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Dairy intake and risk of type 2 diabetes

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Abstract

Background & aims—The effect of total dairy products, milk, and calcium intake on risk of type 2 diabetes (T2D) is uncertain, particularly in the Chinese population.

Methods—The present study was based a prospective cohort of 63,257 Chinese men and women aged 45–74 years during enrollment (1993–1998) in Singapore. Dietary information was obtained using a validated 165-item semi-quantitative food-frequency questionnaire. Information about newly diagnosed T2D was collected by self-report during two follow-up interviews in 1999–2004 and 2006–2010. Cox proportional hazard regression method was used to estimate hazard ratios (HRs) and their 95% confidence intervals (CIs) in 45,411 eligible participants.

Results—Incidence rate (95% CI) of T2D was 10.5 (10.2–10.8) per 1000 person-years. Intake of dairy food was significantly associated with reduced T2D risk; compared with the lowest quartile, HRs (95% CI) for the second, third and fourth quartiles of dairy intake were 0.98 (0.91–1.06), 0.96 (0.89–1.03) and 0.90 (0.83–0.98), respectively, after adjustment for potential confounders at baseline (P-trend= 0.01). Daily drinkers of milk had a significant 12% reduction in T2D risk compared with non-drinkers. While dairy calcium was associated with a decreased risk of T2D (HR comparing extreme quartiles 0.84; 95% CI 0.76–0.93; P-trend= 0.001), no association was found for non-dairy calcium (HR 1.02; 95% CI 0.92–1.14; P-trend= 0.61).

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Conclusions—In this large cohort study of Chinese adults, dairy product intake and daily milk consumption was associated with a statistically significant, although modest, decrease in risk of developing T2D, which may be independent of its calcium content.

Keywords

Dairy Products; Milk; Calcium; Type 2 Diabetes; Prospective Cohort Study; Chinese

Introduction

The number of adults with type 2 diabetes (T2D) has quadrupled since 1980 (1). While mortality due to many causes has declined, there has been a median 9% increase in age-standardized rate of death due to T2D worldwide (2). The large and fast growing burden of T2D in the world (3) has made primary prevention a public health imperative. It is well established that T2D is related to lifestyle, including diet, and in large-scale intervention studies, its progression was reduced by about 40% through the promotion of a healthy diet and physical activity (4).

Dairy products contain many components with potential anti-diabetes effects, including calcium, vitamin D, magnesium, and whey protein (5). However, the benefits of these components may be offset by the diabetogenic effects of saturated fatty acids in dairy products (6). Findings of observational studies have been mixed for the association between total dairy or milk intake and risk of T2D (7, 8). In a meta-analysis of 22 cohort studies, a modest dose-response inverse association was found with total dairy intake, whereas the association with milk was not significant. However a large heterogeneity was noted among these studies (8). Furthermore, the pooled subgroup analysis of three Asian studies showed an inverse but non-statistically significant association between total dairy and milk intake and risk of T2D but with a large heterogeneity among studies (8). Given the observed evidence of a nonlinear association between dairy and T2D risk (7), studying this association in Asian populations will fill in the missing knowledge gap regarding the lower intake range, with the reference group being individuals with no or little dairy intake in their usual diet.

According to the US Food and Drug Administration database, 30% of daily need for calcium could be satisfied by a cup of milk (9). Calcium may have a potential preventive role against glycaemia and weight gain (10), and since dairy food is a rich source for calcium, this mineral may be the mediating factor that accounts for the inverse association between dairy intake and T2D in observational studies. Thus, it is difficult, if not impossible, to distinguish impact of calcium on T2D risk in epidemiological data from populations with high dairy intake. Asian populations tend to have generally lower dairy intake and more varied dietary sources of calcium, but findings that attempted to differentiate the effects of calcium from dairy food in such populations have yielded conflicting results (11, 12). In this study, we aimed to prospectively evaluate the association of total dairy, milk, and calcium (dairy/non-dairy) intake with risk of incident T2D in a cohort of Chinese residing in Singapore.

Materials and Methods

Study population

The Singapore Chinese Health Study is a population-based cohort study established between April 1993 and December 1998 by recruiting 35,303 Chinese women and 27,954 Chinese men aged 45 to 74 years (13). The participants were from two major dialect groups in Singapore: the Hokkiens and Cantonese, who originated from Fujian and Guangdong provinces in Southern China, respectively. Briefly, all participants were interviewed in-person using structured questionnaires at recruitment. Surviving participants were followed-up via telephone call at Follow-up I (1999–2004) and Follow-up II (2006–2010). The Institutional Review Board at the National University of Singapore approved the study and informed consent was obtained from all the study subjects.

Assessment of diet and covariates

Information on usual diet for the past one year was collected using a semi-quantitative 165-item food-frequency questionnaire (FFQ) about commonly consumed food by this population at baseline. The FFQ was subsequently validated in a subset of 810 participants by a repeat administration as well as by comparing with two 24-hour recalls (13). According to validation study, similar distributions were observed by the two methods, and most mean pairs for energy and nutrients were within 10% of each other's values. The correlation coefficients also ranged between 0.24 and 0.79 for energy and nutrient values assessed by these two methods (13), which is comparable with a previous validation study in diverse populations (14). Specifically for calcium intake, the validation study yielded correlation coefficients ranging from 0.51 to 0.62 for energy-adjusted values (13). For dietary intake, the respondents were required to select from 8 categories ranging from “never or hardly ever” to “two or more times a day”, and from 3 portion sizes (small, medium, large) with photographs provided as a guide. Among the items listed in the FFQ were three main items asking about commonly consumed dairy products in the local Chinese population comprising of: 1) milk including powdered, whole, low fat, and chocolate but excluding addition to coffee or tea; 2) Milo, Ovaltine, or Horlicks; and 3) Yakult or Vitagen (probiotic cultured milk drinks). The FFQ also had independent items about added milk to coffee or tea (evaporated or condensed), added butter to bread, as well as ice cream and frozen yogurt. We mainly calculated total dairy intake as the sum of all these items. In addition, to enhance the accuracy of estimated total dairy product intake, we took into account the small amounts of dairy products used in cooking procedures of local dishes (including rice dishes, mashed potatoes, fast foods, etc.). We further assessed total, dietary, dairy, and non-dairy calcium intake (in mg) from the Singapore Food Composition Database that was specifically developed for this cohort study (13).

We also collected self-reported information about subject's body weight, height, educational level, alcohol consumption, smoking status, and physical activity at recruitment. Body mass index (BMI, in kg/m^2) was calculated by body weight in kg divided by square of height in meter. For those with missing weight and/or height, BMI was calculated using imputed weight and/or height derived from the linear regression equation (15). Moreover, the

participants also reported their known medical conditions diagnosed by physicians such as hypertension, cancer, coronary heart disease and stroke at recruitment.

Assessment of T2D

Participants were asked for the history of T2D diagnosed by physician at recruitment and the two follow-up interviews using this question: “Have you been told by a doctor that you have diabetes (high blood sugar)?” If yes: “Please also tell me the age at which you were first diagnosed?” In a separate study on 1651 cohort subjects with self-reported history of physician-diagnosed T2D at baseline, the accuracy of the self-reported diabetes was validated in this cohort and found to be as high as 98.8% (16). Participants with a history of diagnosed T2D at recruitment were excluded from analysis. Individuals were considered as having incident T2D cases if they reported being diagnosed anytime between recruitment and subsequent follow-up interviews.

Statistical Analysis

Among 54,341 participants who were contacted in at least one follow-up interview, 45,411 subjects were eligible for this analysis (Figure 1). We employed Cox proportional hazard models to examine associations of total dairy intake, milk intake, and calcium intake with risk of incident T2D. Intake values were categorized by quartile distribution with the lowest quartile serving as the reference. We used the multivariate nutrient density model that adjusted for total energy intake in addition to the energy-adjusted dietary/nutrient component (exposure of interest) (17). Food/nutrient density is calculated through dividing food/nutrient intake by total energy intake, which is an accepted measure for studying intake with the consideration for total energy in nutritional studies and epidemiologic analyses. Person-years for each participant were calculated from the date of recruitment until the reported time of T2D diagnosis, or the date of last follow-up interview, whichever came first. In the multivariable model, we adjusted for age (continuous), sex, interview year (1993–1995, 1996–1998), dialect group (Hokkien, Cantonese), level of education (none, primary school, secondary school or more), physical activity level (<0.5, 0.5–<4, 4 hours/week), BMI (continuous), cigarette smoking (current, former, and never smoker), alcohol consumption (never or monthly, weekly, daily), baseline history of hypertension, total energy intake (continuous), coffee (quartiles), and soda intakes (glasses/week, continuous) as well as scores of two previously identified dietary patterns through principle component analysis (quartiles), which were associated with T2D risk: “vegetable, fruit, and soy-rich pattern” and “dim sum and meat-rich pattern” (18). In sensitivity analysis, we also adjusted for individual dietary items instead of dietary patterns comprising of red meat, poultry, fish/shellfish, soy, vegetables, and fruits and related juice.

We tested proportionality assumption using Schoenfeld residuals and no violation was seen. Linear trends were tested by assigning the median value of each quartile of dairy intake, and then using this ordinal variable in models. We also stratified analyses by gender using gender-specific quartiles. Potential interactions were tested using likelihood ratio test of the cross-product terms between median intake of quartiles and gender, age (categorized based on cohort median of 54 years at recruitment) and BMI (<23 and ≥23 kg/m²). All the statistical analyses were conducted using Stata Statistical Software, Release 14.2 (Stata

Corporation, College Station, TX), with 2-sided P value less than 5% as the threshold for statistical significance.

Results

The mean age (SD) of 45,411 participants included in this analysis was 55.2 (7.6) years and 19,409 (42.7%) were men. During a median 12 years of follow-up (494741 person-years), we identified 5207 incident T2D cases after baseline interview, resulting in an incidence rate (95% CI) of 10.5 (10.2–10.8) per 1000 person-years. The median (IQR) dairy intake in our study participants was 20.5 (5.19–75.0) g/day. Majority of participants never or hardly ever drank milk (67.4%). Daily milk intake was reported by 6,757 (14.9%) subjects, and 93.5% of them drank one glass of milk a day. Milk intake explained about 80% of dairy intake variation followed by intake of cheese and ice cream in the study population.

Table 1 shows the characteristics of participants according to their dairy intake. Participants with higher dairy intake were more women, smoked less and drank alcohol, coffee, and soda less but they had higher intake of fruits while lower intake of grains. Participants with lowest dairy intake (quartile 1) reported the highest total energy intake, followed by those with the highest dairy intake (quartile 4).

Dairy intake overall was significantly associated with a 10% reduction in risk of T2D after adjustment for potential confounders including dietary patterns, coffee and soda intake (Table 2). Similarly daily intake of milk was significantly associated with a 12% decrease in T2D risk (HR comparing daily drinkers vs. non-drinkers 0.88, 95% CI 0.81–0.96, P for trend=0.01). In sensitivity analysis, we further adjusted for individual dietary items instead of dietary pattern but it did not materially change the findings (data not shown). No significant interaction was observed for dairy or milk intake with sex, age and BMI for its association with T2D risk (all *P*s for interaction >0.15).

Median (IQR) total calcium intake in this cohort was 364 (260–523) mg/day, and this comprised of 18.6% contribution from dairy calcium and 80.4% contribution from non-dairy calcium (median percentage). Only about 3% of this cohort reported taking daily calcium supplements. Dietary calcium intake was inversely associated with T2D risk (Table 3); total calcium intake, which included supplemental calcium, also showed similar associations (data not shown). The association was strengthened when the models were adjusted for potassium, magnesium, phosphorus, and vitamin D. The same inverse association was observed with dairy calcium intake in fully adjusted model; compared to the lowest quartile of intake, those in the highest quartile had a 16% reduction in T2D risk (HR 0.84, 95% CI 0.76–0.93, P for trend=0.001). However, we found a null association between non-dairy calcium intake and T2D risk (HR comparing highest vs. lowest 1.02, 95% CI 0.92–1.14, P for trend=0.61). We also adjusted for individual dietary items in the model for sensitivity analysis, and the findings were essentially the same, with trivial changes to the risk estimates (data not shown). Interactions with sex, age, and BMI were also not statistically significant in these analyses (P for all >0.10).

Discussion

In this prospective study of Chinese middle-aged and elderly population, with relatively low intake of dairy products compared to Western populations, we found an inverse association between dairy intake and T2D risk. Daily intake of milk, the major component of dairy food in this population, was significantly associated with reduced risk of T2D too. Higher intake of dietary and dairy calcium was associated with decreased risk of T2D; however, the association with non-dairy calcium intake was null.

While a previous meta-analysis had reported an inverse association between dairy intake and T2D risk (19), the association became null when the meta-analysis was updated to include three large-scale US cohorts (6). These three studies, which constituted 41% of the weight in the meta-analysis, used reference groups with median dairy intakes that ranged from 0.6 to 0.9 servings/day (6). Later, Gijsbers et al., in a dose-response meta-analysis of 16 prospective cohort studies, reported a 3% decreased risk of T2D per 200 g/d total dairy intake (RR: 0.97; 95% CI: 0.95, 1.00; $P = 0.044$) but with significant heterogeneity among the studies (8). They also reported an inverse association in subgroup of three studies in Asian populations (RR: 0.85 per 200 g/d; 95% CI: 0.65, 1.12) but the association did not reach statistical significance and the studies had substantial heterogeneity (8). As for milk, they found no significant association in a pooled analysis of 11 studies; however, their subgroup analysis suggested divergent associations: a statistically significant 3% increased risk in European populations but an insignificant 13% decreased risk in Asian populations. As they found a non-linear inverse association for yogurt, they finally attributed the observed inverse association for total dairy to this dairy product (8). Total dairy consumption of those studies ranged from 162 to 347 g/d in the United States and from 121 to 400 g/d in Europe (8). In contrast, intake level in our study and three other Asian studies started from nil (12, 20) or <50 g/d (11).

Our findings corroborated well with a study of 64,191 Chinese woman aged 40–70 years from Shanghai, which reported that compared to non-consumers, the HR (95% CI) of T2D was 0.61 (0.54–0.69) for <100 g/d, 0.56 (0.50–0.62) for 100–200 g/d, and 0.46 (0.32–0.64) for >200 g/d milk intake (P for trend <0.001) (12). Zong et al. followed 2091 Chinese older than 50 years for six years, and also found an inverse association between total dairy intake and T2D risk that was independent of favorable changes in BMI and waist circumference. Likewise, they found daily intake of half a serving of milk or other dairy food to be associated with 28% and 31% decreased risk compared to non-consumers, respectively (20). In contrast, in a study in Japanese, an inverse reduction of T2D incidence was found only in women with dairy intake 300 g/d but not in men (11). In a Mendelian randomization study involving 97,811 Danish individuals, no significant association was found between genotypes of lactase persistence favoring higher milk intake and T2D risk. However, the authors themselves pointed out that this study could have been underpowered to achieve statistical significance for weaker associations (21).

Calcium was speculated to improve pancreatic β -cell function by maintaining balance between intracellular and extracellular calcium pool (22), enhance insulin sensitivity through improving insulin signal transduction in primary insulin target tissues (23), and improve

systemic inflammation (22). Previous prospective cohort studies have reported that higher dietary calcium intake could be inversely associated with T2D risk (11, 12, 24–27). However, a meta-analysis suggested that the findings from these studies could possibly be confounded by magnesium intake, since both minerals are found in dairy products (28). Hence, we were careful to include magnesium intake as a covariate in our model. Furthermore, majority of those studies (24–27, 29) were done in Western populations with generally higher range of dietary calcium, and compared calcium intake in excess of 1000 mg/day calcium intake against <500 mg/day as the reference group. Two studies in Asian populations had ranges of intake comparable to our population (439–650 mg/day versus 278–495 mg/day), but while Villegas et al. found an inverse association in Chinese women (12), Kirii et al. only reported a borderline inverse association in Japanese women and no significant association in men (11). Our study did not find a sex specific association for either dairy or calcium intake.

Our findings of a protective effect with intake of dairy but not with non-dairy calcium suggest that the potential beneficial impact of dairy on T2D risk could be due to its other components such as dairy protein (30) or trans-palmitoleic acid (31, 32), or because of its impact on satiety (33), and not due to the direct effect of calcium per se or through its interaction with other dairy ingredients. In Western populations, with up to 80% of total calcium coming from dairy products (9), it is challenging to eliminate residual confounding effect of dairy product on the association between calcium and T2D risk. Conversely, our cohort had a wide range of food sources for calcium other than dairy products (34), and this gave us the unique opportunity to discover the null association between non-dairy calcium and T2D risk. To the best of our knowledge, only Villegas et al. studied intake of calcium from different sources in Chinese women, and although they observed inverse associations regardless of calcium sources (12), we noted that their analysis did not adjust for magnesium intake in the model.

Our findings must be considered in light of the study limitations. First, measurement error due to self-reported dietary intake could have caused non-differential misclassification, which may, in turn, have led to underestimation of the risk reduction. Similarly, misclassification due to self-report of covariates may also lead to residual confounding. Second, our analysis relied on dietary measurements at baseline and subsequent changes in intake may lead to non-differential misclassification and underestimation of the risk estimate. Third, we used self-reported physician-diagnosed T2D as outcome, and would inherently have omitted undiagnosed T2D in our case ascertainment. If dairy intake is associated with asymptomatic disease, this may cause under-estimation of the risk estimate due to non-differential misclassification of undiagnosed cases as non-cases. Fourth, information about fat content of dairy was not collected in this study, thus, we were not able to separately explore the association of low or high fat dairy with T2D risk, although low fat dairy products were generally less common during the 1990s (recruitment period) in Singapore. Finally, milk was the major source of dairy intake, and our results may not be generalizable to other populations with substantial variety of other dairy products such as cheese, butter, yogurt and cream.

In conclusion, we found a modest, but statistically significant inverse association between dairy intake, especially daily milk intake, and risk of T2D. While non-dairy sources substantially contributed to total calcium intake in this population, the association between non-dairy calcium intake and T2D was null. Thus, the potential beneficial impact of dairy on T2D risk was likely to be accounted for by other components and not by its calcium content.

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Abbreviations

BMI	body mass index
FFQ	food-frequency questionnaire
IQR	interquartile range
T2D	type 2 diabetes

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FIGURE 1.
Participant flow

TABLE 1

Participant characteristics according to quartiles of dairy products intake in the Singapore Chinese Health Study

Characteristics	Quartiles of dairy intake			
	Q1	Q2	Q3	Q4
n	11,701	11,518	11,151	11,041
Age, y	54.3 ± 7.2	55.5 ± 7.7	55.5 ± 7.7	55.4 ± 7.7
Female sex, n (%)	4398 (37.6)	7069 (61.4)	7171 (64.3)	7364 (66.7)
Dialect group, n (%)				
Hokkien	5710 (48.8)	5204 (45.2)	5113 (45.8)	5633 (51.0)
Cantonese	5991 (51.2)	6314 (54.8)	6038 (54.1)	5408 (49.0)
Hypertension, n (%)	2178 (18.6)	2313 (20.1)	2166 (19.4)	2063 (18.7)
Education more than secondary school, n (%)	3702 (31.6)	3121 (27.1)	3117 (27.9)	3921 (35.5)
Ever smoker, n (%)	4604 (39.3)	3047 (26.4)	2796 (25.1)	2233 (20.2)
Weekly/daily alcohol drinker, n (%)	2355 (20.1)	1176 (10.2)	953 (8.5)	1048 (9.5)
Daily tea drinker, n (%)	2880 (24.6)	2321 (20.1)	2418 (21.7)	2419 (21.9)
Coffee drinker 2 cups/d, n (%)	5109 (43.7)	3851 (33.4)	3963 (35.5)	3123 (28.3)
Soda > 2 times/w, n (%)	1807 (15.4)	1106 (9.6)	956 (8.6)	901 (8.2)
Weekly moderate activity (%)				
<0.5 hours/wk	9331 (79.7)	9321 (80.9)	8945 (80.2)	7906 (71.6)
0.5–3.4 hours/wk	1521 (13.0)	1417 (12.3)	1436 (12.9)	1982 (17.9)
3.5 hours/wk	849 (7.3)	780 (6.8)	770 (6.9)	1153 (10.4)
Body mass index, kg/m ²	23.1 ± 3.2	23.1 ± 3.2	23.0 ± 3.3	22.8 ± 3.2
Total energy intake, kcal/d	1941 ± 472	1351 ± 373	1311 ± 459	1653 ± 504
Dairy, g/d *	−4.50 ± 14.1	20.3 ± 4.8	43.4 ± 11.6	227 ± 117
Red meat, g/d *	31.5 ± 23.0	31.9 ± 15.4	31.1 ± 14.8	26.2 ± 17.8
Poultry, g/d *	21.1 ± 20.0	21.8 ± 13.7	21.1 ± 13.0	18.6 ± 16.1
Fish and seafood, g/d *	56.5 ± 31.2	56.3 ± 23.7	54.0 ± 22.9	52.9 ± 26.6
Total legumes, g/d *	113 ± 102	116 ± 69.7	113 ± 63.7	117 ± 85.2
Total vegetables, g/d *	110 ± 63.5	113 ± 46.4	110 ± 45.8	115 ± 59.2
Total fruit, g/d *	191 ± 181	204 ± 132	202 ± 127	224 ± 164
Total grains, g/d *	361 ± 94.5	359 ± 85.6	342 ± 86.8	318 ± 85.5
Calcium intake, mg/d *	296 ± 122	350 ± 105	399 ± 112	616 ± 190
Non-dairy calcium intake, mg/d *	285 ± 103	292 ± 71.2	285 ± 67.9	288 ± 88.5
Magnesium, mg/d *	233 ± 38.2	240 ± 29.1	244 ± 29.4	261 ± 36.8

The data are expressed as n (%) or mean ± standard deviation.

* Dietary intakes are energy adjusted using residual method.

TABLE 2

Hazard ratio (95% Confidence Interval) of T2D according to intakes of dairy products and frequency of milk intake

	Quartiles of dairy intake				P for trend*
	Q1	Q2	Q3	Q4	
Median intake (IQR), g/d	1.39 (0.58–2.52)	14.3 (8.13–17.0)	37.7 (28.5–48.2)	252 (122–271)	
Cases/person-years	1358/121105	1399/127320	1323/126803	1127/119513	
Multivariate Model 1 [†]	1.00	1.00 (0.92–1.07)	0.95 (0.88–1.02)	0.86 (0.79–0.93)	<0.001
Multivariate Model 2 [‡]	1.00	1.00 (0.93–1.08)	0.96 (0.89–1.04)	0.91 (0.84–0.99)	0.01
Multivariate Model 3 [§]	1.00	0.98 (0.91–1.06)	0.96 (0.89–1.03)	0.90 (0.83–0.98)	0.01
Milk intake frequency					
	None	once a week	2–6 times/week	Daily	
n(%)	30,600 (67.4)	3,976 (8.8)	4,078 (9.0)	6,757 (14.9)	
Cases/person-years	3664/334935	418/42169	453/43729	672/73908	
Multivariate Model 1 [†]	1.00	0.93 (0.84–1.03)	0.97 (0.88–1.07)	0.84 (0.78–0.92)	
Multivariate Model 2 [‡]	1.00	0.95 (0.86–1.05)	1.00 (0.91–1.11)	0.88 (0.81–0.96)	
Multivariate Model 3 [§]	1.00	0.95 (0.85–1.05)	1.00 (0.91–1.11)	0.88 (0.81–0.96)	

* Linear trend was tested by treating the median value of each quartile as a continuous variable; IQR: interquartile range;

[†] Multivariate model 1: adjusted for age, sex, dialect, year of interview, and educational level;

[‡] Multivariate model 2: further adjusted for body mass index, physical activity, smoking status, alcohol use, baseline history of self-reported hypertension, and total energy intake;

[§] Multivariate model 3: further adjusted for vegetable, fruit, soy-rich pattern and dim sum and meat-rich pattern, coffee, and soda;

TABLE 3

Hazard ratio (95% Confidence Interval) of incident type 2 diabetes according to intakes of dietary, dairy, and non-dairy calcium

	Quartiles of Ca intake				P for trend [*]
	Q1	Q2	Q3	Q4	
Dietary Ca					
Median intake (IQR), mg/d	258 (206–290)	337 (316–354)	411 (390–438)	597 (524–681)	
Cases/person-years	1393/123910	1303/126078	1408/125556	1103/119197	
Multivariate Model 1 [†]	1.00	0.93 (0.93–1.01)	1.02 (0.94–1.10)	0.84 (0.77–0.91)	<0.001
Multivariate Model 2 [‡]	1.00	0.93 (0.86–1.00)	1.01 (0.94–1.09)	0.86 (0.79–0.93)	0.001
Multivariate Model 3 [§]	1.00	0.93 (0.86–1.00)	1.02 (0.94–1.10)	0.86 (0.79–0.94)	0.003
Multivariate Model 4/	1.00	0.89 (0.81–0.97)	0.95 (0.86–1.04)	0.75 (0.66–0.85)	<0.001
Dairy Ca					
Median intake, mg/d	16.8 (0–32.6)	39.0 (20.3–53.6)	100 (81.9–123)	314 (211–368)	
Cases/person-years	1388/121675	1396/128192	1297/126087	1126/118787	
Multivariate Model 1 [†]	1.00	0.97 (0.90–1.05)	0.92 (0.85–0.99)	0.85 (0.78–0.92)	<0.001
Multivariate Model 2 [‡]	1.00	0.97 (0.90–1.05)	0.93 (0.87–1.01)	0.90 (0.83–0.97)	0.009
Multivariate Model 3 [§]	1.00	0.95 (0.88–1.03)	0.93 (0.86–1.00)	0.89 (0.82–0.97)	0.01
Multivariate Model 4/	1.00	0.95 (0.88–1.02)	0.90 (0.83–0.98)	0.84 (0.76–0.93)	0.001
Nondairy Ca					
Median intake, mg/d	203 (169–225)	259 (246–269)	302 (291–316)	376 (348–421)	
Cases/person-years	1291/121851	1287/124496	1323/124885	1306/123509	
Multivariate Model 1 [†]	1.00	0.99 (0.92–1.07)	1.03 (0.95–1.11)	1.03 (0.95–1.12)	0.33
Multivariate Model 2 [‡]	1.00	0.99 (0.91–1.06)	1.00 (0.93–1.09)	0.98 (0.91–1.07)	0.79
Multivariate Model 3 [§]	1.00	0.99 (0.92–1.08)	1.02 (0.94–1.11)	1.01 (0.92–1.11)	0.72
Multivariate Model 4/	1.00	0.99 (0.91–1.07)	1.01 (0.92–1.11)	1.02 (0.92–1.14)	0.61

* Linear trend was tested by treating the median value of each quartile as a continuous variable; IQR: interquartile range;

[†] Multivariate model 1: adjusted for age, sex, dialect, year of interview, and educational level;[‡] Multivariate model 2: further adjusted for body mass index, physical activity, smoking status, alcohol use, baseline history of self-reported hypertension, and total energy intake;[§]

Multivariate model 3: further adjusted for vegetable, fruit, soy-rich pattern and dim sum and meat-rich pattern, coffee, and soda;
§ Multivariate model 5: model 3 plus dietary intake of potassium, magnesium, phosphorus, and vitamin D.