aged 50 years or older for a nominal, monthly fee of four CNY ( $\approx$ 50 US cents). Baseline information was collected using face-to-face computer-assisted interview by trained nurses. Measures of anthropometry, blood pressure, fasting plasma glucose, lipids and inflammatory markers were performed following standard protocols. Reliability and validity of the questionnaire were tested 6 months into recruitment by recalling 200 randomly selected participants for re-interview, and the results were satisfactory [22]. Ethics approval was granted by the Guangzhou Medical Ethics Committee of the Chinese Medical Association, Guangzhou, China. Participants from phase 3 (2006-2008) were not included in this study as the Food Frequency Questionnaire (FFQ) was changed.

## **Exposures**

All participants reported their average frequency of consumption of 282 types of foods and beverages during the past week. The number of portions consumed per week was asked for each dairy product including milk, skim milk and chocolate milk. One portion of milk corresponded to a glass of 250 milliliters. Milk consumption was summed into a single measure of total milk consumption on a continuous scale. Milk consumption was also categorized into 3 groups, i.e., no consumption, moderate consumption (1-3 portions/week) and high consumption (3+ portions/week), based on the frequency of consumption and the usual amount per occasion. We excluded

participants with milk consumption > 45 portions/week, which equals to about 1.6 liters per day, as such amount was implausible in older people. Details of the measurement methods were reported elsewhere [23].

## Outcomes

For the prospective analyses, the primary outcomes were all-cause, CVD and cancer mortality, and the secondary outcomes were ischemic heart disease (IHD), stroke mortality and top five cause-specific cancer deaths. We also conducted cross-sectional analyses to explore the possible mechanisms using baseline data of CVD risk factors including systolic and diastolic blood pressure (SBP), diastolic blood pressure (DBP), lipids (low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglycerides and total cholesterol), fasting glucose, body mass index (BMI) and waist circumference.

Information on causes of death up to December 31, 2017 was mostly obtained via record linkage with the Guangzhou Center for Disease Control and Prevention (GCDC). Causes of death were coded according to the 10th Revisions of the International Classification of Diseases (ICD-10) by trained clinical coding officers in each hospital (Supplementary Tables 1). For death certificates that were not issued by medical institutions, the causes of death were verified by GCDC as part of their quality assurance programmed by cross-checking past medical histories and

conducting verbal autopsies. From 2015 to 2018, eleven verbal autopsy meetings were also conducted in the Guangzhou 12th Hospital to clarify the deaths with unclear causes.

#### **Potential confounders**

As both the dietary pattern and mortality risk may be influenced by sex, age, social-economic position (family income, education, occupation), lifestyle factors (smoking status, alcohol use and physical activity), BMI, self-rated health status and chronic disease history (diabetes, hypertension and hyperlipidemia), these factors were considered potential confounders and included in the regression model. To further examine whether milk consumption within different dietary patterns altered the associations of milk consumption with all-cause, CVD and cancer mortality, we included scores of three dietary patterns in separate regression models, i.e., alternate Mediterranean diet (aMED) [24], Dietary Approaches to Stop Hypertension (DASH) [25] and the alternate Healthy Eating Index 2010 (aHEI-2010) [26]. Detailed information on scoring standards for each component of the aMED, DASH and aHEI-2010, and the correlations between milk consumption and these scores are shown in the Supplementary Tables 2 and 3.

#### **Statistical analysis**

Chi-square tests were used to compare baseline categorical variables by milk

consumption, and one-way analysis of variance (ANOVA) and Kruskal-Wallis rank sum test for continuous variables. Generalized linear modeling was used to assess the associations of milk consumption with CVD risk factors at baseline giving regression coefficients ( $\beta$ s) and 95% confidence intervals (CIs). Cox proportional hazard regression was used to assess the associations of milk consumption with risk of all-cause, CVD and cancer mortality. Schoenfeld's residuals were used to assess the proportional hazard assumption. If the proportional hazard assumption was violated, Cox regression with time varying covariate was used to estimate hazard ratios (HRs) with 95% CIs for categories of milk consumption. Model 1 was a crude model without any adjustment and Model 2 was adjusted for sex, age, SEP (family income, education and occupation), lifestyle factors (smoking status, alcohol use and physical activity), BMI, self-rated health and chronic disease history (diabetes, hypertension and hyperlipidemia). Model 3 was additionally adjusted for daily dietary energy intake and plus each of the three dietary patterns: aMED, DASH and aHEI-2010 separately. All potential confounders were categorized as in Table 1. In addition, we assessed the potential non-linear association between milk consumption and mortality using restricted cubic spline regression.

In sensitivity analyses, we excluded deaths occurring within the first 2 years of follow-up to reduce the influence from reverse causality. We also excluded participants with history of cancer at baseline to examine the association of milk

intake and cancer mortality. Log likelihood ratio test was used to assess the model fitness comparing models with and without interaction terms between milk consumption and some potential effect modifiers such as sex, age, education, lifestyle factors (smoking status, alcohol use and physical activity), BMI, self-rated health status, chronic disease history (diabetes, hypertension and hyperlipidemia) and dietary quality (aHEI-2010). For significant interaction terms, we conducted subgroup analyses stratifying by the effect modifiers. Moreover, to examine whether the results would be different if different methods of categorizing milk consumption were used, we categorized milk consumption into four (0, 1-3, 4-6, 7+ portions/week) and five groups (0, 1-2, 3-4, 5-6, 7+ portions/week) respectively in sensitivity analyses. We also examined the association of all dairy products with all-cause, cardiovascular disease and cancer mortality, despite other subtypes of dairy products such as cheese, yogurt, cream and butter were rarely consumed in our population. All statistical analyses were done using Stata version 15.0 (STATA Corp LP). All tests were two-sided with  $P < 0.05$  as statistically significant.

## Results

In 20,548 participants, after excluding individuals with duplicate information (N=88) and missing information on energy intake (N=38), self-reported history of CVD at baseline (N=1,825), nonsensical milk consumption ( $> 45$  portions/week; N=1), and loss to follow-up for vital status (N=382), 18,214 individuals with information of milk

consumption were included in the main analysis (Supplemental Figure 1). Of the 18,214 participants, 12,670 (69.6%) did not consume milk (no consumption), 2,669 (14.7%) consumed 1-3 portions/week (moderate consumption; 1 portion=250 ml) and 2,875 (15.8%) consumed 3+ portions/week (high consumption) including 2,020 (11.1%) who consumed 7+ portions/week. During an average follow-up of 11.5 (SD=2.3) years with 222,120 person-years, 2,697 deaths occurred, including 917 CVD (384 IHD and 374 stroke) and 1029 cancer deaths.

Table 1 shows that, compared with no consumption, participants who consumed milk were younger, with BMI in the normal range (18.6-22.9), had more never smokers, less manual workers, higher education and family income (all  $P < 0.01$ ). Milk consumption was also associated with higher intake of fruits, nuts, eggs, total energy, carbohydrate, protein, fat, saturated fat, monounsaturated fat, polyunsaturated fat and cholesterol (all  $P < 0.001$ ). There was no association with alcohol use, self-rated health or hypertension ( $P > 0.05$ ), while more hyperlipidemia was found in those with moderate milk consumption ( $P < 0.01$ ). Participants with moderate milk consumption also had lowest prevalence of diabetes, intake of vegetables and scores of three dietary patterns ( $P < 0.001$ ).

Table 2 shows that in Model 3, after adjusting for 15 potential confounders as above, higher milk consumption was negatively associated with SBP, DBP, triglycerides,

fasting glucose, BMI and waist circumference, but positively associated with LDL-cholesterol, HDL-cholesterol and total cholesterol (all P for trend < 0.05).

Figure 1 shows that after adjusting for potential confounders in Model 3 plus aHEI-2010 score, compared with no consumption, the HRs (95% CIs) of all-cause, CVD, IHD, and stroke mortality for moderate milk consumption were 0.92 (0.81-1.04), 0.72 (0.57-0.92), 0.57 (0.38-0.85) and 0.77 (0.63-0.94), respectively. High consumption was associated with a higher risk of total cancer and esophagus cancer mortality, with the adjusted HRs (95% CIs) being 1.33 (1.12-1.57) and 3.20 (1.21-8.43) respectively. No significant association of high consumption with lung cancer, liver cancer, gastrointestinal cancer, or colorectal and anal cancer was found, and the adjusted HRs (95% CIs) were 1.08 (0.79-1.48), 1.18 (0.72-1.93), 1.42 (0.72-2.78), and 1.15 (0.71-1.88), respectively. The associations were consistent in different models with different sets of potential confounding factors (Supplementary Tables 4 to 6). The results were similar after excluding 146 deaths within the first 2 years of follow-up (Supplementary Table 4).

Figure 2 shows that, in the full adjustment model (Model 3 plus aHEI-2010 score), increasing milk consumption (from 0 to 10+ portions/week) did not significantly increase the risk of all-cause mortality, even up to 10+ portions/week. Milk consumption of 2-6 portions/week was significantly associated with a lower risk of

CVD and stroke mortality. Results from the restricted cubic spline regression did not support the non-linearity assumptions between milk consumption and risk of CVD and stroke mortality (both P value for non-linearity  $> 0.05$ ). However, the association of milk consumption with IHD mortality tended to be non-linear (P value for non-linearity = 0.03), with the nadir at about 2 portions/week. Moreover, linear associations of milk consumption and risk of total cancer and esophagus cancer mortality were found, with P values for linearity from  $<0.01$  to 0.03 and P values for non-linearity from 0.91 to 0.97.

Table 3 shows that the association of milk consumption with CVD mortality did not vary by sex, education, lifestyle factors (smoking status, alcohol use and physical activity), BMI, self-rated health status, chronic disease history (diabetes, hypertension and hyperlipidemia) or dietary quality (aHEI-2010) in the full adjustment model (P values for interaction from 0.11 to 0.80). However, the inverse association was more pronounced in participants younger than 65 years (P for interaction  $< 0.01$ ), and the adjusted HR (95% CIs) for milk consumption of 1-3 portions/week and 3+ portions/week was 0.52 (0.22-0.84) and 0.46 (0.27-0.77) respectively.

The association of milk consumption with all-cause mortality did not vary by most of the risk factors except for aHEI-2010 score. The adjusted HR (95% CIs) for moderate milk consumption was 0.85 (0.71-1.01) in those with a lower aHEI-2010 score and



1.05 (0.86-1.28) in those with a higher aHEI-2010 score (P value for interaction < 0.01) (Supplementary Table 7). The associations of milk consumption with cancer mortality did not vary by the selected factors (all P values for interaction > 0.05) (Supplementary Table 8). Sensitivity analyses showed similar associations of milk consumption with IHD mortality across different subgroups (Supplementary Table 9). However, the inverse association with stroke mortality was more pronounced in participants younger than 65 years (P for interaction < 0.01) and with lower education (P for interaction = 0.03). In participants younger than 65, the adjusted HR (95% CIs) for moderate and high milk consumption was 0.48 (0.22-1.06) and 0.21 (0.06-0.66), respectively. The adjusted HR (95% CIs) for moderate milk consumption was 0.52 (0.29-0.94) in participants with lower education and 0.74 (0.44-1.26) in those with higher education (Supplementary Table 10). Sensitivity analyses using different categorical cut-off points for milk consumption and excluding 146 deaths within the first 2 years of follow-up showed similar results (Supplementary Tables 11 to 12). The association between milk intake and cancer mortality after excluding participants with history of cancer at baseline were similar (Supplementary Table 13). Results on the association of all dairy products with all-cause, cardiovascular disease and cancer mortality were similar (Supplementary Table 14).

## Discussion

In this large cohort of older Chinese with an average follow-up of 11.5 years, we

found that moderate milk consumption (1-3 portions/week; 1 portion=250 ml) versus no consumption was associated with 28% lower risk of CVD mortality, 43% lower risk of IHD mortality and 23% lower risk of stroke mortality. However, those with high milk consumption (3+ portions/week) had 33% higher risk of total cancer mortality and about three-fold higher risk of esophagus cancer mortality. No significant association between moderate milk consumption and all-cause mortality was found. Our findings support potential benefits of milk consumption on CVD mortality. However, the potential detrimental effect on cancer mortality warrants attention and further investigation.

We found that baseline milk consumption was cross-sectionally associated with lower systolic and diastolic blood pressure but higher total cholesterol, which was consistent with a prospective cohort study with 22.8-year follow-up showing that individuals with higher milk intake (>586 ml/day) had lower SBP than those who did not consume milk [27]. We also found that higher milk consumption was associated with lower triglycerides, which was supported by the existing evidence from randomized controlled trials [28, 29]. These results indicate that milk consumption may be beneficial for cardiovascular health. However, results of previous studies on the association between milk consumption and CVD mortality were inconsistent, with some studies from western populations showing a positive or null association [10, 14, 15, 19], while studies in Asia with lower consumption than those in the West tended

to show an inverse association [11, 12, 18]. A meta-analysis found the same difference on the association between milk consumption and fatal stroke, with the pooled RR for low-to-moderate (38 g/day) versus high (266 g/day) daily consumption being 0.82 (95% CI 0.75 to 0.90) in East Asian populations and 0.98 (95% CI 0.95 to 1.01) in western populations [30]. In Chinese, a Singapore study showed that higher dairy product (median intake 193 g/d) intake was associated with a lower risk of stroke mortality, and the association was more pronounced in men (HR 0.71, 95% CI 0.55 to 0.92) [17]. Our findings further support the inverse association of moderate milk consumption with stroke mortality (HR 0.77, 95% CI 0.63 to 0.93) in the East where milk and dairy product consumption was much lower.

Previous prospective studies on the association of milk intake with cancer also showed mixed results [11, 14, 15, 18, 19]. Two of them found no association [11, 14], probably due to small sample size (N=2,275) [11] or short follow-up duration (mean 6.3 years) [14]. The study from Sweden showed that higher intake (>600 g/day) was associated with a higher risk for cancer mortality in women only (HR 1.07, 95% CI 1.02 to 1.11), but the reference group with <200 g/day milk intake would be classified to high intake according to our study [15]. A recent study from the US also showed that individuals with higher ( $\geq 480$  ml/week) versus lower milk intake (<240 ml/month) had a higher risk of cancer mortality, with HR being 1.13 (95% CI 1.07 to 1.19) [19]. However, another study from Japan found a lower risk for cancer mortality in men for

milk intake of 3-4 times/week versus never (HR 0.85, 95% CI 0.76 to 0.94) [18]. A meta-analysis of case-control studies found non-significant association between milk intake and esophagus cancer (pooled OR 0.93, 95% CI 0.74 to 1.16), but significant heterogeneity among studies was observed ( $I^2=52.9\%$ ) [31]. However, an additional case-control study in the eastern Nebraska showed that a “high milk” dietary pattern was associated with a 2.5-fold risk of esophageal cancer [32]. A meta-analysis of ten cohort studies showed an inverse association between milk intake and colorectal cancer (pooled RR 0.83, 95% CI 0.74–0.93) with low heterogeneity ( $I^2=14\%$ ). But there was no substantial association between milk intake and colorectal cancer with milk intake of 200 g/day or below [33].

In our study, a non-significant negative association between milk consumption and all-cause mortality was found, which was notably due to the opposite directions of the associations with CVD and cancer. Our results were in line with four meta-analyses of cohort studies (pooled RR from 0.99 to 1.01) [14, 34-36] and three additional cohort studies not in these meta-analyses [10, 11, 37]. Notably, three of the meta-analyses [34-36] showed significant heterogeneity among studies ( $I^2$  from 70% to 97.4%), which could be due to a study including participants with very high level of milk consumption (10% women and 18% men with daily intake of >600 gram) [15]. This study and another recent study from the US both showed positive associations of milk intake with the risk of all-cause, CVD and cancer mortality [15,

19]. The heterogeneity might also be due to the variation in milk intake patterns across different countries. For example, daily milk intake ranged from less than 200 grams to more than 600 grams in the western populations [10, 15] but from less than 42.4 grams to more than 82.6 grams in the Asia populations [12, 17]. Notably, the highest category of milk consumption in this US study was  $\geq 480$  ml/week [19], which was much lower than that in other western ( $>600$  g/day) [10, 15] or Asian populations ( $>82.6$  g/day) [12, 17]. Furthermore, different studies accounted for different confounding factors, which might have also biased the results and led to different estimates. Some studies adjusted for history of hypertension and diabetes [17, 18] and some did not account for any personal disease history [10, 15]. In addition, different sets of confounding factors and the same confounders with opposite directions of confounding might reveal effects on the association between milk consumption and outcomes. For example, individuals with higher levels of milk consumption would not be associated with socioeconomic position (SEP) because milk is cheap and widely consumed in the west or high-income countries, whereas in low-to-middle income countries higher levels of milk consumption tends to be associated with higher SEP. Moreover, the consumption of milk or other dairy products was often accompanied by some specific dietary patterns in different populations. As high-quality diets (adherence to the dietary pattern with high scores) were inversely associated with risks of CVD [24-26] and some site-specific cancer, i.e., colorectal [38] and hepatocellular cancer [39], we additionally adjusted for three common dietary patterns

in the results to minimize the confounding effects. Failure to account for SEP or related dietary patterns might lead to residual confounding [9, 10, 13-16, 37]. In our study, we found that participants who consumed milk had higher SEP, and those with moderate milk consumption had the lowest scores of three dietary patterns. Therefore, after comprehensively accounting for these confounding factors such as SEP factors and dietary patterns, our results should have been less confounded than previous studies.

The exact mechanisms by which moderate milk consumption lead to a lower risk of CVD remain unclear. One possible explanation may be due to the potential beneficial effects on blood pressure [27]. Two meta-analyses of randomized trials on effects of lactotripeptides originating from milk showed a significant reduction in SBP and DBP, and such effects were mostly attributed to the inhibition of angiotensin converting enzyme [40, 41]. Moreover, milk and dairy products are rich in calcium, magnesium and potassium, which may be responsible for an antihypertensive effect [42-44]. High milk consumption might increase circulating concentrations of insulin-like growth factor (IGF)-I and IGF binding protein-3 which were associated with an increased risk of common cancers [45]. However, as the associations with cancer were modest in effect size and varied across organ sites [46, 47], further studies to confirm the results are necessary.

This is the first prospective study in China mainland examining the association between milk consumption and risk of all-cause and cause-specific mortality. Mendelian randomization studies mostly showed no association of milk or dairy consumption with metabolic traits, ischemic heart disease or cancer [48-52]. However, the interpretation of such null Mendelian randomization studies warrants greater caution, given the high potential for false-negative findings due to very small proportion of variance explained by genetic instrumental variables in studies of milk consumption and the difficulties in verifying the restriction exclusion assumption. Moreover, we found no Mendelian randomization study examining the effects of milk intake on cardiovascular disease or cancer in Asian populations, which are of great heterogeneity in terms of genetic background and milk consumption patterns compared to the western populations. Thus our study provided important additional evidence that moderate milk consumption was associated with a lower risk of CVD mortality, but high milk consumption was associated with a higher risk of total cancer mortality in Chinese. Strengths of this study included the comprehensive collection of baseline information, a long duration of follow-up, and adjustment for multiple confounding factors and dietary patterns. Moreover, we focused on milk rather than whole dairy products since butter, cream, cheese or yogurt are rarely consumed in older Chinese people [21]. As other dairy products may have differential effects on CVD or cancer [9, 10, 37], our results on milk only would be less confounded by other dairy products.

423

424 Our study had several limitations. Firstly, measurement errors during dietary  
425 assessments in large population-based cohort studies are inevitable and might have  
426 biased our results towards the null. Secondly, dietary intake was assessed only at  
427 one-time point, which might have changed during the long-term follow-up, although  
428 our previous study showed that dietary pattern in our older Chinese sample was  
429 relatively stable [53]. Thirdly, although we adjusted for multiple covariates, residual  
430 confounding could not be fully ruled out. Fourthly, our results may not be applicable  
431 to younger populations or other populations in the West.

432

433 In conclusion, in our sample of Chinese with much lower milk consumption than  
434 those in the West, compared with no consumption, moderate milk consumption  
435 showed a lower risk of CVD mortality including IHD and stroke, but high milk  
436 consumption showed a higher risk of total cancer mortality. Given the observational  
437 study design, further studies are warranted to verify the differential effects of milk on  
438 CVD and cancer.

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444

445 **Authorship statement**

446 XJW, LX, THL, CQJ, WSZ, FZ, YLJ, JW and KKC have substantial contributions to  
447 conception and design, acquisition of funding, data and interpretation of data; XJW  
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451

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453 **Conflict of interest** The authors declare that they have no conflict of interest.

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462

**References**

- [1] World Health Organization. Cardiovascular diseases (CVDs) fact sheet. current. Available from: [www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](http://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)). Accessed May 27 2017.
- [2] World Health Organization. Latest global cancer data IARC PRESS RELEASE. current. Available from: <https://www.who.int/news-room/fact-sheets/detail/cancer>. Accessed September 20 2018.
- [3] National Bureau of Statistics of China. Proportional Mortality Ratio data. Current. Available from: <http://data.stats.gov.cn/easyquery.htm?cn=C01>. Accessed December 26 2018.
- [4] Canada's food guides. Eat protein foods. current. Available from: <https://www.canada.ca/en/health-canada/services/food-nutrition/canada-food-guide/changing-foods/milk-alternatives.html>. Accessed May 1 2019.
- [5] US Department of Health and Human Services; US Department of Agriculture. 2015-2020 Dietary Guidelines for Americans. 8th Edition. Available from: <https://health.gov/dietaryguidelines/2015/guidelines/>. Accessed January 1 2016.
- [6] National Health and Family Planning Commission of PRC. Balanced Diet Pagoda for Chinese Consumers (2016) current. Available from: <http://www.chinadaily.com.cn/m/chinahealth/index.html>. Accessed May 23 2016.
- [7] Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston Miller N, Hubbard VS, et al.

- 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 2014;63:2960-84.
- [8] Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). *European heart journal*. 2012;33:1635-701.
- [9] Dalmeijer GW, Struijk EA, van der Schouw YT, Soedamah-Muthu SS, Verschuren WM, Boer JM, et al. Dairy intake and coronary heart disease or stroke--a population-based cohort study. *International journal of cardiology*. 2013;167:925-9.
- [10] Goldbohm RA, Chorus AM, Galindo Garre F, Schouten LJ, Brandt PA. Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in the Netherlands. *Am J Clin Nutr*. 2011;93.
- [11] Huang LY, Wahlqvist ML, Huang YC, Lee MS. Optimal dairy intake is predicated on total, cardiovascular, and stroke mortalities in a Taiwanese cohort. *Journal of the American College of Nutrition*. 2014;33:426-36.
- [12] 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

- 505 general population: the NIPPON DATA80. *Journal of epidemiology*. 2013;23:47-54.
- 506 [13] Louie J, Flood V, Burlutsky G, Rangan A, Gill T, Mitchell P. Dairy Consumption  
507 and the Risk of 15-Year Cardiovascular Disease Mortality in a Cohort of Older  
508 Australians. *Nutrients*. 2013;5:441.
- 509 [14] Mazidi M, Mikhailidis DP, Sattar N, Howard G, Graham I, Banach M.  
510 Consumption of dairy product and its association with total and cause specific  
511 mortality – A population-based cohort study and meta-analysis. *Clinical Nutrition*.  
512 2018.
- 513 [15] Michaelsson K, Wolk A, Langenskiöld S, Basu S, Warensjö Lemming E, Melhus  
514 H, et al. Milk intake and risk of mortality and fractures in women and men: cohort  
515 studies. *BMJ (Clinical research ed)*. 2014;349:g6015.
- 516 [16] Praagman J, Franco OH, Ikram MA, Soedamah-Muthu SS, Engberink MF, van  
517 Rooij FJA, et al. Dairy products and the risk of stroke and coronary heart disease: the  
518 Rotterdam Study. *European Journal of Nutrition*. 2015;54:981-90.
- 519 [17] Talaei M, Koh WP, Yuan JM, Pan A. The association between dairy product  
520 intake and cardiovascular disease mortality in Chinese adults. *Eur J Nutr*.  
521 2017;56:2343-52.
- 522 [18] Wang C, Yatsuya H, Tamakoshi K, Iso H, Tamakoshi A. Milk drinking and  
523 mortality: findings from the Japan collaborative cohort study. *Journal of epidemiology*.  
524 2015;25:66-73.
- 525 [19] Ding M, Li J, Qi L, Ellervik C, Zhang X, Manson JE, et al. Associations of dairy

- 526 intake with risk of mortality in women and men: three prospective cohort studies.  
527 BMJ (Clinical research ed). 2019;367:l6204.
- 528 [20] Alford SC. Lactose intolerance in Asians. *Nature*. 1969;221:562-3.
- 529 [21] Liu Z, Pang S, Li Y, Man Q, Li L, Zhang J. [Consumption status of dairy  
530 products in Chinese aged 60 and above in 2010-2012]. *Wei sheng yan jiu = Journal of  
531 hygiene research*. 2016;45:708-13.
- 532 [22] Jiang C, Thomas GN, Lam TH, Schooling CM, Zhang W, Lao X, et al. Cohort  
533 Profile: The Guangzhou Biobank Cohort Study, a Guangzhou–Hong Kong–  
534 Birmingham collaboration. *International Journal of Epidemiology*. 2006;35:844-52.
- 535 [23] Sun Y, Jiang C, Cheng KK, Zhang W, Leung GM, Lam TH, et al. Milk  
536 consumption and cardiovascular risk factors in older Chinese: the Guangzhou  
537 Biobank Cohort Study. *PloS one*. 2014;9:e84813.
- 538 [24] Fung TT, Rexrode KM, Mantzoros CS, Manson JE, Willett WC, Hu FB.  
539 Mediterranean diet and incidence of and mortality from coronary heart disease and  
540 stroke in women. *Circulation*. 2009;119:1093-100.
- 541 [25] Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB.  
542 Adherence to a DASH-style diet and risk of coronary heart disease and stroke in  
543 women. *Archives of internal medicine*. 2008;168:713-20.
- 544 [26] Chiuve SE, Fung TT, Rimm EB, Hu FB, McCullough ML, Wang M, et al.  
545 Alternative dietary indices both strongly predict risk of chronic disease. *The Journal  
546 of nutrition*. 2012;142:1009-18.

- 547 [27] Livingstone KM, Lovegrove JA, Cockcroft JR, Elwood PC, Pickering JE, Givens  
548 DI. Does dairy food intake predict arterial stiffness and blood pressure in men?:  
549 Evidence from the Caerphilly Prospective Study. *Hypertension* (Dallas, Tex : 1979).  
550 2013;61:42-7.
- 551 [28] Drouin-Chartier J-P, Côté JA, Labonté M-È, Brassard D, Tessier-Grenier M,  
552 Desroches S, et al. Comprehensive Review of the Impact of Dairy Foods and Dairy  
553 Fat on Cardiometabolic Risk. *Advances in Nutrition*. 2016;7:1041-51.
- 554 [29] Huth PJ, Park KM. Influence of dairy product and milk fat consumption on  
555 cardiovascular disease risk: a review of the evidence. *Advances in nutrition* (Bethesda,  
556 Md). 2012;3:266-85.
- 557 [30] de Goede J, Soedamah-Muthu SS, Pan A, Gijsbers L, Geleijnse JM. Dairy  
558 Consumption and Risk of Stroke: A Systematic Review and Updated Dose-Response  
559 Meta-Analysis of Prospective Cohort Studies. *Journal of the American Heart*  
560 *Association*. 2016;5.
- 561 [31] Li BL, Jiang GX, Xue Q, Zhang H, Wang C, Zhang GX, et al. Dairy  
562 consumption and risk of esophageal squamous cell carcinoma: A meta-analysis of  
563 observational studies. *Asia-Pacific journal of clinical oncology*. 2016;12:e269-79.
- 564 [32] Chen H, Ward MH, Graubard BI, Heineman EF, Markin RM, Potischman NA, et  
565 al. Dietary patterns and adenocarcinoma of the esophagus and distal stomach. *Am J*  
566 *Clin Nutr*. 2002;75:137-44.
- 567 [33] Aune D, Lau R, Chan DSM, Vieira R, Greenwood DC, Kampman E, et al. Dairy

- 568 products and colorectal cancer risk: a systematic review and meta-analysis of cohort  
569 studies. *Ann Oncol.* 2012;23:37-45.
- 570 [34] Guo J, Astrup A, Lovegrove JA, Gijsbers L, Givens DI, Soedamah-Muthu SS.  
571 Milk and dairy consumption and risk of cardiovascular diseases and all-cause  
572 mortality: dose-response meta-analysis of prospective cohort studies. *European*  
573 *journal of epidemiology.* 2017;32:269-87.
- 574 [35] Mullie P, Pizot C, Autier P. Daily milk consumption and all-cause mortality,  
575 coronary heart disease and stroke: a systematic review and meta-analysis of  
576 observational cohort studies. *BMC public health.* 2016;16:1236.
- 577 [36] Soedamah-Muthu SS, Ding EL, Al-Delaimy WK, Hu FB, Engberink MF, Willett  
578 WC, et al. Milk and dairy consumption and incidence of cardiovascular diseases and  
579 all-cause mortality: dose-response meta-analysis of prospective cohort studies. *The*  
580 *American Journal of Clinical Nutrition.* 2011;93:158-71.
- 581 [37] Dehghan M, Mente A, Rangarajan S, Sheridan P, Mohan V, Iqbal R, et al.  
582 Association of dairy intake with cardiovascular disease and mortality in 21 countries  
583 from five continents (PURE): a prospective cohort study. *The Lancet.*  
584 2018;392:2288-97.
- 585 [38] Park SY, Boushey CJ, Wilkens LR, Haiman CA, Le Marchand L. High-Quality  
586 Diets Associate With Reduced Risk of Colorectal Cancer: Analyses of Diet Quality  
587 Indexes in the Multiethnic Cohort. *Gastroenterology.* 2017;153:386-94.e2.
- 588 [39] Ma Y, Yang W, Simon TG, Smith-Warner SA, Fung TT, Sui J, et al. Dietary

- 589 Patterns and Risk of Hepatocellular Carcinoma Among U.S. Men and Women.  
590 Hepatology (Baltimore, Md). 2019;70:577-86.
- 591 [40] Turpeinen AM, Jarvenpaa S, Kautiainen H, Korpela R, Vapaatalo H.  
592 Antihypertensive effects of bioactive tripeptides-a random effects meta-analysis.  
593 Annals of medicine. 2013;45:51-6.
- 594 [41] Xu JY, Qin LQ, Wang PY, Li W, Chang C. Effect of milk tripeptides on blood  
595 pressure: a meta-analysis of randomized controlled trials. Nutrition (Burbank, Los  
596 Angeles County, Calif). 2008;24:933-40.
- 597 [42] Gaucheron F. Milk and dairy products: a unique micronutrient combination.  
598 Journal of the American College of Nutrition. 2011;30:400s-9s.
- 599 [43] Griffith LE, Guyatt GH, Cook RJ, Bucher HC, Cook DJ. The influence of dietary  
600 and nondietary calcium supplementation on blood pressure: an updated metaanalysis  
601 of randomized controlled trials. American journal of hypertension. 1999;12:84-92.
- 602 [44] Pereira PC. Milk nutritional composition and its role in human health. Nutrition  
603 (Burbank, Los Angeles County, Calif). 2014;30:619-27.
- 604 [45] Harrison S, Lennon R, Holly J, Higgins JPT, Gardner M, Perks C, et al. Does  
605 milk intake promote prostate cancer initiation or progression via effects on  
606 insulin-like growth factors (IGFs)? A systematic review and meta-analysis. Cancer  
607 causes & control : CCC. 2017;28:497-528.
- 608 [46] Renehan AG, Zwahlen M, Minder C, O'Dwyer ST, Shalet SM, Egger M.  
609 Insulin-like growth factor (IGF)-I, IGF binding protein-3, and cancer risk: systematic



- 610 review and meta-regression analysis. *Lancet* (London, England). 2004;363:1346-53.
- 611 [47] Roddam AW, Allen NE, Appleby P, Key TJ, Ferrucci L, Carter HB, et al.
- 612 Insulin-like growth factors, their binding proteins, and prostate cancer risk: analysis of
- 613 individual patient data from 12 prospective studies. *Annals of internal medicine*.
- 614 2008;149:461-71, w83-8.
- 615 [48] Dairy Consumption and Body Mass Index Among Adults: Mendelian
- 616 Randomization Analysis of 184802 Individuals from 25 Studies. *Clin Chem*.
- 617 2018;64:183-91.
- 618 [49] Dairy Intake and Body Composition and Cardiometabolic Traits among Adults:
- 619 Mendelian Randomization Analysis of 182041 Individuals from 18 Studies. *Clin*
- 620 *Chem*. 2019;65:751-60.
- 621 [50] Bergholdt HKM, Nordestgaard BG, Varbo A, Ellervik C. Milk intake is not
- 622 associated with ischaemic heart disease in observational or Mendelian randomization
- 623 analyses in 98,529 Danish adults. *International journal of epidemiology*.
- 624 2015;44:587-603.
- 625 [51] Bergholdt HKM, Nordestgaard BG, Varbo A, Ellervik C. Lactase persistence,
- 626 milk intake, and mortality in the Danish general population: a Mendelian
- 627 randomization study. *European journal of epidemiology*. 2018;33:171-81.
- 628 [52] Ding M, Huang T, Bergholdt HK, Nordestgaard BG, Ellervik C, Qi L. Dairy
- 629 consumption, systolic blood pressure, and risk of hypertension: Mendelian
- 630 randomization study. *BMJ* (Clinical research ed). 2017;356:j1000.

- 631 [53] Xu L, Lam TH, Jiang CQ, Zhang WS, Zhu F, Jin YL, et al. Egg consumption and  
632 the risk of cardiovascular disease and all-cause mortality: Guangzhou Biobank Cohort  
633 Study and meta-analyses. *Eur J Nutr.* 2019;58:785-96.
- 634 [54] Koh-Banerjee P, Franz M, Sampson L, Liu S, Jacobs DR, Jr, Spiegelman D, et al.  
635 Changes in whole-grain, bran, and cereal fiber consumption in relation to 8-y weight  
636 gain among men. *The American Journal of Clinical Nutrition.* 2004;80:1237-45.
- 637 [55] Liu AD, Li JW, Liu ZP, Zhou PP, Mao WF, Li N, et al. Trans Fatty Acid Levels in  
638 Foods and Intakes among Population Aged 3 Years and above in Beijing and  
639 Guangzhou Cities, China. *Biomedical and environmental sciences : BES.*  
640 2015;28:477-85.
- 641
- 642

**Table 1.** Baseline characteristics by milk consumption groups in 18,214 participants of the Guangzhou Biobank Cohort Study from September 2003 to May 2006.

	Milk consumption, 1 portion=250 ml			P
	0	1-3 portions/week	3+ portions/week	
Number of participants	12,670	2,669	2,875	
Sex, men, %	29.8	26.6	28.0	0.002
Age, years, mean (CI)	62.8 (62.7, 62.9)	60.9 (60.7, 61.2)	62.6 (62.3, 62.8)	<0.001
Age group, years, %				
<65	58.6	69.4	59.2	
≥65	41.4	30.7	40.8	<0.001
Social-economic position				
Family income, CNY/year, %				

<10,000	6.7	4.5	4.1	
10,000-29,999	33.8	31.0	32.1	
30,000-49,999	17.6	22.8	22.7	
≥50,000	12.1	18.2	19.9	
Don't know	29.8	23.5	21.2	<0.001
Education, %				
Primary or below	50.3	36.9	32.0	
Secondary	42.2	53.1	53.6	
College or above	7.5	10.0	14.4	<0.001
Occupation, %				
Manual	64.8	55.7	49.0	
Non-manual	23.5	22.7	32.6	

Others	11.7	21.6	18.4	<0.001
Smoking status, %				
Never	78.6	83.4	83.2	
Former	10.0	8.0	9.9	
Current	11.4	8.6	6.9	<0.001
Physical activity, %				
Inactive	8.1	10.4	7.5	
Minimally active	46.1	52.2	49.1	
Active	45.8	37.4	43.4	<0.001
Alcohol use, %				
Never	81.0	81.7	81.6	
Former	2.7	2.3	2.3	

Current	16.3	16.0	16.1	0.45
BMI, kg/m <sup>2</sup> , %				
≤18.5	4.8	4.1	5.2	
18.6-22.9	37.5	40.7	39.4	
23-27.4	45.0	44.4	46.0	
≥27.5	12.7	10.8	9.4	<0.001
Vegetable consumption <sup>†</sup> , g/day, %				
≤100	8.8	9.5	7.1	
101-150	15.0	17.2	14.9	
151-200	18.9	22.1	19.9	
201-250	14.9	17.7	15.7	
251-300	12.1	10.0	11.4	

≥301	30.3	23.4	31	<0.001
Fruit consumption <sup>†</sup> , g/day, %				
≤50	24.0	17.8	14.3	
51–100	22.1	22.9	19.4	
101–150	19.8	21.6	19.9	
151–200	14.1	15.3	17.1	
201–250	8.4	9.5	11.1	
≥251	11.6	12.9	18.2	<0.001
Nut consumption <sup>†</sup> , portions/week, %				
None	60.6	54.5	54.5	
1-3	26.1	30.8	26.7	
3+	13.3	14.7	18.8	<0.001

Egg consumption<sup>†</sup>, times/week, (%)

0	23.1	17.3	16.8	
1-2	57.5	64.3	54.7	
≥3	19.4	18.4	28.5	<0.001
Energy, kcal/day, mean (CI)	1795.9 (1786.6, 1805.3)	1848.1 (1829.2, 1867.0)	1995.7 (1976.2, 2015.3)	<0.001
Nutrient intakes (energy-adjusted as appropriate) <sup>†</sup> , g/day, mean (CI)				
Carbohydrates <sup>‡</sup>	259.4 (257.8, 260.9)	259.2 (256.1, 262.3)	275.2 (272.1, 278.4)	<0.001
Protein <sup>‡</sup>	70.1 (69.7, 70.5)	73.4 (72.5, 74.2)	81.9 (81.0, 82.8)	<0.001
Fat <sup>‡</sup>	55.9 (55.5, 56.3)	60.3 (59.4, 61.2)	66.1 (65.2, 67)	<0.001
Saturated fat <sup>‡</sup>	9.1 (9.0, 9.2)	10.7 (10.5, 10.9)	13.7 (13.5, 13.9)	<0.001
Monounsaturated fat <sup>‡</sup>	16.7 (16.5, 16.8)	18.3 (17.9, 18.6)	19.7 (19.3, 20.0)	<0.001
Polyunsaturated fat <sup>‡</sup>	12.7 (12.5, 12.8)	13.3 (13.0, 13.7)	14.3 (13.9, 14.6)	<0.001



Fiber <sup>†</sup>	12.9 (12.8, 13.0)	12.6 (12.4, 12.9)	14.8 (14.5, 15.1)	<0.001
Cholesterol <sup>†</sup>	141.5 (139.7, 143.4)	156.9 (153.8, 159.9)	177.2 (174.3, 180.2)	<0.001
aMED diet score, mean (CI)	4.7 (4.6, 4.7)	4.6 (4.5, 4.6)	4.6 (4.6, 4.7)	0.003
DASH diet score, mean (CI)	23.2 (23.2, 23.3)	23.0 (22.9, 23.2)	23.9 (23.8, 24.1)	<0.001
aHEI-2010 score, mean (CI)	54.4 (54.3, 54.5)	54.1 (53.8, 54.4)	55 (54.7, 55.3)	<0.001
Self-rated health, % good	85.4	85.6	85.0	0.80
Diabetes, % yes	12.8	11.9	15.0	0.001
Hypertension, % yes	27.9	27.5	26.9	0.54
Hyperlipidemia, % yes	8.6	10.3	10.1	0.003

Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; BMR, basal metabolic rate; CI, confidence interval;

DASH, Dietary Approaches to Stop Hypertension.

Note: one dollar almost equals to 7 CNY.

<sup>†</sup>: 18,707 participants with data on daily dietary energy intake.

‡: Energy-adjusted mean and 95% confidence interval (CI).

**Table 2.** Regression coefficients ( $\beta$ s) and 95% confidence intervals (CIs) of cardiovascular risk factors by baseline milk consumption in 18,214 participants based on information collected from September 2003 to May 2006.

	Milk consumption, 1 portion=250 ml			P for
	0	1-3 portions/week	3+ portions/week	trend
<b>Systolic blood pressure, mmHg</b>				
Model 1	Reference (0)	-4.03 (-4.95, -3.11)***	-3.85 (-4.75, -2.96)***	<0.001
Model 2	Reference (0)	-1.84 (-2.73, -0.96)***	-2.93 (-3.79, -2.07)***	<0.001
Model 3 plus dietary patterns				
aMED diet score	Reference (0)	-1.88 (-2.77, -0.99)***	-2.99 (-3.87, -2.12)***	<0.001
DASH diet score	Reference (0)	-1.89 (-2.77, -1.00)***	-3.09 (-3.96, -2.22)***	<0.001
aHEI-2010 score	Reference (0)	-1.88 (-2.77, -0.99)***	-3.09 (-3.96, -2.21)***	<0.001
<b>Diastolic blood pressure, mmHg</b>				

Model 1	Reference (0)	-1.56 (-2.04, -1.09)***	-2.09 (-2.55, -1.64)***	<0.001
Model 2	Reference (0)	-1.08 (-1.53, -0.64)***	-1.60 (-2.04, -1.17)***	<0.001
Model 3 plus dietary patterns				
aMED diet score	Reference (0)	-1.09 (-1.54, -0.65)***	-1.65 (-2.09, -1.21)***	<0.001
DASH diet score	Reference (0)	-1.10 (-1.55, -0.65)***	-1.68 (-2.12, -1.24)***	<0.001
aHEI-2010 score	Reference (0)	-1.10 (-1.55, -0.65)***	-1.71 (-2.15, -1.27)***	<0.001
<b>LDL-cholesterol, mmol/l</b>				
Model 1	Reference (0)	0.13 (0.1, 0.16)***	0.09 (0.07, 0.12)***	<0.001
Model 2	Reference (0)	0.09 (0.06, 0.12)***	0.07 (0.04, 0.10)***	<0.001
Model 3 plus dietary patterns				
aMED diet score	Reference (0)	0.09 (0.06, 0.12)***	0.07 (0.04, 0.10)***	<0.001
DASH diet score	Reference (0)	0.09 (0.06, 0.12)***	0.08 (0.05, 0.10)***	<0.001

aHEI-2010 score	Reference (0)	0.09 (0.06, 0.12)***	0.07 (0.05, 0.12)***	<0.001
<b>HDL-cholesterol, mmol/l</b>				
Model 1	Reference (0)	0.02 (-0.001, 0.03)	0.02 (0.01, 0.04)**	0.002
Model 2	Reference (0)	0.01 (-0.004, 0.03)	0.02 (-0.001, 0.03)	0.03
Model 3 plus dietary patterns				
aMED diet score	Reference (0)	0.01 (-0.002, 0.03)	0.02 (0.01, 0.04)*	0.005
DASH diet score	Reference (0)	0.01 (-0.003, 0.03)	0.02 (0.01, 0.04)**	0.004
aHEI-2010 score	Reference (0)	0.02 (-0.002, 0.03)	0.02 (0.004, 0.04)*	0.007
<b>Triglycerides, mmol/l</b>				
Model 1	Reference (0)	-0.10 (-0.15, -0.05)***	-0.10 (-0.15, -0.05)***	<0.001
Model 2	Reference (0)	-0.10 (-0.16, -0.05)***	-0.09 (-0.14, -0.04)**	<0.001
Model 3 plus dietary patterns				

aMED diet score	Reference (0)	-0.11 (-0.16, -0.06)***	-0.09 (-0.14, -0.04)***	<0.001
DASH diet score	Reference (0)	-0.11 (-0.16, -0.06)***	-0.09 (-0.14, -0.04)***	<0.001
aHEI-2010 score	Reference (0)	-0.11 (-0.16, -0.05)***	-0.09 (-0.14, -0.04)***	<0.001
<b>Total cholesterol, mmol/l</b>				
Model 1	Reference (0)	0.11 (0.06, 0.16)***	0.09 (0.04, 0.14)***	<0.001
Model 2	Reference (0)	0.07 (0.02, 0.12)**	0.07 (0.02, 0.11)**	0.001
Model 3 plus dietary patterns				
aMED diet score	Reference (0)	0.08 (0.03, 0.12)**	0.07 (0.03, 0.12)**	<0.001
DASH diet score	Reference (0)	0.07 (0.02, 0.12)**	0.08 (0.03, 0.12)**	<0.001
aHEI-2010 score	Reference (0)	0.07 (0.02, 0.12)**	0.07 (0.02, 0.12)**	0.001
<b>Fasting glucose, mmol/l</b>				
Model 1	Reference (0)	-0.19 (-0.26, -0.12)***	-0.003 (-0.07, 0.07)	0.10

Model 2	Reference (0)	-0.11 (-0.18, -0.03)**	0.04 (-0.03, 0.11)	0.02
Model 3 plus dietary patterns				
aMED diet score	Reference (0)	-0.10 (-0.17, -0.03)**	0.05 (-0.02, 0.13)	0.02
DASH diet score	Reference (0)	-0.10 (-0.18, -0.03)**	0.04 (-0.02, 0.12)	0.01
aHEI-2010 score	Reference (0)	-0.11 (-0.19, -0.04)**	0.05 (-0.03, 0.12)	0.01
<b>Body mass index, kg/m<sup>2</sup></b>				
Model 1	Reference (0)	-0.14 (-0.28, -0.004)*	-0.30 (-0.43, -0.16)***	<0.001
Model 2	Reference (0)	-0.17 (-0.30, -0.03)*	-0.26 (-0.39, -0.13)***	<0.001
Model 3 plus dietary patterns				
aMED diet score	Reference (0)	-0.17 (-0.30, -0.03)*	-0.28 (-0.41, -0.15)***	<0.001
DASH diet score	Reference (0)	-0.18 (-0.31, -0.04)*	-0.30 (-0.43, -0.17)***	<0.001
aHEI-2010 score	Reference (0)	-0.18 (-0.31, -0.04)*	-0.31 (-0.45, -0.18)***	<0.001

**Waist circumference, cm**

Model 1	Reference (0)	-1.58 (-1.95, -1.21)***	-1.58 (-1.94, -1.22)***	<0.001
Model 2	Reference (0)	-0.92 (-1.28, -0.57)***	-1.23 (-1.58, -0.88)***	<0.001
Model 3 plus dietary patterns				
aMED diet score	Reference (0)	-0.92 (-1.27, -0.56)***	-1.30 (-1.66, -0.95)***	<0.001
DASH diet score	Reference (0)	-0.95 (-1.31, -0.60)***	-1.34 (-1.69, -1.00)***	<0.001
aHEI-2010 score	Reference (0)	-0.97 (-1.33, -0.62)***	-1.37 (-1.72, -1.02)***	<0.001

Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension; LDL, low density lipoprotein; HDL, high density lipoprotein.

Model 1: Crude model.

Model 2: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension and hyperlipidemia, as appropriate.

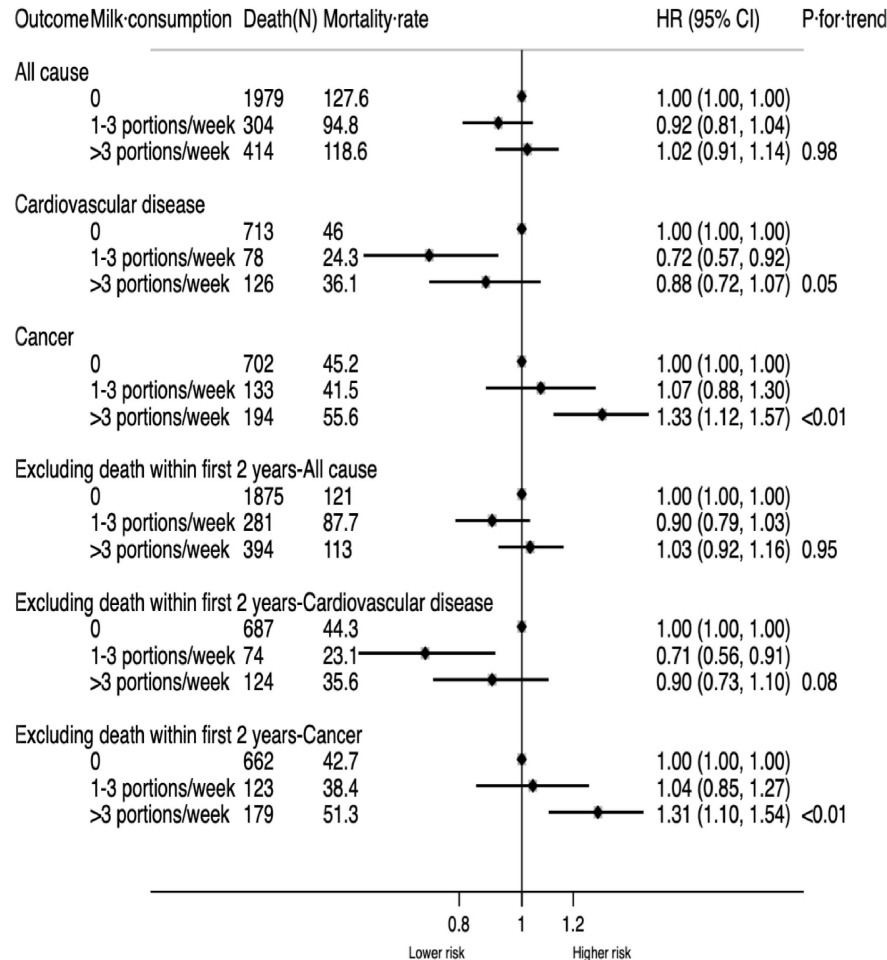
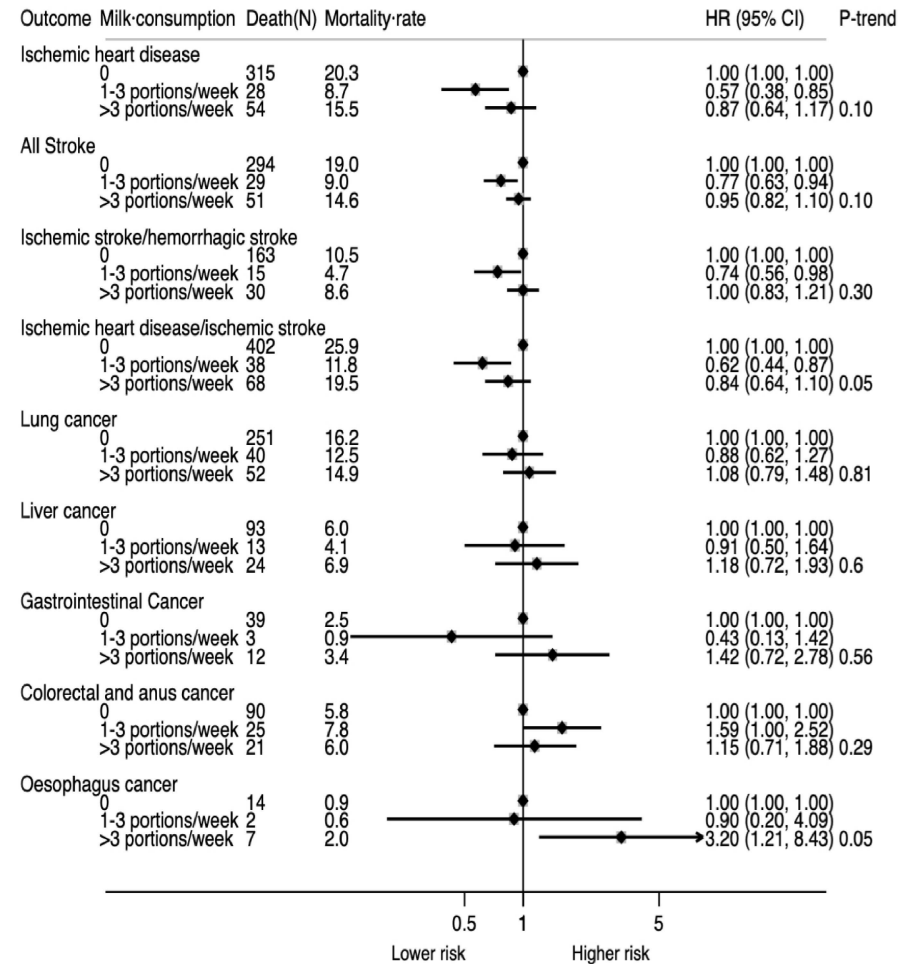
Model 3: Additionally adjusted for daily dietary energy intake.



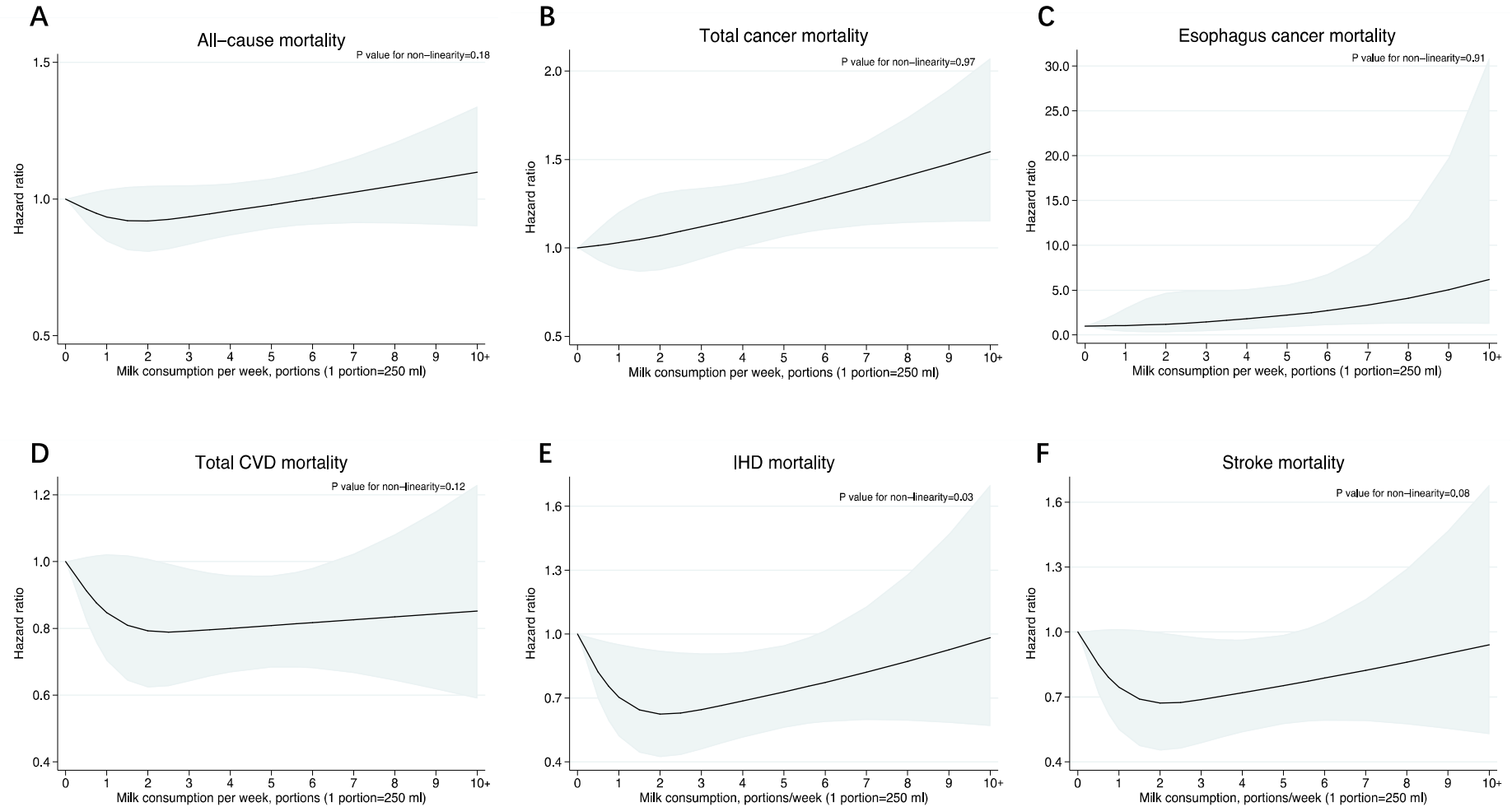
\*:  $P < 0.05$ ; \*\*:  $P < 0.01$ ; \*\*\*:  $P < 0.001$

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**Figure 1.** (A) Associations between milk consumption and all-cause, CVD and cancer mortality; (B) Associations between milk consumption and cause-specific death of CVD and cancer. The HRs and 95% CIs above were adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension and hyperlipidemia, daily dietary energy intake and dietary quality (aHEI-2010 score). One portion of milk consumption was equal to 250 ml; unit of mortality rate was per 10,000 person-years.

**A****B**

**Figure 2.** Restricted cubic spline plots to assess associations between milk consumption and mortality. (A) All-cause mortality; (B) Total cancer mortality; (C) Esophagus cancer mortality; (D) CVD mortality; (E) IHD mortality; (F) Stroke mortality. The HRs and 95% CIs above were adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension and hyperlipidemia, daily dietary energy intake and dietary quality (aHEI-2010 score).



**Table 3.** Adjusted hazards ratios (HRs)<sup>†</sup> and 95% confidence interval (CIs) of CVD mortality related to milk consumption stratified by selected baseline characteristics.

	Milk consumption, 1 portion=250 ml			P value for
	0	1-3 portions/week	3+ portions/week	interaction
Sex				
Male	Reference (1)	0.58 (0.39, 0.87)	0.94 (0.70, 1.27)	0.31
Female	Reference (1)	0.87 (0.64, 1.17)	0.88 (0.67, 1.15)	
Age group, years				
<65	Reference (1)	0.52 (0.32, 0.84) <sup>**</sup>	0.46 (0.27, 0.77) <sup>**</sup>	<0.01
≥65	Reference (1)	0.82 (0.63, 1.09)	1.06 (0.85, 1.32)	
Education				
Primary or below	Reference (1)	0.69 (0.50, 0.97) <sup>*</sup>	0.96 (0.71, 1.29)	

Secondary or above	Reference (1)	0.68 (0.48, 0.97)*	0.98 (0.75, 1.28)	0.11
Smoking status				
Never	Reference (1)	0.81 (0.61, 1.07)	1.00 (0.79, 1.26)	
Ever	Reference (1)	0.60 (0.38, 0.95)*	0.70 (0.47, 1.04)	0.27
Alcohol use				
Never	Reference (1)	0.76 (0.58, 0.99)*	0.87 (0.69, 1.09)	
Ever	Reference (1)	0.64 (0.37, 1.11)	1.05 (0.68, 1.61)	0.63
Physical activity				
Inactive or minimally active	Reference (1)	0.82 (0.60, 1.11)	0.99 (0.76, 1.28)	
Active	Reference (1)	0.62 (0.42, 0.91)*	0.81 (0.60, 1.10)	0.36
BMI, kg/m <sup>2</sup>				
<25	Reference (1)	0.74 (0.54, 1.00)	0.94 (0.73, 1.21)	

$\geq 25$	Reference (1)	0.71 (0.49, 1.05)	0.85 (0.61, 1.18)	0.80
Self-rated health				
Good	Reference (1)	0.79 (0.61, 1.03)	0.97 (0.78, 1.20)	
Poor	Reference (1)	0.50 (0.27, 0.93)*	0.64 (0.38, 1.07)	0.22
History of diabetes				
Yes	Reference (1)	0.50 (0.28, 0.91)*	1.11 (0.76, 1.63)	
No	Reference (1)	0.79 (0.61, 1.02)	0.84 (0.66, 1.06)	0.19
History of hypertension				
Yes	Reference (1)	0.90 (0.62, 1.30)	0.81 (0.57, 1.15)	
No	Reference (1)	0.64 (0.47, 0.87)**	0.96 (0.75, 1.23)	0.19
History of hyperlipidemia				
Yes	Reference (1)	0.61 (0.30, 1.25)	0.64 (0.32, 1.27)	



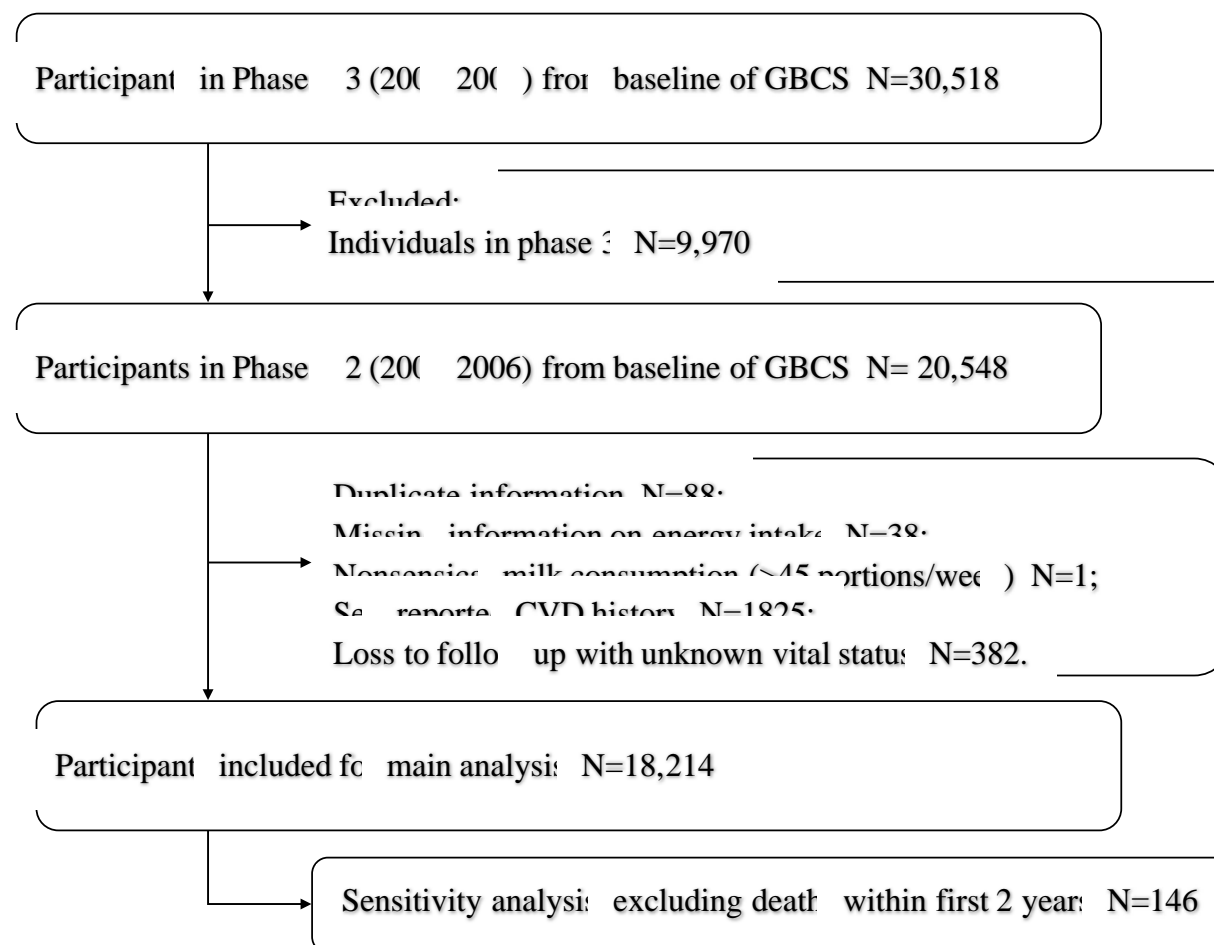
No	Reference (1)	0.74 (0.57, 0.95)*	0.94 (0.76, 1.16)	0.71
aHEI-2010 score				
< median	Reference (1)	0.65 (0.46, 0.91)*	0.95 (0.72, 1.26)	
≥ median	Reference (1)	0.84 (0.60, 1.18)	0.87 (0.65, 1.16)	0.56

Abbreviations: aHEI, alternate Healthy Eating Index.

†: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension, hyperlipidemia and aHEI-2010 score respectively.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001

**Supplementary Figure 1.** Flowchart showing selection of participants included in the main analysis from Guangzhou Biobank Cohort Study



**Supplementary Table 1.** ICD-10 codes for deaths of cardiovascular disease and cancer.

Causes of deaths	ICD-10
Cardiovascular disease	I00-I25, I28-I99
Ischemic heart disease	I20-I25
Stroke	I60-I69
Ischemic stroke or hemorrhagic stroke	I61, I63
Ischemic heart disease or ischemic stroke	I20-I25, I63
Cancer	C-codes
Lung cancer	C34
Liver cancer	C22
Gastrointestinal cancer	C16
Colorectal and anal cancer	C18-C19, C20-21
Esophagus cancer	C15

**Supplementary Table 2.** Scoring standards for each component of the aMED, DASH and aHEI-2010.

Component	aMED <sup>1</sup>		DASH <sup>2</sup>		aHEI-2010 <sup>3</sup>	
	Minimum DPS (0)	Maximum DPS	Minimum DPS	Maximum DPS	Minimum	Maximum
	(1)	(1)	(1)	(5)	DPS (0)	DPS (10)
Vegetables, servings/day <sup>4</sup>	Less than median	Median or greater	Lowest quintile	Highest quintile	0	≥5
Fruits, servings /day <sup>5</sup>	Less than median	Median or greater	Lowest quintile	Highest quintile	0	≥4
Nuts, servings /day <sup>6</sup>	Less than median	Median or greater	-	-	-	-
Legumes, servings/day <sup>7</sup>	Less than median	Median or greater	-	-	-	-
Whole grains, servings/day <sup>8</sup>	Less than median	Median or greater	Lowest quintile	Highest quintile	0	5
Fish, servings/day <sup>7</sup>	Less than median	Median or greater	-	-	-	-
Red and processed meat, servings/day <sup>9</sup>	Median or greater	Less than median	Highest quintile	Lowest quintile	≥1.5	0

Alcohol, drinks/day <sup>10</sup>	lower or greater	5-15	-	-	$\geq 3$	0.5-1.5
Ratio <sup>11</sup>	Less than median	Median or greater	-	-	-	-
Nuts and legumes, servings/day <sup>12</sup>	-	-	Lowest quintile	Highest quintile	0	$\geq 1$
Sweetened beverages, servings/day <sup>13</sup>	-	-	Highest quintile	Lowest quintile	$\geq 1$	0
Low-fat dairy, servings/day <sup>14</sup>	-	-	Lowest quintile	Highest quintile	-	-
Trans-fat, % of energy <sup>15</sup>	-	-	-	-	$\geq 4$	$\leq 0.5$
Long-chain (n-3) fats, mg/day	-	-	-	-	0	250
Polyunsaturated fat, % of energy	-	-	-	-	$\leq 2$	$\geq 10$
Sodium, mg/day	-	-	Highest quintile	Lowest quintile	Highest	Lowest

decile

decile

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Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; DASH; Dietary Approaches to Stop Hypertension; DPS, dietary pattern score.

<sup>1</sup> aMED, nine components included vegetables (excluding potatoes), fruits, nuts, whole grains, legumes, fish, ratio of monounsaturated to saturated fat, red and processed meats, and alcohol. Participants with intake above the median intake received 1 point. Red and processed meat consumption below the median received 1 point. We assigned 1 point for alcohol intake between 5 and 15 g/d. This represents approximately 12-oz can of regular beer, 5 oz of wine, or 1.5 oz of liquor. The possible score range for aMED was 0 to 9, with a higher score representing closer resemblance to the Mediterranean diet [24].

<sup>2</sup> DASH, eight components, for intake of fruits (all fruits and fruit juices), vegetables (all vegetables except potatoes and legumes), nuts and legumes (nuts and peanut butter, dried beans, peas and tofu), whole grains (brown rice, dark breads, cooked cereal, whole grain cereal, other grains, popcorn, wheat germ and bran), low-fat dairy (skim milk, yogurt and cottage cheese), the lowest quintile was assigned 1 point and the highest quintile was assigned 5 points. For intake of sodium (sum of sodium content of all foods in FFQ), sweetened beverages (carbonated and noncarbonated sweetened beverages), and red and processed meats (beef, pork, lamb, deli meats, organ meats, hot dogs and bacon), the lowest

quintile was assigned 5 points and the highest quintile was assigned 1 point. Total DASH score ranged from 8 to 40 [25].

<sup>3</sup> aHEI-2010, eleven components included vegetables (excluding potatoes), fruits (excluding fruit juice), whole grains (excluding refined grains), sweetened beverages (including soda and fruit drinks), nuts and legumes, red and processed meats, trans fat, long-chain (n-3) fats, polyunsaturated fat, sodium and alcohol. Intermediate intakes were scored proportionately between 0 and 10. Nondrinkers received a score of 2.5 points. All aHEI-2010 components were scored from 0 (worst) to 10 (best), and the total aHEI-2010 score ranged from 0 (non-adherence) to 110 (perfect adherence) [26].

<sup>4</sup> For aMED and DASH, one serving of vegetable is 50 g; for aHEI-2010, one serving is 0.5 cup of vegetables or 1 cup of green leafy vegetables (1 cup = 236.59 g).

<sup>5</sup> For aMED and DASH, one serving of fruit is 50 g; for aHEI-2010, one serving is 1 medium piece of fruit or 0.5 cup of berries (1 cup = 236.59 g).

<sup>6</sup> For aMED, one serving of nut is 25 g.

<sup>7</sup> For aMED, one serving of legume or fish is 50 g.

<sup>8</sup> For aMED and DASH, one serving is 200 g wheat noodle or 200 g porridge or 25 g corn flakes or 50 g whole wheat bread; for aHEI-2010, one

serving is 16 g wheat noodle or porridge or com flakes or whole wheat bread [54].

<sup>9</sup> For aMED and DASH, one serving is 50 g red meat or 25 g processed meat; for aHEI-2010, one serving is 4 oz of unprocessed meat or 1.5 oz of processed meat (1oz = 28.35 g).

<sup>10</sup> For aMED, one drink is 1 g ethanol; for aHEI-2010, one drink is 2 oz of ethanol (1 oz = 28.35 g).

<sup>11</sup> Monounsaturated to saturated fat ratio.

<sup>12</sup> For DASH, one serving is 25 g nut or 50 g legume; for aHEI-2010, one serving is 1 oz (1 oz = 28.35 g) of nuts or 1 tablespoon (15 mL) of peanut butter.

<sup>13</sup> One serving of sweetened beverage is 250 ml.

<sup>14</sup> One serving of low-fat dairy is 250 ml skim liquid milk or 7 g dried skimmed milk or 150 g low-fat yurt or 20 g cheese.

<sup>15</sup> The major source of dietary trans-fat was vegetable edible oils (content: 0.86 g/100g), milk and yogurt (0.16 g/100g), mutton and beef (0.3 g/100g), bakery foods (0.41 g/100g), fast foods (0.11 g/100g), fried noodle (0.31 g/100g), snacks (0.24 g/100g), chocolate and candy (0.89 g/100g), ice creams (0.09 g/100g), poultry and products (0.16 g/100g), margarine (0.86 g/100g), condiments (0.35 g/100g), puffing foods (0.16 g/100g), pork products (0.04 g/100g) and solid beverages (0.25 g/100g) [55].



**Supplementary Table 3.** Correlation coefficients R among milk consumption and total scores for aMED, DASH, aHEI-2010 in the Guangzhou Biobank Cohort Study.

	Milk	aMED	DASH	aHEI-2010
Milk	1.00			
aMED	-0.02**	1.00		
DASH	0.05***	0.55***	1.00	
aHEI-2010	0.02**	0.58***	0.72***	1.00

Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001

**Supplementary Table 4.** Adjusted hazards ratios (HRs) and 95% confidence interval (CIs) of mortality from all-cause, cardiovascular disease and cancer by baseline milk consumption in 18,214 participants in 2003-2006 and followed up until December 2017.

	Milk consumption, 1 portion=250 ml			P for trend
	0	1-3 portions/week	3+ portions/week	
<b>Person-years</b>	155,144	32,075	34,901	
<b>All-cause</b>				
No. of deaths	1,979	304	414	
Mortality rate, per 10,000 person-year	127.6	94.8	118.6	
Model 1	Reference (1)	0.76 (0.68, 0.86) <sup>***</sup>	0.94 (0.85, 1.05)	0.02
Model 2	Reference (1)	0.93 (0.82, 1.05)	1.03 (0.93, 1.15)	0.83
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.92 (0.82, 1.05)	1.02 (0.91, 1.14)	0.93

DASH diet score	Reference (1)	0.92 (0.82, 1.05)	1.03 (0.92, 1.15)	0.92
aHEI-2010 score	Reference (1)	0.92 (0.81, 1.04)	1.02 (0.91, 1.14)	0.98

### Cardiovascular disease

No. of deaths	713	78	126	
Mortality rate, per 10,000 person-year	46.0	24.3	36.1	
Model 1	Reference (1)	0.55 (0.44, 0.70) <sup>***</sup>	0.80 (0.66, 0.97) <sup>*</sup>	<0.01
Model 2	Reference (1)	0.72 (0.57, 0.91) <sup>**</sup>	0.88 (0.72, 1.07)	0.05
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.72 (0.57, 0.91) <sup>**</sup>	0.87 (0.72, 1.06)	0.04
DASH diet score	Reference (1)	0.72 (0.57, 0.91) <sup>**</sup>	0.87 (0.71, 1.06)	0.04
aHEI-2010 score	Reference (1)	0.72 (0.57, 0.92) <sup>**</sup>	0.88 (0.72, 1.07)	0.05

### Cancer

No. of deaths	702	133	194	
Mortality rate, per 10,000 person-year	45.2	41.5	55.6	
Model 1	Reference (1)	0.93 (0.77, 1.11)	1.24 (1.05, 1.45)**	0.03
Model 2	Reference (1)	1.08 (0.89, 1.32)	1.36 (1.16, 1.61)***	<0.01
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	1.08 (0.89, 1.31)	1.34 (1.13, 1.58)**	<0.01
DASH diet score	Reference (1)	1.08 (0.89, 1.31)	1.35 (1.14, 1.59)**	<0.01
aHEI-2010 score	Reference (1)	1.07 (0.88, 1.30)	1.33 (1.12, 1.57)**	<0.01
<b>Excluding deaths within first 2 years</b>				
<b>Person-years</b>	155,020	32,048	34,877	
<b>All-cause</b>				
No. of deaths	1875	281	394	

Mortality rate, per 10,000 person-year	121.0	87.7	113.0	
Model 1	Reference (1)	0.75 (0.66, 0.85) <sup>***</sup>	0.95 (0.85, 1.06)	0.02
Model 2	Reference (1)	0.91 (0.80, 1.03)	1.04 (0.93, 1.16)	0.81
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.91 (0.80, 1.03)	1.03 (0.91, 1.15)	0.98
DASH diet score	Reference (1)	0.91 (0.80, 1.03)	1.04 (0.93, 1.16)	0.86
aHEI-2010 score	Reference (1)	0.90 (0.79, 1.03)	1.03 (0.92, 1.16)	0.95
<b>Cardiovascular disease</b>				
No. of deaths	687	74	124	
Mortality rate, per 10,000 person-year	44.3	23.1	35.6	
Model 1	Reference (1)	0.54 (0.43, 0.69) <sup>***</sup>	0.82 (0.68, 0.99) <sup>*</sup>	<0.01
Model 2	Reference (1)	0.71 (0.55, 0.90) <sup>**</sup>	0.90 (0.74, 1.09)	0.07

## Model 3 plus dietary patterns

aMED diet score	Reference (1)	0.71 (0.55, 0.90)**	0.89 (0.73, 1.09)	0.06
DASH diet score	Reference (1)	0.70 (0.55, 0.90)**	0.89 (0.73, 1.08)	0.06
aHEI-2010 score	Reference (1)	0.71 (0.56, 0.91)**	0.90 (0.73, 1.10)	0.08

**Cancer**

No. of deaths	662	123	179	
Mortality rate, per 10,000 person-year	42.7	38.4	51.3	
Model 1	Reference (1)	0.91 (0.75, 1.10)	1.21 (1.03, 1.43)*	0.08
Model 2	Reference (1)	1.06 (0.87, 1.29)	1.34 (1.13, 1.58)**	<0.01
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	1.06 (0.87, 1.29)	1.32 (1.11, 1.57)**	<0.01
DASH diet score	Reference (1)	1.05 (0.86, 1.29)	1.33 (1.12, 1.58)**	<0.01

aHEI-2010 score	Reference (1)	1.04 (0.85, 1.27)	1.31 (1.10, 1.56)**	<0.01
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Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension.

Model 1: Crude model.

Model 2: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension and hyperlipidemia, as appropriate.

Model 3: Additionally adjusted for daily dietary energy intake.

\*:  $P < 0.05$ ; \*\*:  $P < 0.01$ ; \*\*\*:  $P < 0.001$

**Supplementary Table 5.** Adjusted hazards ratios (HRs) and 95% confidence interval (CIs) of cause-specific death of cardiovascular disease by baseline milk consumption in 18,214 participants in 2003-2006 and followed up until December 2017.

	Milk consumption, 1 portion=250 ml			P for trend
	0	1-3 portions/week	3+ portions/week	
<b>Person-years</b>	155,144	32,075	34,901	
<b>Ischemic heart disease</b>				
No. of deaths	315	28	54	
Mortality rate, per 10,000 person-year	20.3	8.7	15.5	
Model 1	Reference (1)	0.45 (0.30, 0.66)***	0.78 (0.58, 1.04)	<0.01
Model 2	Reference (1)	0.56 (0.38, 0.84)**	0.86 (0.64, 1.16)	0.08
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.57 (0.38, 0.84)**	0.86 (0.64, 1.16)	0.09



DASH diet score	Reference (1)	0.56 (0.38, 0.83) <sup>**</sup>	0.85 (0.63, 1.15)	0.07
aHEI-2010 score	Reference (1)	0.57 (0.38, 0.85) <sup>**</sup>	0.87 (0.64, 1.17)	0.10
<b>All Stroke</b>				
No. of deaths	294	29	51	
Mortality rate, per 10,000 person-year	19.0	9.0	14.6	
Model 1	Reference (1)	0.69 (0.57, 0.84) <sup>***</sup>	0.92 (0.81, 1.06)	0.01
Model 2	Reference (1)	0.78 (0.64, 0.94) <sup>**</sup>	0.95 (0.83, 1.10)	0.09
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.78 (0.64, 0.94) <sup>**</sup>	0.96 (0.83, 1.10)	0.10
DASH diet score	Reference (1)	0.78 (0.64, 0.94) <sup>**</sup>	0.96 (0.83, 1.10)	0.10
aHEI-2010 score	Reference (1)	0.77 (0.63, 0.94) <sup>**</sup>	0.95 (0.82, 1.10)	0.10
<b>Ischemic stroke/hemorrhagic stroke</b>				

No. of deaths	163	15	30	
Mortality rate, per 10,000 person-year	10.5	4.7	8.6	
Model 1	Reference (1)	0.65 (0.49, 0.85) <sup>**</sup>	0.97 (0.81, 1.16)	0.08
Model 2	Reference (1)	0.73 (0.55, 0.96) <sup>*</sup>	1.00 (0.83, 1.20)	0.28
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.73 (0.56, 0.97) <sup>*</sup>	1.01 (0.84, 1.21)	0.32
DASH diet score	Reference (1)	0.73 (0.55, 0.97) <sup>*</sup>	1.00 (0.83, 1.20)	0.25
aHEI-2010 score	Reference (1)	0.74 (0.56, 0.98) <sup>*</sup>	1.00 (0.83, 1.21)	0.30
<b>Ischemic heart disease/ischemic stroke</b>				
No. of deaths	402	38	68	
Mortality rate, per 10,000 person-year	25.9	11.8	19.5	
Model 1	Reference (1)	0.47 (0.34, 0.66) <sup>***</sup>	0.76 (0.59, 0.99) <sup>*</sup>	<0.01

Model 2	Reference (1)	0.60 (0.43, 0.85)**	0.83 (0.64, 1.08)	0.03
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.61 (0.43, 0.86)**	0.84 (0.64, 1.09)	0.04
DASH diet score	Reference (1)	0.60 (0.43, 0.85)**	0.82 (0.63, 1.07)	0.03
aHEI-2010 score	Reference (1)	0.62 (0.44, 0.87)**	0.84 (0.64, 1.10)	0.05

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Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension.

Model 1: Crude model.

Model 2: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension and hyperlipidemia, as appropriate.

Model 3: Additionally adjusted for daily dietary energy intake.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001

**Supplementary Table 6.** Adjusted hazards ratios (HRs) and 95% confidence interval (CIs) of top five cause-specific death of cancer by baseline milk consumption in 18,214 participants in 2003-2006 and followed up until December 2017.

	Milk consumption, 1 portion=250 ml			P for trend
	0	1-3 portions/week	3+ portions/week	
<b>Person-years</b>	155,144	32,075	34,901	
<b>Lung cancer</b>				
No. of deaths	251	40	52	
Mortality rate, per 10,000 person-year	16.2	12.5	14.9	
Model 1	Reference (1)	0.77 (0.55, 1.08)	0.92 (0.68, 1.24)	0.35
Model 2	Reference (1)	0.90 (0.63, 1.29)	1.10 (0.81, 1.49)	0.71
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.90 (0.63, 1.29)	1.07 (0.78, 1.46)	0.84

DASH diet score	Reference (1)	0.88 (0.61, 1.27)	1.11 (0.81, 1.52)	0.69
aHEI-2010 score	Reference (1)	0.88 (0.62, 1.27)	1.08 (0.79, 1.48)	0.81

### Liver cancer

No. of deaths	93	13	24	
Mortality rate, per 10,000 person-year	6.0	4.1	6.9	
Model 1	Reference (1)	0.68 (0.38, 1.22)	1.15 (0.73, 1.80)	0.86
Model 2	Reference (1)	0.91 (0.51, 1.64)	1.22 (0.76, 1.97)	0.50
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.93 (0.51, 1.67)	1.27 (0.78, 2.06)	0.42
DASH diet score	Reference (1)	0.91 (0.51, 1.65)	1.21 (0.75, 1.96)	0.53
aHEI-2010 score	Reference (1)	0.91 (0.50, 1.64)	1.18 (0.72, 1.93)	0.60

### Gastrointestinal Cancer

No. of deaths	39	3	12	
Mortality rate, per 10,000 person-year	2.5	0.9	3.4	
Model 1	Reference (1)	0.37 (0.12, 1.21)	1.37 (0.72, 2.63)	0.67
Model 2	Reference (1)	0.45 (0.14, 1.47)	1.53 (0.78, 2.97)	0.42
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.44 (0.13, 1.43)	1.43 (0.73, 2.80)	0.55
DASH diet score	Reference (1)	0.44 (0.14, 1.43)	1.43 (0.73, 2.81)	0.54
aHEI-2010 score	Reference (1)	0.43 (0.13, 1.42)	1.42 (0.72, 2.78)	0.56
<b>Colorectal and anal cancer</b>				
No. of deaths	90	25	21	
Mortality rate, per 10,000 person-year	5.8	7.8	6.0	
Model 1	Reference (1)	1.36 (0.87, 2.12)	1.04 (0.65, 1.68)	0.57

Model 2	Reference (1)	1.59 (1.01, 2.52)	1.14 (0.70, 1.86)	0.30
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	1.58 (1.00, 2.51)	1.14 (0.70, 1.86)	0.32
DASH diet score	Reference (1)	1.59 (1.00, 2.51)	1.14 (0.70, 1.87)	0.30
aHEI-2010 score	Reference (1)	1.59 (1.00, 2.52)	1.15 (0.71, 1.88)	0.29
<b>Esophagus cancer</b>				
No. of deaths	14	2	7	
Mortality rate, per 10,000 person-year	0.9	0.6	2	
Model 1	Reference (1)	0.69 (0.16, 3.02)	2.21 (0.89, 5.48)	0.14
Model 2	Reference (1)	0.83 (0.19, 3.73)	2.85 (1.11, 7.29)*	0.05
Model 3 plus dietary patterns				
aMED diet score	Reference (1)	0.91 (0.20, 4.13)	3.23 (1.22, 8.57)*	0.03

DASH diet score	Reference (1)	0.83 (0.19, 3.72)	2.87 (1.10, 7.48)*	0.05
aHEI-2010 score	Reference (1)	0.90 (0.20, 4.09)	3.20 (1.21, 8.43)*	0.03

Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension.

Model 1: Crude model.

Model 2: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension and hyperlipidemia, as appropriate.

Model 3: Additionally adjusted for daily dietary energy intake.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001



**Supplementary Table 7.** Adjusted hazards ratios (HRs)<sup>†</sup> and 95% confidence interval (CIs) of all-cause mortality related to milk consumption stratified by selected baseline characteristics.

	Milk consumption, 1 portion=250 ml			P value for
	0	1-3 portions/week	3+ portions/week	interaction
Sex				
Male	Reference (1)	0.92 (0.77, 1.11)	1.01 (0.85, 1.20)	0.54
Female	Reference (1)	0.95 (0.81, 1.13)	1.08 (0.93, 1.26)	
Age group, years				
<65	Reference (1)	0.95 (0.78, 1.17)	0.98 (0.79, 1.21)	0.76
≥65	Reference (1)	0.92 (0.79, 1.08)	1.07 (0.94, 1.22)	
Education				
Primary or below	Reference (1)	0.94 (0.79, 1.12)	1.12 (0.94, 1.32)	

Secondary or above	Reference (1)	0.86 (0.72, 1.03)	1.09 (0.94, 1.27)	0.58
Smoking status				
Never	Reference (1)	0.96 (0.82, 1.12)	1.11 (0.97, 1.26)	
Ever	Reference (1)	0.91 (0.74, 1.13)	0.92 (0.75, 1.13)	0.30
Alcohol use				
Never	Reference (1)	0.94 (0.82, 1.08)	1.02 (0.90, 1.16)	
Ever	Reference (1)	0.93 (0.72, 1.21)	1.15 (0.91, 1.45)	0.79
Physical activity				
Inactive or minimally active	Reference (1)	0.94 (0.80, 1.11)	1.06 (0.92, 1.23)	
Active	Reference (1)	0.93 (0.76, 1.13)	1.02 (0.86, 1.21)	0.96
BMI, kg/m <sup>2</sup>				
<25	Reference (1)	0.87 (0.74, 1.02)	1.05 (0.91, 1.20)	

$\geq 25$	Reference (1)	1.05 (0.86, 1.28)	1.05 (0.87, 1.26)	0.33
Self-rated health				
Good	Reference (1)	0.97 (0.84, 1.11)	1.09 (0.96, 1.23)	
Poor	Reference (1)	0.82 (0.61, 1.10)	0.87 (0.67, 1.15)	0.48
History of diabetes				
Yes	Reference (1)	0.81 (0.60, 1.10)	1.26 (1.01, 1.58)*	
No	Reference (1)	0.96 (0.84, 1.10)	0.99 (0.87, 1.12)	0.07
History of hypertension				
Yes	Reference (1)	1.04 (0.82, 1.30)	1.00 (0.81, 1.23)	
No	Reference (1)	0.90 (0.77, 1.04)	1.07 (0.94, 1.22)	0.34
History of hyperlipidemia				
Yes	Reference (1)	0.69 (0.44, 1.09)	0.84 (0.56, 1.26)	

No	Reference (1)	0.96 (0.84, 1.10)	1.07 (0.95, 1.20)	0.35
aHEI-2010 score				
< median	Reference (1)	0.85 (0.71, 1.01)	1.10 (0.94, 1.28)	
≥ median	Reference (1)	1.05 (0.88, 1.25)	1.01 (0.86, 1.19)	<0.01

Abbreviations: aHEI, alternate Healthy Eating Index.

†: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension, hyperlipidemia and aHEI-2010 score respectively.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001

**Supplementary Table 8.** Adjusted hazards ratios (HRs)<sup>†</sup> and 95% confidence interval (CIs) of cancer mortality by baseline milk consumption stratified by selected baseline characteristics.

	Milk consumption, 1 portion=250 ml			P value for interaction
	0	1-3 portions/week	3+ portions/week	
Sex				
Male	Reference (1)	1.10 (0.83, 1.46)	1.24 (0.96, 1.60)	0.35
Female	Reference (1)	1.01 (0.77, 1.32)	1.40 (1.12, 1.74)**	
Age group, years				
<65	Reference (1)	1.16 (0.88, 1.54)	1.40 (1.07, 1.84)*	0.65
≥65	Reference (1)	0.95 (0.72, 1.25)	1.27 (1.02, 1.57)	
Education (%)				
Primary or below	Reference (1)	1.08 (0.81, 1.44)	1.34 (1.02, 1.76)	

Secondary or above	Reference (1)	0.97 (0.75, 1.26)	1.39 (1.12, 1.72)**	0.19
Smoking status				
Never	Reference (1)	1.01 (0.79, 1.30)	1.42 (1.17, 1.74)**	
Ever	Reference (1)	1.11 (0.81, 1.53)	1.11 (0.81, 1.50)	0.11
Alcohol use				
Never	Reference (1)	1.04 (0.83, 1.31)	1.33 (1.10, 1.61)**	
Ever	Reference (1)	1.07 (0.72, 1.58)	1.32 (0.93, 1.87)	0.98
Physical activity (%)				
Inactive or minimally active	Reference (1)	1.03 (0.80, 1.32)	1.35 (1.08, 1.69)**	
Active	Reference (1)	1.09 (0.81, 1.48)	1.29 (1.00, 1.66)	0.90
BMI, kg/m <sup>2</sup>				
<25	Reference (1)	0.96 (0.75, 1.23)	1.32 (1.07, 1.62)*	

$\geq 25$	Reference (1)	1.21 (0.88, 1.64)	1.35 (1.02, 1.77)*	0.52
Self-rated health				
Good or very good	Reference (1)	1.08 (0.87, 1.34)	1.34 (1.12, 1.61)**	
Poor or very poor	Reference (1)	0.90 (0.56, 1.46)	1.25 (0.84, 1.86)	0.86
History of diabetes				
Yes	Reference (1)	0.90 (0.53, 1.53)	1.49 (1.02, 2.17)*	
No	Reference (1)	1.07 (0.87, 1.32)	1.29 (1.07, 1.56)**	0.47
History of hypertension				
Yes	Reference (1)	1.28 (0.87, 1.87)	1.42 (1.01, 1.99)*	
No	Reference (1)	0.99 (0.79, 1.24)	1.30 (1.07, 1.58)**	0.65
History of hyperlipidemia				
Yes	Reference (1)	0.91 (0.44, 1.89)	0.98 (0.50, 1.91)	

No	Reference (1)	1.07 (0.87, 1.30)	1.36 (1.14, 1.62) <sup>***</sup>	0.75
aHEI-2010 score				
< median	Reference (1)	0.97 (0.74, 1.28)	1.29 (1.02, 1.65) <sup>*</sup>	
≥ median	Reference (1)	1.13 (0.86, 1.50)	1.38 (1.09, 1.74) <sup>**</sup>	0.73

Abbreviations: aHEI, alternate Healthy Eating Index.

†: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension, hyperlipidemia and aHEI-2010 score respectively.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001



**Supplementary Table 9.** Adjusted hazards ratios (HRs)<sup>†</sup> and 95% confidence interval (CIs) of IHD mortality by baseline milk consumption stratified by selected baseline characteristics.

	Milk consumption, 1 portion=250 ml			P value for
	0	1-3 portions/week	3+ portions/week	interaction
Sex				
Male	Reference (1)	0.50 (0.26, 0.95)*	0.88 (0.56, 1.39)	0.83
Female	Reference (1)	0.65 (0.39, 1.07)	0.89 (0.60, 1.33)	
Age group, years				
<65	Reference (1)	0.57 (0.28, 1.14)	0.62 (0.31, 1.25)	0.45
≥65	Reference (1)	0.57 (0.35, 0.92)*	0.96 (0.69, 1.34)	
Education (%)				
Primary or below	Reference (1)	0.49 (0.27, 0.88)*	0.82 (0.51, 1.33)	

Secondary or above	Reference (1)	0.59 (0.34, 1.00)	1.06 (0.72, 1.56)	0.35
Smoking status				
Never	Reference (1)	0.57 (0.35, 0.94)*	1.04 (0.74, 1.48)	
Ever	Reference (1)	0.61 (0.32, 1.18)	0.56 (0.30, 1.05)	0.21
Alcohol use				
Never	Reference (1)	0.62 (0.40, 0.95)*	0.87 (0.63, 1.22)	
Ever	Reference (1)	0.39 (0.14, 1.09)	0.91 (0.46, 1.81)	0.79
Physical activity (%)				
Inactive or minimally active	Reference (1)	0.65 (0.39, 1.07)	0.95 (0.64, 1.41)	
Active	Reference (1)	0.46 (0.24, 0.88)*	0.82 (0.52, 1.29)	0.70
BMI, kg/m <sup>2</sup>				
<25	Reference (1)	0.68 (0.42, 1.10)	1.05 (0.73, 1.51)	

$\geq 25$	Reference (1)	0.42 (0.20, 0.86)*	0.65 (0.38, 1.12)	0.17
Self-rated health				
Good or very good	Reference (1)	0.67 (0.44, 1.01)	0.90 (0.65, 1.25)	
Poor or very poor	Reference (1)	0.23 (0.06, 0.96)*	0.87 (0.42, 1.82)	0.20
History of diabetes				
Yes	Reference (1)	0.38 (0.15, 0.95)*	0.99 (0.57, 1.70)	
No	Reference (1)	0.65 (0.42, 1.01)	0.85 (0.59, 1.22)	0.55
History of hypertension				
Yes	Reference (1)	0.70 (0.39, 1.29)	0.77 (0.46, 1.29)	
No	Reference (1)	0.50 (0.30, 0.85)*	0.96 (0.66, 1.39)	0.49
History of hyperlipidemia				
Yes	Reference (1)	0.74 (0.31, 1.81)	0.74 (0.30, 1.81)	

No	Reference (1)	0.53 (0.34, 0.83)**	0.91 (0.66, 1.25)	0.56
aHEI-2010 score				
< median	Reference (1)	0.58 (0.34, 0.97)*	0.87 (0.57, 1.32)	
≥ median	Reference (1)	0.56 (0.30, 1.05)	0.92 (0.60, 1.42)	0.95

Abbreviations: aHEI, alternate Healthy Eating Index.

†: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension, hyperlipidemia and aHEI-2010 score respectively.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001

**Supplementary Table 10.** Adjusted hazards ratios (HRs)<sup>†</sup> and 95% confidence interval (CIs) of stroke mortality by baseline milk consumption stratified by selected baseline characteristics.

	Milk consumption, 1 portion=250 ml			P value for
	0	1-3 portions/week	3+ portions/week	interaction
Sex				
Male	Reference (1)	0.57 (0.30, 1.06)	0.99 (0.63, 1.54)	0.67
Female	Reference (1)	0.77 (0.46, 1.28)	0.81 (0.52, 1.27)	
Age group, years				
<65	Reference (1)	0.48 (0.22, 1.06)	0.21 (0.06, 0.66)**	<0.01
≥65	Reference (1)	0.74 (0.47, 1.16)	1.15 (0.82, 1.60)	
Education (%)				
Primary or below	Reference (1)	0.52 (0.29, 0.94)*	1.10 (0.71, 1.70)	

Secondary or above	Reference (1)	0.74 (0.44, 1.26)	0.85 (0.54, 1.33)	0.03
Smoking status				
Never	Reference (1)	0.76 (0.48, 1.18)	0.97 (0.67, 1.40)	
Ever	Reference (1)	0.48 (0.21, 1.09)	0.72 (0.38, 1.36)	0.48
Alcohol use				
Never	Reference (1)	0.62 (0.39, 0.99)*	0.84 (0.59, 1.22)	
Ever	Reference (1)	0.79 (0.38, 1.67)	1.03 (0.55, 1.94)	0.73
Physical activity (%)				
Inactive or minimally active	Reference (1)	0.71 (0.42, 1.18)	0.98 (0.65, 1.49)	
Active	Reference (1)	0.62 (0.34, 1.16)	0.77 (0.47, 1.25)	0.74
BMI, kg/m <sup>2</sup>				
<25	Reference (1)	0.68 (0.41, 1.10)	0.84 (0.56, 1.27)	

$\geq 25$	Reference (1)	0.64 (0.33, 1.23)	0.96 (0.58, 1.58)	0.94
Self-rated health				
Good or very good	Reference (1)	0.69 (0.45, 1.06)	1.01 (0.73, 1.41)	
Poor or very poor	Reference (1)	0.53 (0.21, 1.34)	0.36 (0.13, 1.01)	0.16
History of diabetes				
Yes	Reference (1)	0.29 (0.07, 1.22)	1.14 (0.58, 2.28)	
No	Reference (1)	0.72 (0.48, 1.08)	0.82 (0.58, 1.18)	0.28
History of hypertension				
Yes	Reference (1)	0.38 (0.15, 0.93)*	0.75 (0.41, 1.37)	
No	Reference (1)	0.77 (0.50, 1.19)	0.96 (0.66, 1.39)	0.35
History of hyperlipidemia				
Yes	Reference (1)	0.22 (0.03, 1.64)	0.41 (0.09, 1.80)	

No	Reference (1)	0.70 (0.47, 1.04)	0.93 (0.68, 1.30)	0.27
aHEI-2010 score				
< median	Reference (1)	0.54 (0.30, 0.97)*	1.00 (0.64, 1.56)	
≥ median	Reference (1)	0.80 (0.47, 1.35)	0.78 (0.50, 1.23)	0.47

Abbreviations: aHEI, alternate Healthy Eating Index.

†: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension, hyperlipidemia and aHEI-2010 score respectively.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001



**Supplementary Table 11.** Adjusted hazards ratios (HRs) and 95% confidence interval (CIs) of mortality from all-cause, cardiovascular disease and cancer by baseline milk consumption for four groups in 18,214 participants in 2003-2006 and followed up until December 2017.

	Milk consumption, 1 portion=250 ml				P for trend
	0	1-3 portions/week	4-6 portions/week	7+ portions/week	
<b>Person-years</b>	155,144	32,075	10,439	24,476	
<b>All-cause</b>					
No. of deaths	1,979	304	105	309	
Mortality rate, per 10,000 person-year	127.6	94.8	100.6	126.2	
Model 1	Reference (1)	0.76 (0.68, 0.86) <sup>***</sup>	0.80 (0.66, 0.98) <sup>*</sup>	1.00 (0.89, 1.13)	0.14
Model 2	Reference (1)	0.93 (0.82, 1.05)	0.96 (0.79, 1.17)	1.07 (0.94, 1.20)	0.60
Model 3 plus dietary patterns					
aMED diet score	Reference (1)	0.92 (0.82, 1.05)	0.95 (0.78, 1.16)	1.04 (0.92, 1.18)	0.84

DASH diet score	Reference (1)	0.92 (0.82, 1.05)	0.96 (0.79, 1.18)	1.05 (0.93, 1.19)	0.69
aHEI-2010 score	Reference (1)	0.92 (0.81, 1.04)	0.95 (0.78, 1.17)	1.05 (0.92, 1.19)	0.77
<b>Cardiovascular disease</b>					
No. of deaths	713	78	39	87	
Mortality rate, per 10,000 person-year	46.0	24.3	37.4	35.6	
Model 1	Reference (1)	0.55 (0.44, 0.70) <sup>***</sup>	0.84 (0.61, 1.15)	0.78 (0.63, 0.98) <sup>*</sup>	<0.01
Model 2	Reference (1)	0.72 (0.57, 0.91) <sup>**</sup>	1.04 (0.75, 1.45)	0.82 (0.65, 1.03)	0.06
Model 3 plus dietary patterns					
aMED diet score	Reference (1)	0.72 (0.57, 0.91) <sup>**</sup>	1.05 (0.75, 1.46)	0.81 (0.64, 1.02)	0.05
DASH diet score	Reference (1)	0.72 (0.57, 0.91) <sup>**</sup>	1.05 (0.76, 1.46)	0.81 (0.64, 1.02)	0.04
aHEI-2010 score	Reference (1)	0.72 (0.57, 0.92) <sup>**</sup>	1.07 (0.76, 1.49)	0.81 (0.64, 1.03)	0.06

**Cancer**

No. of deaths	702	133	46	148	
Mortality rate, per 10,000 person-year	45.2	41.5	44.1	60.5	
Model 1	Reference (1)	0.93 (0.77, 1.11)	0.98 (0.73, 1.32)	1.34 (1.12, 1.60)**	<0.01
Model 2	Reference (1)	1.08 (0.89, 1.31)	1.16 (0.86, 1.58)	1.44 (1.20, 1.73)***	<0.01
Model 3 plus dietary patterns					
aMED diet score	Reference (1)	1.08 (0.89, 1.31)	1.16 (0.85, 1.57)	1.41 (1.17, 1.69)***	<0.01
DASH diet score	Reference (1)	1.08 (0.89, 1.31)	1.17 (0.86, 1.58)	1.42 (1.18, 1.71)***	<0.01
aHEI-2010 score	Reference (1)	1.07 (0.88, 1.30)	1.13 (0.83, 1.54)	1.40 (1.17, 1.69)***	<0.01
<b>Excluding deaths within first 2 years</b>					
<b>Person-years</b>	155,020	32,048	10,433	24,458	
<b>All-cause</b>					
No. of deaths	1875	281	102	292	

Mortality rate, per 10,000 person-year	121.0	87.7	97.8	119.4	
Model 1	Reference (1)	0.75 (0.66, 0.85) <sup>***</sup>	0.83 (0.68, 1.01)	1.00 (0.88, 1.13)	0.15
Model 2	Reference (1)	0.91 (0.80, 1.03)	0.99 (0.81, 1.22)	1.06 (0.93, 1.20)	0.59
Model 3 plus dietary patterns					
aMED diet score	Reference (1)	0.91 (0.80, 1.03)	0.99 (0.80, 1.21)	1.04 (0.92, 1.18)	0.79
DASH diet score	Reference (1)	0.91 (0.80, 1.03)	1.00 (0.81, 1.22)	1.05 (0.93, 1.20)	0.64
aHEI-2010 score	Reference (1)	0.90 (0.79, 1.03)	0.99 (0.80, 1.21)	1.05 (0.92, 1.19)	0.72
<b>Cardiovascular disease</b>					
No. of deaths	687	74	38	86	
Mortality rate, per 10,000 person-year	44.3	23.1	36.4	35.2	
Model 1	Reference (1)	0.54 (0.43, 0.69) <sup>***</sup>	0.85 (0.61, 1.17)	0.81 (0.64, 1.01)	<0.01
Model 2	Reference (1)	0.71 (0.55, 0.90) <sup>**</sup>	1.05 (0.75, 1.47)	0.84 (0.67, 1.06)	0.09

## Model 3 plus dietary patterns

aMED diet score	Reference (1)	0.71 (0.55, 0.90)**	1.06 (0.76, 1.48)	0.83 (0.66, 1.05)	0.08
DASH diet score	Reference (1)	0.70 (0.55, 0.90)**	1.06 (0.76, 1.49)	0.83 (0.66, 1.04)	0.07
aHEI-2010 score	Reference (1)	0.71 (0.56, 0.91)**	1.08 (0.77, 1.51)	0.84 (0.66, 1.06)	0.10

**Cancer**

No. of deaths	662	123	45	134	
Mortality rate, per 10,000 person-year	42.7	38.4	43.1	54.8	
Model 1	Reference (1)	0.91 (0.75, 1.10)	1.02 (0.75, 1.38)	1.29 (1.07, 1.55)**	0.03
Model 2	Reference (1)	1.06 (0.87, 1.29)	1.20 (0.88, 1.64)	1.39 (1.15, 1.68)**	<0.01

## Model 3 plus dietary patterns

aMED diet score	Reference (1)	1.06 (0.87, 1.29)	1.20 (0.88, 1.64)	1.36 (1.12, 1.66)**	<0.01
DASH diet score	Reference (1)	1.05 (0.86, 1.29)	1.21 (0.89, 1.65)	1.38 (1.13, 1.67)**	<0.01

aHEI-2010 score	Reference (1)	1.04 (0.85, 1.27)	1.18 (0.86, 1.61)	1.36 (1.12, 1.65)**	<0.01
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Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension.

Model 1: Crude model.

Model 2: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension and hyperlipidemia, as appropriate.

Model 3: Additionally adjusted for daily dietary energy intake.

\*:  $P < 0.05$ ; \*\*:  $P < 0.01$ ; \*\*\*:  $P < 0.001$

**Supplementary Table 12.** Adjusted hazards ratios (HRs) and 95% confidence interval (CIs) of mortality from all-cause, cardiovascular disease and cancer by baseline milk consumption for five groups in 18,214 participants in 2003-2006 and followed up until December 2017.

	Milk consumption, 1 portion=250 ml					P for trend
	0	1-2 portions/week	3-4 portions/week	5-6 portions/week	7+ portions/week	
<b>Person-years</b>	155,144	18,880	19,094	4,540	24,462	
<b>All-cause</b>						
No. of deaths	1,979	173	197	30	309	
Mortality rate, per 10,000 person-year	127.6	91.6	103.2	85.9	126.3	
Model 1	Reference (1)	0.74 (0.63, 0.86) <sup>***</sup>	0.83 (0.72, 0.96) <sup>*</sup>	0.68 (0.50, 0.94) <sup>*</sup>	1.00 (0.89, 1.13)	0.13
Model 2	Reference (1)	0.91 (0.77, 1.07)	1.00 (0.86, 1.16)	0.78 (0.56, 1.09)	1.06 (0.94, 1.20)	0.66
Model 3 plus dietary patterns						

aMED diet score	Reference (1)	0.91 (0.77, 1.07)	0.99 (0.85, 1.15)	0.77 (0.56, 1.08)	1.04 (0.92, 1.18)	0.91
DASH diet score	Reference (1)	0.90 (0.77, 1.06)	1.00 (0.86, 1.16)	0.78 (0.56, 1.08)	1.05 (0.93, 1.19)	0.76
aHEI-2010 score	Reference (1)	0.90 (0.77, 1.06)	0.99 (0.85, 1.15)	0.77 (0.55, 1.08)	1.05 (0.92, 1.19)	0.84
<b>Cardiovascular disease</b>						
No. of deaths	713	43	60	14	87	
Mortality rate, per 10,000 person-year	46.0	22.8	31.4	30.8	35.6	
Model 1	Reference (1)	0.52 (0.38, 0.70) <sup>***</sup>	0.71 (0.55, 0.93) <sup>*</sup>	0.68 (0.40, 1.16)	0.79 (0.63, 0.98) <sup>*</sup>	<0.01
Model 2	Reference (1)	0.71 (0.52, 0.97) <sup>*</sup>	0.87 (0.67, 1.14)	0.82 (0.47, 1.43)	0.82 (0.65, 1.03)	0.04
Model 3 plus dietary patterns						
aMED diet score	Reference (1)	0.72 (0.53, 0.98) <sup>*</sup>	0.88 (0.67, 1.15)	0.82 (0.47, 1.42)	0.81 (0.64, 1.02)	0.03
DASH diet score	Reference (1)	0.71 (0.52, 0.97) <sup>*</sup>	0.88 (0.67, 1.15)	0.81 (0.47, 1.41)	0.80 (0.64, 1.01)	0.03





**2 years**

<b>Person-years</b>	155,020	18,869	19,074	4,538	24,444
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**All-cause**

No. of deaths	1,875	162	183	38	292
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Mortality rate, per 10,000	121.0	85.9	95.9	83.7	119.5
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person-year

Model 1	Reference (1)	0.73 (0.62, 0.86)***	0.82 (0.70, 0.95)**	0.70 (0.51, 0.97)*	1.00 (0.88, 1.13)	0.13
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Model 2	Reference (1)	0.91 (0.77, 1.07)	0.86 (0.84, 1.15)	0.81 (0.58, 1.13)	1.06 (0.93, 1.20)	0.70
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Model 3 plus dietary patterns

aMED diet score	Reference (1)	0.91 (0.77, 1.07)	0.97 (0.83, 1.14)	0.80 (0.57, 1.12)	1.04 (0.91, 1.18)	0.92
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DASH diet score	Reference (1)	0.90 (0.77, 1.07)	0.98 (0.84, 1.15)	0.81 (0.58, 1.13)	1.05 (0.93, 1.20)	0.75
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aHEI-2010 score	Reference (1)	0.90 (0.76, 1.07)	0.97 (0.83, 1.14)	0.80 (0.57, 1.13)	1.05 (0.92, 1.19)	0.84
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**Cardiovascular disease**

No. of deaths	687	41	58	13	86	
Mortality rate, per 10,000 person-year	44.3	21.7	30.4	28.6	35.2	
Model 1	Reference (1)	0.51 (0.37, 0.70) <sup>***</sup>	0.72 (0.55, 0.94) <sup>*</sup>	0.66 (0.38, 1.14)	0.81 (0.64, 1.01)	<0.01
Model 2	Reference (1)	0.70 (0.51, 0.96) <sup>*</sup>	0.88 (0.67, 1.15)	0.79 (0.44, 1.39)	0.84 (0.67, 1.06)	0.06
Model 3 plus dietary patterns						
aMED diet score	Reference (1)	0.71 (0.51, 0.97) <sup>*</sup>	0.88 (0.67, 1.15)	0.83 (0.44, 1.38)	0.83 (0.66, 1.05)	0.05
DASH diet score	Reference (1)	0.70 (0.51, 0.96) <sup>*</sup>	0.88 (0.67, 1.16)	0.78 (0.44, 1.38)	0.83 (0.65, 1.04)	0.05
aHEI-2010 score	Reference (1)	0.71 (0.51, 0.97) <sup>**</sup>	0.90 (0.68, 1.18)	0.76 (0.42, 1.38)	0.83 (0.66, 1.06)	0.06

**Cancer**

No. of deaths	662	76	73	19	134
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Mortality rate, per 10,000 person-year	42.7	40.3	38.3	41.9	54.8	
Model 1	Reference (1)	0.95 (0.75, 1.21)	0.91 (0.71, 1.15)	0.98 (0.62, 1.55)	1.29 (1.07, 1.55)**	0.04
Model 2	Reference (1)	1.13 (0.88, 1.44)	1.06 (0.82, 1.36)	1.13 (0.71, 1.81)	1.39 (1.14, 1.68)**	<0.01
Model 3 plus dietary patterns						
aMED diet score	Reference (1)	1.13 (0.88, 1.44)	1.05 (0.82, 1.36)	1.12 (0.70, 1.79)	1.36 (1.12, 1.66)**	<0.01
DASH diet score	Reference (1)	1.11 (0.88, 1.43)	1.06 (0.83, 1.36)	1.12 (0.70, 1.80)	1.37 (1.13, 1.67)**	<0.01
aHEI-2010 score	Reference (1)	1.11 (0.87, 1.42)	1.02 (0.79, 1.32)	1.13 (0.71, 1.81)	1.36 (1.12, 1.65)**	<0.01

Abbreviations: aMED, alternate Mediterranean diet; aHEI, alternate Healthy Eating Index; DASH, Dietary Approaches to Stop Hypertension.

Model 1: Crude model.

Model 2: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension and hyperlipidemia, as appropriate.

Model 3: Additionally adjusted for daily dietary energy intake.

\*:  $P < 0.05$ ; \*\*:  $P < 0.01$ ; \*\*\*:  $P < 0.001$

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**Supplementary Table 13.** Adjusted hazards ratios (HRs) and 95% confidence interval (CIs) of death of cancer by baseline milk consumption after excluding participants with history of cancer at baseline in 19,618 participants in 2003-2006 and followed up until December 2017.

	Milk consumption, 1 portion=250 ml			P for trend
	0	1-3 portions/week	3+ portions/week	
<b>Person-years</b>	178,735	36,983	39,839	
<b>Total cancer</b>				
No. of deaths	843	150	216	
Mortality rate, per 10,000 person-year	47.2	40.6	54.2	
Model 3 plus aHEI-2010 score	Reference (1)	1.02 (0.85, 1.22)	1.24 (1.06, 1.45)**	0.01
<b>Lung cancer</b>				
No. of deaths	304	43	57	
Mortality rate, per 10,000 person-year	17.0	11.6	14.3	

Model 3 plus aHEI-2010 score	Reference (1)	0.82 (0.59, 1.15)	0.97 (0.72, 1.30)	0.60
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### Liver cancer

No. of deaths	106	14	28	
Mortality rate, per 10,000 person-year	5.9	3.8	7.0	
Model 3 plus aHEI-2010 score	Reference (1)	0.85 (0.48, 1.50)	1.22 (0.78, 1.92)	0.51

### Gastrointestinal Cancer

No. of deaths	42	5	14	
Mortality rate, per 10,000 person-year	2.3	1.4	3.5	
Model 3 plus aHEI-2010 score	Reference (1)	0.69 (0.27, 1.77)	1.60 (0.85, 3.00)	0.24

### Colorectal and anal cancer

No. of deaths	115	26	22	
Mortality rate, per 10,000 person-year	6.4	7.0	5.5	

Model 3 plus aHEI-2010 score	Reference (1)	1.29 (0.83, 2.01)	0.93 (0.58, 1.49)	0.94
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### Esophagus cancer

No. of deaths	17	4	9	
Mortality rate, per 10,000 person-year	1.0	1.1	2.3	
Model 3 plus aHEI-2010 score	Reference (1)	1.69 (0.55, 5.21)	3.62 (1.51, 8.65)**	<0.01

Abbreviations: aHEI, alternate Healthy Eating Index.

Model 3: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension, hyperlipidemia and daily dietary energy intake, as appropriate.

\*: P<0.05; \*\*: P<0.01; \*\*\*: P<0.001



**Supplementary Table 14.** Adjusted hazards ratios (HRs) and 95% confidence interval (CIs) of mortality from all-cause, cardiovascular disease and cancer by baseline all dairy products consumption for four groups in 18,214 participants in 2003-2006 and followed up until December 2017.

	Milk consumption, 1 portion=250 ml				P for trend
	0	1 portion/week	2 portions/week	3+ portions/week	
<b>Person-years</b>	149,165	33,410	35,950	3,595	
<b>All-cause</b>					
No. of deaths	1,929	310	417	41	
Mortality rate, per 10,000 person-year	129.3	92.8	116.0	114.1	
Model 3 plus aHEI-2010 score	Reference (1)	0.91 (0.80, 1.03)	1.01 (0.90, 1.13)	1.21 (0.88, 1.66)	0.88
<b>Cardiovascular disease</b>					
No. of deaths	689	84	125	19	

Mortality rate, per 10,000 person-year	46.2	25.1	34.8	52.9	
Model 3 plus aHEI-2010 score	Reference (1)	0.74 (0.59, 0.94)*	0.87 (0.71, 1.06)	1.75 (1.09, 2.81)*	0.32
<b>Cancer</b>					
No. of deaths	686	135	195	13	
Mortality rate, per 10,000 person-year	46.0	40.4	54.2	36.2	
Model 3 plus aHEI-2010 score	Reference (1)	1.01 (0.84, 1.23)	1.29 (1.09, 1.52)**	0.92 (0.52, 1.64)	0.02
<b>Excluding deaths within first 2 years</b>					
<b>Person-years</b>	149,041	33,383	35,927	3,595	
<b>All-cause</b>					
No. of deaths	1,826	287	397	40	
Mortality rate, per 10,000 person-year	122.5	86.0	110.5	111.3	
Model 3 plus aHEI-2010 score	Reference (1)	0.88 (0.78, 1.01)	1.02 (0.91, 1.14)	1.26 (0.91, 1.74)	0.75

**Cardiovascular disease**

No. of deaths	664	80	123	18	
Mortality rate, per 10,000 person-year	44.6	24.0	34.2	50.1	
Model 3 plus aHEI-2010 score	Reference (1)	0.74 (0.58, 0.93)*	0.89 (0.72, 1.09)	1.73 (1.06, 2.82)*	0.40

**Cancer**

No. of deaths	646	125	180	13	
Mortality rate, per 10,000 person-year	43.3	37.4	50.1	36.2	
Model 3 plus aHEI-2010 score	Reference (1)	0.99 (0.81, 1.21)	1.27 (1.07, 1.51)**	0.99 (0.56, 1.77)	0.03

Abbreviations: aHEI, alternate Healthy Eating Index.

Note: All dairy products were milk, cheese, cream, yogurt and butter. One portion of dairy products equals to 250 ml for milk or 20 g for cheese or 150 ml for cream or 150 g for yogurt, or 10 g for butter.

Model 3: Adjusted for sex, age, family income, education, occupation, smoking status, alcohol use, physical activity, body mass index, self-rated health, diabetes, hypertension, hyperlipidemia and daily dietary energy intake, as appropriate.

\*:  $P < 0.05$ ; \*\*:  $P < 0.01$ ; \*\*\*:  $P < 0.001$

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