REVIEW

Consumption of Dairy Products and the Risk of Overweight or Obesity, Hypertension, and Type 2 Diabetes Mellitus: A Dose–Response Meta-Analysis and Systematic Review of Cohort Studies

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ABSTRACT

Dairy products have been suggested to be related to the prevention of overweight or obesity, hypertension, and type 2 diabetes mellitus (T2DM). These associations are currently controversial, however, and a systematic quantitative meta-analysis is lacking. In this study, we examined the associations between dairy products and the risk of overweight or obesity, hypertension, and T2DM and tested for dose–response relations. We comprehensively searched PubMed, Embase, and Web of Science up to April 2021. Cohort studies were included if dairy food consumption was reported at a minimum of 3 levels or as continuous variables, and the associations were assessed with overweight or obesity, hypertension, and T2DM. Summary RRs and 95% CIs were estimated for the dose–response association. Restricted cubic splines were used to evaluate the linear or nonlinear relations. Among the 9887 articles retrieved, 42 articles were included. For overweight or obesity, a linear association was observed for total dairy, milk, and yogurt. The risk decreased by 25%, 7%, and 12% per 200-g/d increase for total dairy, high-fat dairy, and milk, respectively, and by 13% per 50-g/d increment of yogurt. For hypertension, a nonlinear association was observed with total dairy, whereas significant inverse associations were found for low-fat dairy (RR: 0.94; 95% CI: 0.90, 0.98) and milk (RR: 0.94; 95% CI: 0.92, 0.97) per 200-g/d intake increase. For T2DM, all types of dairy food consumption except for milk and low-fat dairy products showed nonlinear associations, with total dairy and yogurt intake associated with 3% and 7% lower risk per 200-g/d and 50-g/d intake increase, respectively. In conclusion, our study suggests that total dairy is associated with a low risk of overweight or obesity, hypertension, and T2DM, especially milk and yogurt for overweight or obesity, low-fat dairy and milk for hypertension, and yogurt for T2DM. *Adv Nutr* 2022;13:2165–2179.

Statement of Significance: The meta-analysis examined a wide range of well-specified dairy foods in relation to overweight or obesity, hypertension, and type 2 diabetes mellitus (T2DM) risk based on cohort studies. The results suggest that total dairy intake, including any other type of dairy product, is protective for overweight or obesity, hypertension, and T2DM, although the separate effects of various types of dairy products on these 3 outcomes are inconsistent.

Keywords: dairy, overweight/obesity, hypertension, type 2 diabetes mellitus, cohort studies, meta-analysis

Introduction

Dairy product consumption is recommended in most dietary guidelines in Western and Asian countries as an important component of a healthy dietary pattern (1–4). Dairy products are a high-quality protein source, providing a substantial proportion of the recommended adult nutrient intake of calcium, iodine, riboflavin, and vitamin B-12 (5). The International Dairy Federation has indicated that the

consumption of dairy products is increasing worldwide. From 2006 to 2013, global per capita consumption of dairy products increased sharply. In particular, Asia, Africa, and Latin America are growing markets for dairy products (6). Recently, researchers have tended to focus on teasing out different dairy products by type (those with low-fat and high-fat content, fermented products, milk, yogurt, and cheese). Possessing different nutrients, bioactive compounds, and processes of fermentation, these various types of dairy product are inherently different (7). In addition, the popularity and contribution of a particular type of dairy product to total intake varies widely among different populations, which may have an impact on outcomes (8). Moreover, consumption of dairy products might be influenced by other variables affecting health status (8).

In the past decades, the number of studies investigating the potential association between dairy product consumption and health outcomes has increased exponentially. Although some epidemiologic studies have suggested a potential role for dairy product consumption in the prevention of overweight or obesity (9, 10), hypertension (11, 12), and type 2 diabetes mellitus (T2DM) (13, 14), other studies have failed to find such an effect (15–20). For overweight or obesity, only 1 meta-analysis (21) explored the association by comparing the highest and lowest categories of dairy intake. There are no dose–response effect analyses. Four meta-analyses (22–25) investigated the association with hypertension; however, the 2 recently updated ones (24, 25) in 2017 included only 8 more studies and drew contradictory conclusions, in particular not taking into account subgroup analyses based on different types of dairy products. Although several previous meta-analyses explored the association for T2DM based on cohort studies, their conclusions are widely inconsistent. More recent evidence (13, 19, 20, 26–31) shows that a more comprehensive systematic review is necessary.

Accordingly, this comprehensive systematic review and dose–response meta-analysis, based on cohort studies, aimed to synthesize knowledge of the associations between different types of dairy product consumption (total dairy, low-fat dairy, high-fat dairy, fermented dairy, milk, yogurt, and cheese) and risk of overweight or obesity, hypertension, and T2DM, as well as to explore their dose–response relations.

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Supplemental Figures 1–5 and Supplemental Tables 1–7 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances/.
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Abbreviations used: IPP, isoleucine–proline–proline; NUQUEST, NUtrition QUality Evaluation Strengthening Tools; T2DM, type 2 diabetes mellitus; VPP, valine–proline–proline.

Methods

The present meta-analysis was registered in the PROSPERO International Prospective Register of Systematic Reviews (www.crd.york.ac.uk/prospero/index.asp, identifier CRD42021276429). This systematic review was conducted according to the PRISMA Protocols 2015 (32). We also followed the 12-item PRISMA extension when writing the abstract (33).

Search strategy

Cohort studies published up to 22 April 2021 were searched using PubMed, Embase, and Web of Science for relevant publications, restricted to the English language, using a comprehensive list of search terms (**Supplemental Table 1**). In addition, the reference lists from the retrieved articles were checked to identify further relevant studies. Published systematic reviews and meta-analyses were also used as a data source. Two investigators (YF and YZ) independently conducted systematic searches, screened the articles, and reviewed the full text of articles, with any disagreements discussed with a third investigator (DH).

Study selection

Studies were included in this meta-analysis if they met the following inclusion criteria: *1*) they were cohort studies; *2*) they included the general adult population aged ≥18 y; *3*) the exposure of interest was dairy food consumption (including total dairy, low-fat dairy, high-fat dairy, fermented dairy, milk, yogurt, and cheese); *4*) they reported dairy food consumption at a minimum of 3 levels or as continuous variables; *5*) the outcome of interest was overweight or obesity (defined by BMI, waist circumference, or waist-to-height ratio), hypertension, or T2DM; and *6*) they reported quantitative estimates and their 95% CIs or provided sufficient data to calculate these estimates. We excluded reviews, comments, letters, and editorials. If >1 article was based on the same data, the study with the most detailed report and/or the largest sample size was chosen.

Data extraction and quality assessment

Data were extracted from published articles with the use of a predefined protocol. Two investigators (YF and YZ) independently extracted the following information from the included studies: first author's last name, publication year, study location, study design, study name, mean age, sex, number of participants, number of cases, follow-up duration, outcome assessment, dairy food type, dairy food measurement, number of cases and person-years/number of participants per dairy foods category, most adjusted risk estimates (ORs, RRs, or HRs) with their corresponding 95% CIs for each category, and adjustment factors. Any disagreement was resolved by consensus involving a third author (DH).

The NUtrition QUality Evaluation Strengthening Tools (NUQUEST), a risk of bias tool developed specifically for nutrition studies, was used to assess the study quality of the included cohort studies in 4 sections based on 16 items (34).

Each of the NUQUEST sections and the overall assessment were rated independently by each rater as "good," "neutral," or "poor." The overall evaluation of each study was based on the results of 4 sections.

Data synthesis and analysis

Dairy food consumption in included studies was reported inconsistently, so we converted it to grams per day for the dose–response meta-analysis. The conversions were in accordance with the definitions in the original articles. When studies did not define the servings, times, or portions per day, week, or month, we converted the intake to grams per day with the use of standard units of 177 g for total, low-fat, high-fat, and fermented dairy; 244 g for milk and yogurt; and 43 g for cheese (35, 36). We used the RRs as the unified effect measure for the association with dairy product consumption. Due to the high incidence of overweight or obesity, hypertension, and T2DM (>10%), the ORs may present an overestimation of the true RRs; therefore, we converted the ORs reported by included studies into RRs using a previously published correction method (37). Articles reporting data separately for men and women, or from different cohorts, or reporting >1 health outcome within an article were treated as separate studies. If the number of cases or participants in each category was not provided, we calculated it from the available data (38). When the lowest category was not the reference category, the method of Hamling et al. (39) was used to recalculate risk estimates. When exposures were reported as a range, we took the midpoint value for analyses. If the highest or lowest categories were open-ended, the range was assumed to be the same width as the closest range, and we estimated the midpoint value accordingly (40).

Generalized least squares regression was used to estimate study-specific dose–response associations, and the random-effects model was used to pool the study-specific dose–response effect estimates (41, 42). Study-specific effect estimates were calculated per 200-g/d increase in total, high-fat, low-fat, and milk dairy consumption; per 50 g/d in yogurt; per 40 g/d in fermented dairy; and per 30 g/d in cheese. Restricted cubic splines with 3 knots at the 25th, 50th, and 75th percentiles of the distribution were used to examine the linear/nonlinear dose–response association (42). *P*-nonlinearity was calculated by testing the null hypothesis that the coefficient of the second spline is equal to 0 (43).

The heterogeneity between studies was evaluated by Cochran's *Q* and I^2 statistic (44). $P < 0.05$ was considered significant for the Cochran's *Q* statistic. I^2 values of 25%, 50%, and 75% represented low, moderate, and high degrees of heterogeneity, respectively. Subgroup analyses by sex, age (≤50 and >50 y), country (Asia, United States, Australia, Europe, and multicountry), follow-up period (≤10 and >10 y), and confounding variables (smoking, alcohol consumption, total energy intake, BMI, and physical exercise) were performed to access potential sources of heterogeneity. Publication bias was evaluated with the Egger test (45), and if statistically significant bias was found, the trim-and-fill method was used for adjustment. Subgroup analyses and publication bias assessments were not completed if there were <8 cohort comparisons available.

All analyses were performed with Stata 14.0 (StataCorp). All tests were 2-sided, with $P < 0.05$ considered statistically significant.

Results

Study characteristics

Study selection processes are summarized in **Figure 1**. We identified 9887 potential eligible articles. After removing duplicate articles ($n = 2352$) and those that did not fit the inclusion criteria ($n = 7284$), 251 articles were retrieved for critical full-text review. Finally, an overview of 42 articles (13, 14, 16–20, 26–31, 46–74) (52 studies: 7 on overweight or obesity, 17 on hypertension, and 28 on T2DM) was included in the meta-analysis, representing a total of 1,212,693 participants with the average age of 48.88 y (50.04 y for overweight or obesity, 47.28 y for hypertension, and 49.60 y for T2DM). Among these articles, 2 articles reporting data from several different cohorts (46, 66), 2 reporting different health outcomes (18, 74), and 4 stratifying by sex were treated as independent studies (31, 47, 67, 73). Twenty studies reported the unit of dairy products by using grams (13, 14, 16, 20, 26, 27, 29, 47, 48, 52–54, 60–62, 67, 68, 72), 27 studies using serving size (17, 19, 28, 30, 31, 46, 49–51, 55, 57, 59, 64–66, 69–71, 73), 6 using frequency (18, 56, 63, 74), and 1 using portion size (58). The sample size of the cohorts ranged from 463 (67) to 85,884 (46), and the duration of follow-up ranged from 2 y (60) to 30 y (46). Geographically, 12 studies were conducted in Asia (13, 14, 18, 47, 57, 67, 68, 73), 18 in Europe (16, 17, 20, 26, 29, 31, 48, 52–54, 58, 60–62, 69, 71, 72), 2 in Australia (27, 50), 21 in the United States (19, 28, 30, 46, 49, 51, 55, 56, 59, 63, 64, 66, 70, 74), and 1 in multiple countries (65). **Supplemental Table 2** shows the main characteristics of the included studies. The risk of bias was neutral for 36 of 42 articles but poor for the remaining 6 articles, as detailed in **Supplemental Table 3**.

Dairy product consumption and risk of overweight or obesity

Total dairy.

Five studies (18, 70, 73, 74) were included to assess the dose–response association between total dairy and overweight or obesity, with a total of 31,054 individuals and 11,103 overweight or obesity cases. A linear inverse association was observed (*P*-nonlinearity = 0.895; **Supplemental Figure 1**A). The pooled RR and 95% CI for per 200 g/d was 0.75 (0.60, 0.92), with high heterogeneity found ($I^2 = 92.8\%$, *P*-heterogeneity < 0.001).

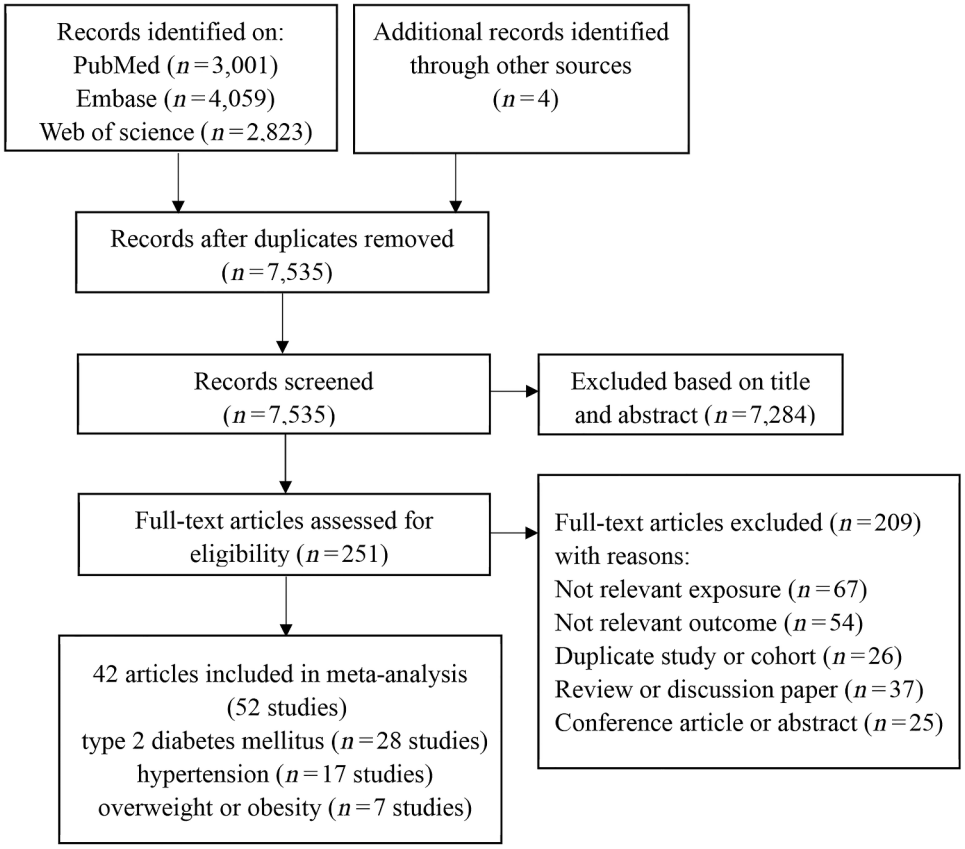

FIGURE 1 Flowchart of article selection.

Milk.

Six studies reported data for milk and overweight or obesity (18, 70, 72–74), comprising 32,534 individuals and 11,439 cases. Similarly, a linear negative dose–response relation was observed (P-nonlinearity = 0.971; Supplemental Figure 1B). The summary RR for per 200-g/d increment was 0.88 (95% CI: 0.82, 0.95) with low heterogeneity (I^2 = 23.7%, P-heterogeneity = 0.256).

Yogurt.

Associations with yogurt and overweight or obesity were assessed in 5 studies (70, 71, 73, 74) that included 32,330 individuals and 11,947 cases. Restricted cubic spline modeling showed a linear association (P-nonlinearity = 0.270; Supplemental Figure 1C). For per 50-g/d increment in yogurt, the pooled RR was 0.87 (95% CI: 0.77, 0.99) with high heterogeneity (I^2 = 94.3%, P-heterogeneity < 0.001).

Low-fat, high-fat dairy and cheese.

Two studies (70, 74) examined the relation of low-fat and high-fat dairy with a total of 19,112 individuals and 8612 overweight or obesity cases but only 1 (70) study for cheese. The RRs and 95% CIs were 1.02 (0.99, 1.05), 0.93 (0.89, 0.97), and 1.00 (0.98, 1.02) with per 200-g/d increment for low-fat and high-fat dairy and per 30 g for cheese, respectively. Restricted cubic spline modeling was not performed due to the low number of studies. Similarly, because of the small number of studies (n < 8) exploring the relation between dairy intake and overweight or obesity, subgroup analyses and publication bias assessments were not performed.

Dairy product consumption and risk of hypertension

Total dairy.

Seventeen studies assessed the association between total dairy and hypertension incidence (16–18, 60–69, 74), representing 375,975 participants and 133,319 hypertensive cases. A nonlinear association was observed (P-nonlinearity = 0.032; **Figure 2**A) in the dose–response analysis, with a steeper inverse association lower than ~310 g/d, but further reductions in risk were observed with higher levels of total dairy intake. With per 200-g/d increment, the pooled risk of hypertension was reduced by 5% (RR: 0.95; 95% CI: 0.93, 0.97; I^2 = 65.2%, P-heterogeneity < 0.001; **Figure 3**). We found that no publication bias existed (Egger test, P = 0.911; **Supplemental Figure 4**A). Heterogeneity was not detected between subgroups (**Table 1**). Subgroup analyses showed a nonsignificant association for studies of European and Asian residents, men, cases ≤1000, and those without adjustment for BMI, physical activity, and smoking.

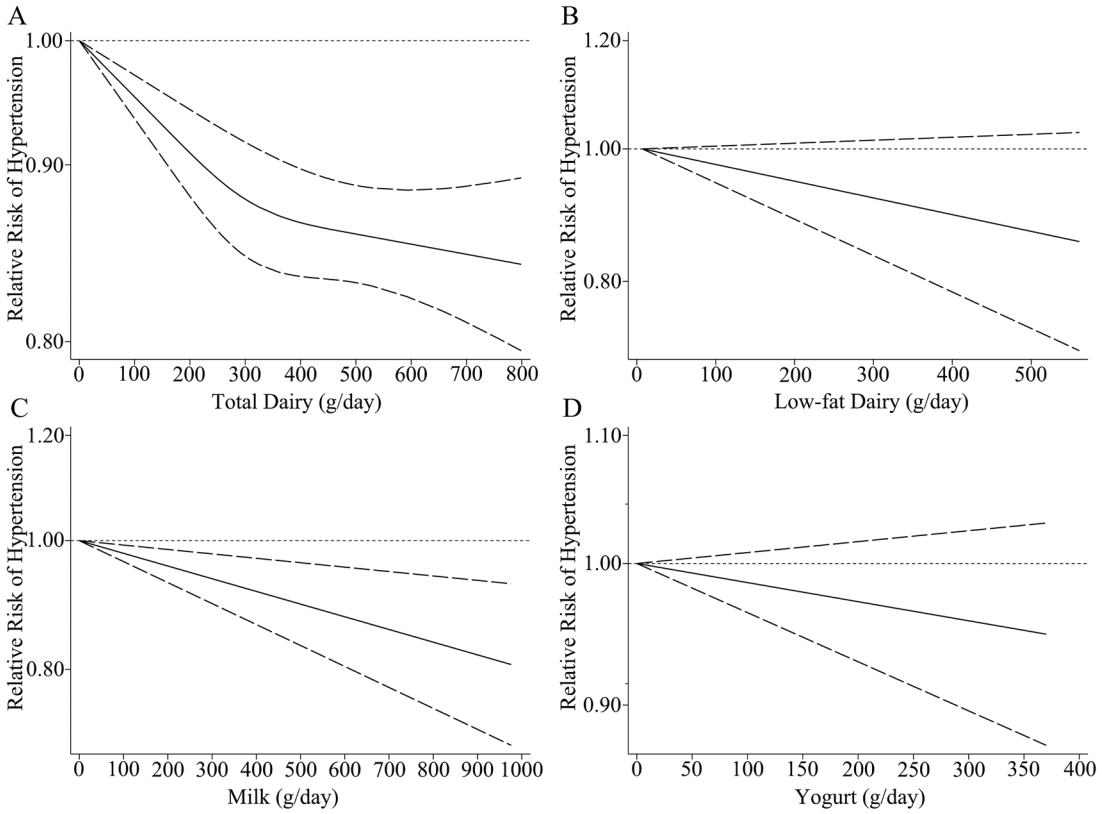

FIGURE 2 Dose–response association of total dairy (A), low-fat dairy (B), milk (C), and yogurt (D) intakes and risk of hypertension in adults modeled by restricted cubic splines.

Low-fat and high-fat dairy.

Consumption of low-fat dairy and high-fat dairy was assessed in 10 studies (16, 60–62, 64, 65, 67, 69, 74), with a total of 144,624 participants. Low-fat dairy was linearly and inversely associated with hypertension incidence (*P*-nonlinearity = 0.429; Figure 2B), with the pooled RR per 200-g/d increment being 0.94 (95% CI: 0.90, 0.98). Intake of high-fat dairy was not associated with hypertension (RR per 200 g/d, 0.96; 95% CI: 0.89, 1.03), although the cubic spline model showed a linear trend (*P*-nonlinearity = 0.788; **Supplemental Figure 2**A). A low level of heterogeneity was apparent for the association with intake of low-fat dairy (I^2 = 46.2%, *P*-heterogeneity = 0.053), with a moderate level of heterogeneity for high-fat dairy (I^2 = 61.8%, *P*-heterogeneity = 0.005). Egger test showed no evidence of publication bias for either low-fat (*P* = 0.841; **Supplemental Figure 5**B) or high-fat dairy (*P* = 0.895; Supplemental Figure 4C). In subgroup analyses, no evidence of heterogeneity was found for low-fat and high-fat dairy. The results were stable for high-fat dairy in overall subgroup analyses, whereas the results for low-fat dairy showed only studies with age cohorts >50 y and cases >1000 were more stable (**Supplemental Table 4**).

Milk.

Fourteen studies (17, 18, 61–64, 66–69, 74) assessing the consumption of milk and incident hypertension included 310,696 participants and 118,766 cases. A significant inverse linear association was found (*P*-nonlinearity = 0.063; Figure 2C), with a pooled RR of 0.94 (95% CI: 0.92, 0.97) per increment of 200 g/d. Moderate heterogeneity (I^2 = 64.1%, *P*-heterogeneity = 0.001) and no evidence of publication bias with Egger test (*P* = 0.354; Supplemental Figure 4D) were found. In subgroup analyses, no evidence was found for the source of heterogeneity (Table 1); however, the results from studies of Asian residents, cohorts aged ≤50 y, cases ≤1000, follow-up periods ≤10 y, and those without adjustment for physical activity, smoking, and alcohol consumption were nonsignificant.

Total fermented dairy, yogurt, and cheese.

Six studies reported data for total fermented dairy (16, 61, 62, 67, 69), comprising 10,876 individuals and 3699 hypertension cases. A linear dose–response association was observed (*P*-nonlinearity = 0.823; Supplemental Figure 2B) and the pooled RR of per 40-g/d increment was 0.99 (95% CI: 0.97, 1.01) with low heterogeneity (I^2 = 25.6%, *P*-heterogeneity = 0.242). Egger test and subgroup analyses were not performed for fermented dairy due to the small number of included studies.

Associations with yogurt intake and hypertension incidence were assessed in 11 studies (17, 61, 63, 64, 66, 67, 69, 74), which included 265,684 individuals and 103,686 cases. Restricted cubic spline modeling showed a linear

	No of studies	No of participants	No of cases	Relative risk (95% CI)	Heterogeneity I^2 (P value)	Egger's test P value
Obesity						
Total dairy	5	31,054	11,103	0.75 (0.60–0.92)	92.8% (<0.001)	-
Low-fat dairy	2	19,112	8,612	1.02 (0.99–1.05)	75.4% (0.044)	-
High-fat dairy	2	19,112	8,612	0.93 (0.89–0.97)	59.6% (0.115)	-
Milk	6	32,534	11,439	0.88 (0.82–0.95)	23.7% (0.256)	-
Yogurt	5	32,330	11,947	0.87 (0.77–0.99)	94.3% (<0.001)	-
Cheese	1	18,438	8,238	1.00 (0.98–1.02)	-	-
Hypertension						
Total dairy	17	375,975	133,319	0.95 (0.93–0.97)	65.2% (<0.001)	0.911
Low-fat dairy	10	144,624	NA	0.94 (0.90–0.98)	46.2% (0.053)	0.841
High-fat dairy	10	144,624	NA	0.96 (0.89–1.03)	61.8% (0.005)	0.895
Fermented dairy	6	10,876	3,699	0.99 (0.97–1.01)	25.6% (0.242)	-
Milk	14	310,696	118,766	0.94 (0.92–0.97)	64.1% (0.001)	0.354
Yogurt	11	265,684	103,686	0.98 (0.96–1.00)	81.5% (<0.001)	0.192
Cheese	11	267,020	104,507	0.99 (0.97–1.01)	60.4% (0.010)	0.824
T2DM						
Total dairy	20	560,852	36,291	0.97 (0.95–0.99)	57.7% (0.001)	0.272
Low-fat dairy	16	562,380	37,065	0.96 (0.92–1.00)	68.7% (<0.001)	0.007
High-fat dairy	14	384,863	25,310	0.99 (0.95–1.03)	37.6% (0.076)	0.916
Fermented dairy	7	52,741	5,115	1.00 (0.98–1.02)	39.3% (0.130)	-
Milk	19	531,979	35,467	0.97 (0.92–1.03)	84.9% (<0.001)	0.416
Yogurt	14	483,090	32,896	0.93 (0.89–0.97)	79.3% (<0.001)	0.025
Cheese	19	545,721	32,408	1.00 (0.99–1.01)	41.2% (0.029)	0.567

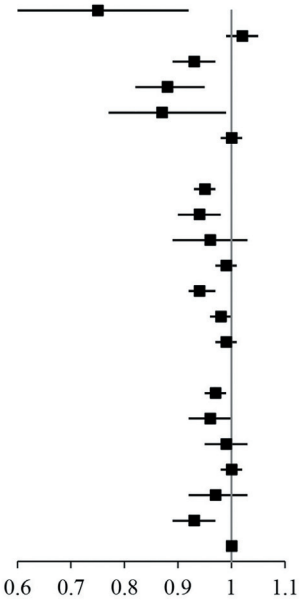

FIGURE 3 Summary of relative risk of dose–response association of dairy product intakes and risk of overweight or obesity, hypertension, and type 2 diabetes mellitus in adults (per 200-g/d increment for total dairy, low-fat dairy, high-fat dairy, fermented dairy, and milk; per 50 g/d for yogurt; and per 30 g for cheese, respectively). NA, not available.

association (P-nonlinearity = 0.075; Figure 2D). A borderline inverse association was found, with a pooled RR of 0.98 (95% CI: 0.96, 1.00) per 50-g/d increment with high heterogeneity (I^2 = 81.5%, P-heterogeneity < 0.001). There was no evidence of publication bias (Egger test, P = 0.192; Supplemental Figure 4E). Subgroup analyses suggested that heterogeneity existed in the study that stratified by adjustment of BMI with the lower heterogeneity (I^2 = 0%). No significant changes of heterogeneity occurred in other subgroup analyses (**Supplemental Table 5**).

Associations with cheese and hypertension incidence were assessed in 11 studies (17, 61–64, 66, 67, 69) covering 267,020 individuals and 104,507 cases. A linear dose–response association was observed (P-nonlinearity = 0.845; Supplemental Figure 2C), whereas a nonsignificant association was found per 50-g/d increment with moderate heterogeneity (I^2 = 60.4%, P-heterogeneity = 0.010), the pooled RR being 0.98 (95% CI: 0.96, 1.00). There was no evidence of publication bias (Egger test, P = 0.824; Supplemental Figure 4E). In general, the association was consistent in most subgroup analyses. No evidence of heterogeneity was detected between subgroups (Supplemental Table 5).

Dairy product consumption and risk of T2DM

Total dairy.

Data from 20 studies (13, 20, 26–29, 46, 47, 49–51, 53–55, 57–59) were included in the dose–response analysis of total dairy and T2DM, comprising a total of 560,869 participants and 36,281 cases. A nonlinear association was observed (P-nonlinearity = 0.048; **Figure 4**A) in the dose–response analysis, with a steeper inverse association lower than ∼350 g/d, but further slow reductions in risk were observed with higher levels of total dairy intake. With per 200-g/d increment, the pooled risk of T2DM was reduced by 3% (RR: 0.97; 95% CI: 0.95, 0.99; I^2 = 57.7%, P-heterogeneity = 0.001; Figure 3). Visual inspection of the funnel plots and nonsignificant Egger test (P = 0.272) suggested no evidence of publication bias (Supplemental Figure 5A). Subgroup analyses showed a significant association for the subgroup aged ≤50 y; for studies conducted with >1000 cases; for adjusted BMI, physical activity, smoking, and alcohol consumption; and for nonadjusted energy intake (**Table 2**).

Low-fat dairy.

For low-fat dairy, 16 studies (19, 26, 28, 30, 46, 48–51, 53–55, 58, 59) were included in the dose–response analysis, with a total of 562,380 participants and 37,065 cases. A borderline inverse association with T2DM was observed (RR: 0.96 per 200-g/d increment; 95% CI: 0.92, 1.00; I^2 = 68.7%, P-heterogeneity < 0.001; Figure 3). Restricted cubic spline modeling showed a linear relation (P-nonlinearity = 0.629; Figure 4B). Publication bias was detected using Egger test (P = 0.007) and with visual inspection of funnel plots (Supplemental Figure 5B). After applying the trim-and-fill method, the results did not change (RR: 0.96; 95% CI: 0.92, 1.00). Subgroup analyses showed a strong inverse association in population groups from America, in those aged >50 y, in

TABLE 1 Dose–response subgroup analyses of total dairy and milk intakes and risk of hypertension in adults

Subgroup	Total dairy (per 200-g/d increment)				Milk (per 200-g/d increment)			
	n	RR (95% CI)	I^2, %	*P* value[1]	*N*	RR (95% CI)[1]	I^2, %	*P* value[1]
All	17	0.95 (0.93, 0.97)	65.2	<0.001	14	0.94 (0.92, 0.97)	64.1	0.001
Region								
United States	6	0.94 (0.92, 0.97)	68.3	0.008	6	0.97 (0.95, 0.98)	32.2	0.219
Europe	6	0.96 (0.92, 1.00)	42.0	0.125	4	0.92 (0.86, 0.99)	59.9	0.058
Asia	4	1.04 (0.88, 1.21)	76.3	0.005	4	1.04 (0.86, 1.24)	73.7	0.010
Multicountry	1	0.97 (0.93, 0.99)	—	—	0	—	—	—
Sex								
Both	9	0.93 (0.90, 0.98)	16.5	0.296	10	0.93 (0.90, 0.97)	61.6	0.011
Men	2	1.15 (0.76, 1.72)	90.6	0.001	1	1.90 (1.22, 2.95)	—	—
Women	6	0.96 (0.94, 0.98)	77.5	<0.001	3	0.95 (0.90, 1.01)	39.6	0.191
Age, y								
≤50	10	0.96 (0.92, 0.99)	73.1	<0.001	8	0.97 (0.91, 1.04)	66.4	0.011
>50	7	0.95 (0.93, 0.97)	48.3	0.071	6	0.92 (0.88, 0.96)	61.9	0.022
No. of cases								
≤1000	9	0.95 (0.88, 1.03)	63.3	0.005	7	0.96 (0.89, 1.04)	61.3	0.017
>1000	8	0.95 (0.94, 0.97)	71	0.001	7	0.95 (0.92, 0.97)	71.3	0.007
Follow-up years								
≤10	11	0.95 (0.92, 0.99)	58.2	0.008	8	0.95 (0.90, 1.01)	64.5	0.006
>10	6	0.95 (0.93, 0.98)	77.3	0.001	6	0.92 (0.87, 0.98)	71.7	0.014
Adjustments								
BMI								
Yes	15	0.95 (0.93, 0.97)	60.6	0.001	12	0.95 (0.92, 0.98)	67.6	0.001
No	2	0.99 (0.96, 1.01)	0.0	0.383	2	0.91 (0.85, 0.98)	0	0.530
Energy intake								
Yes	17	0.95 (0.93, 0.97)	65.2	<0.001	14	0.94 (0.92, 0.97)	64.1	0.001
No	0	—	—	—	0	—	—	—
Physical activity								
Yes	14	0.95 (0.93, 0.97)	69.3	<0.001	12	0.94 (0.91, 0.97)	67.2	0.001
No	3	0.95 (0.89, 1.03)	44	0.168	2	0.96 (0.87, 1.07)	66.8	0.083
Smoking								
Yes	16	0.95 (0.93, 0.97)	65.6	<0.001	13	0.94 (0.91, 0.97)	65.8	0.001
No	1	1.02 (0.93, 1.11)	—	—	1	1.02 (0.93, 1.12)	—	—
Alcohol consumption								
Yes	10	0.95 (0.92, 0.98)	54.4	0.020	8	0.94 (0.91, 0.97)	46.5	0.070
No	7	0.96 (0.93, 0.98)	75.8	<0.001	6	1.01 (0.85, 1.19)	80.6	0.001

[1] *P* for heterogeneity within each subgroup estimated by the Cochran *Q* test.

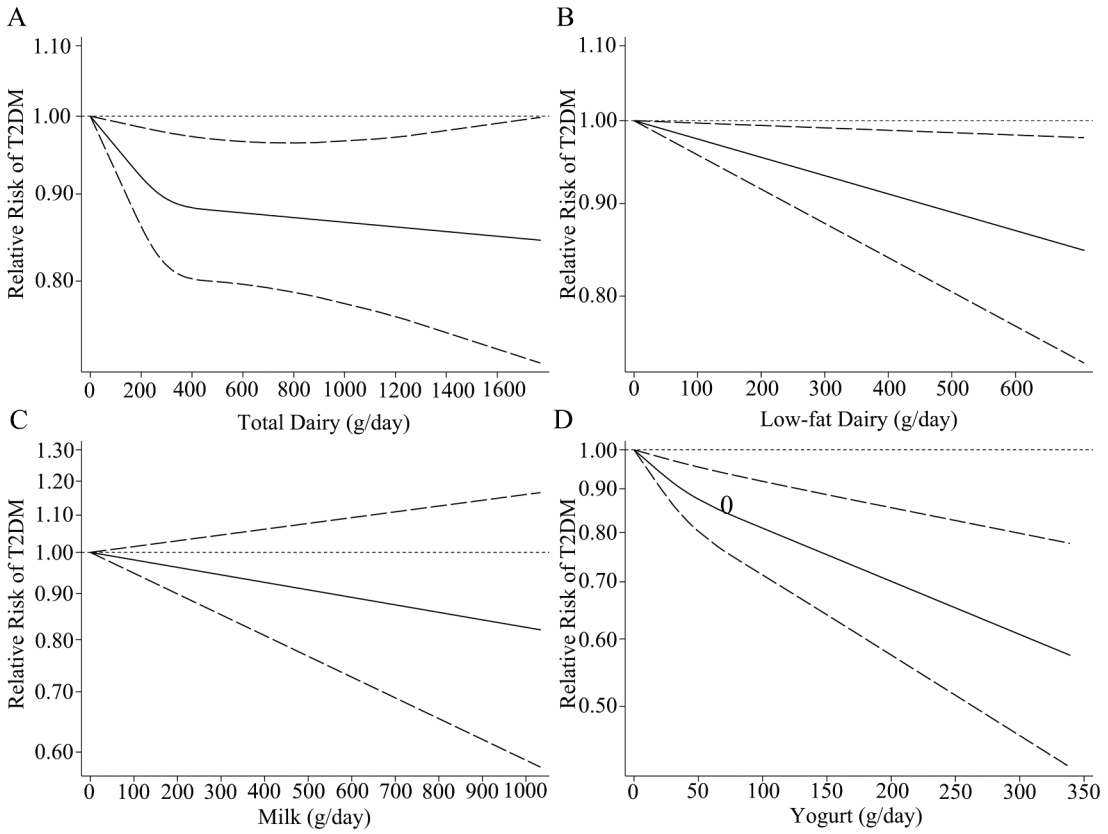

FIGURE 4 Dose–response association of total dairy (A), low-fat dairy (B), milk (C), and yogurt (D) intakes and risk of type 2 diabetes mellitus in adults modeled by restricted cubic splines.

groups with a follow-up period >10 y, and for nonadjusted energy intake cases (**Supplemental Table 6**).

High-fat dairy.

High-fat dairy (14 studies; 26, 28–30, 46, 48, 49, 53–55, 58, 59) showed no association with T2DM risk in the dose–response analysis (RR: 0.99 per 200-g/d increment; 95% CI: 0.95, 1.03; I^2 = 37.6%; *P*-heterogeneity = 0.076; Figure 3). These studies included a total of 384,863 participants and 25,310 cases. A potential nonlinear association was observed (*P*-nonlinearity = 0.045; **Supplemental Figure 3**A) by restricted cubic spline, with an inverse association lower than ∼115 g/d, but the risk was increased with further higher levels of high-fat dairy intake. Visual inspection of the funnel plots and nonsignificant Egger test (*P* = 0.916) suggested no evidence of publication bias (Supplemental Figure 5C). A nonsignificant association was found across most subgroups, but a positive association found with nonadjusted physical activity and alcohol consumption (Supplemental Table 6).

Yogurt.

Yogurt (14 studies; 19, 26–29, 46, 47, 49, 51, 53, 59), including 483,090 participants and 32,896 cases, was nonlinearly (*P*-nonlinearity = 0.035; Figure 4D) inversely related to T2DM, with a steeper inverse association lower than ∼45 g/d, but further reductions in risk were observed with higher levels of yogurt intake and a 7% lower risk per 50-g/d increment (RR: 0.93; 95% CI: 0.89, 0.97; I^2 = 79.3%, *P*-heterogeneity < 0.001; Figure 3). Publication bias was detected with Egger test (*P* = 0.025) and visual inspection of funnel plots (Supplemental Figure 5E). With application of the trim-and-fill method, the results did not change (RR: 0.93; 95% CI: 0.89, 0.97). Subgroup analyses indicated a stronger inverse association for studies in America, in women, where cases numbered >1000, and where study follow-up years were >10 (**Supplemental Table 7**).

Fermented dairy, milk, and cheese.

Seven studies (20, 26, 27, 29, 53, 54, 58) were pooled to estimate the relation between fermented dairy and risk of T2DM in the dose–response analysis, the studies comprising a total of 52,741 participants and 5115 cases. There was a potential nonlinear trend by restricted cubic spline (*P*-nonlinearity = 0.742; Supplemental Figure 3B), but no association was found (RR: 1.00 per 200-g/d increment; 95% CI: 0.98, 1.02; I^2 = 39.3%, *P*-heterogeneity = 0.130; Figure 3). Subgroup analyses and publication bias assessments were not performed because there were <8 included studies.

Milk intake (19 studies; 13, 14, 20, 26, 28, 29, 46, 47, 49, 52–54, 56–59), including 505,049 participants and 32,607

TABLE 2 Dose–response subgroup analyses of total dairy and milk intakes and risk of type 2 diabetes mellitus in adults

Subgroup	Total dairy (per 200-g/d increment)				Milk (per 200-g/d increment)			
	n	RR (95% CI)	I^2, %	*P* value[1]	*n*	RR (95% CI)	I^2, %	*P* value[1]
All	20	0.97 (0.95, 0.99)	57.7	0.001	19	0.96 (0.90, 1.03)	85.0	<0.001
Region								
United States	8	0.96 (0.93, 1.00)	71.0	0.001	7	1.05 (0.98, 1.12)	28.5	0.211
Europe	6	0.99 (0.94, 1.05)	43.0	0.118	7	1.03 (1.00, 1.06)	0.0	0.534
Asia	4	0.93 (0.84, 1.03)	60.0	0.057	5	0.82 (0.65, 1.05)	94.0	<0.001
Australia	2	0.99 (0.87, 1.13)	0.0	0.604	—	—	—	—
Sex								
Both	9	0.96 (0.91, 1.00)	42.4	0.084	10	0.99 (0.95, 1.03)	45.2	0.058
Men	4	0.98 (0.91, 1.07)	75.3	0.007	4	1.05 (0.97, 1.14)	22.5	0.276
Women	7	0.97 (0.93, 1.01)	65.7	0.008	5	0.86 (0.61, 1.22)	95.2	<0.001
Age, y								
≤50	16	0.96 (0.93, 0.99)	56.2	0.003	3	1.05 (0.94, 1.18)	37.6	0.202
>50	4	1.00 (0.97, 1.03)	31.5	0.223	16	0.95 (0.88, 1.02)	86.8	<0.001
No. of cases								
≤1000	11	0.97 (0.91, 1.04)	42.8	0.065	11	0.99 (0.96, 1.03)	0.0	0.898
>1000	9	0.97 (0.94, 0.99)	70.8	0.001	8	0.96 (0.83, 1.11)	93.9	<0.001
Follow-up years								
≤10	11	0.95 (0.90, 1.00)	48.8	0.034	9	0.88 (0.73, 1.05)	88.6	<0.001
>10	9	0.98 (0.95, 1.00)	64.7	0.004	10	1.02 (0.98, 1.07)	59.4	0.008
Adjustments								
BMI								
Yes	19	0.97 (0.94, 0.99)	59.9	<0.001	17	0.96 (0.89, 1.04)	86.6	<0.001
No	1	0.97 (0.81, 1.16)	0.0	—	2	0.99 (0.94, 1.05)	0.0	0.511
Energy intake								
Yes	17	0.98 (0.96, 1.00)	48.8	0.012	15	0.97 (0.90, 1.05)	88.1	<0.001
No	3	0.85 (0.79, 0.92)	0.0	0.636	4	0.98 (0.93, 1.04)	0.0	0.555
Physical activity								
Yes	18	0.97 (0.95, 0.99)	58.9	0.001	15	0.96 (0.88, 1.05)	88.3	<0.001
No	2	0.85 (0.73, 1.00)	0.0	0.466	4	1.00 (0.95, 1.04)	0.0	0.889
Smoking								
Yes	19	0.97 (0.94, 0.99)	59.7	<0.001	18	0.96 (0.89, 1.03)	85.8	<0.001
No	1	1.12 (0.69, 1.82)	0.0	—	1	1.00 (0.94, 1.06)	0.0	—
Alcohol consumption								
Yes	18	0.97 (0.95, 0.99)	59.0	0.001	16	0.96 (0.88, 1.05)	87.4	<0.001
No	2	0.88 (0.67, 1.17)	31.0	0.229	3	1.00 (0.95, 1.04)	0.0	0.730

[1] *P* for heterogeneity within each subgroup estimated by the Cochran *Q* test.

cases, was not associated with T2DM risk (RR: 0.96 per 200-g/d increment; 95% CI: 0.90, 1.03; I^2 = 85.0%; *P*-heterogeneity < 0.001; Figure 3). A linear trend with T2DM was observed (*P*-nonlinearity = 0.077; Figure 4C). Publication bias was not evident using Egger test (Supplemental Figure 5D; $P = 0.416$). All subgroup analyses were consistent with the main results except for studies conducted in Europe, which showed that milk was positively associated with T2DM (Table 2).

Cheese (19 studies; 20, 26–29, 31, 46–49, 53, 54, 56, 58, 59), including 518,791 participants and 29,548 cases, was not associated with T2DM risk in the dose–response analysis (RR: 1.00 per 10-g/d increment; 95% CI: 0.99, 1.01; I^2 = 42.3%, *P*-heterogeneity = 0.027; Figure 3). There was a potential nonlinear relation by restricted cubic spline (*P*-nonlinearity = 0.001; Supplemental Figure 3C). Publication bias was not evident with Egger test (Supplemental Figure 5F; $P = 0.567$). Subgroup analyses were consistent with the main results (Supplemental Table 7).

Discussion

In our meta-analysis, we systematically assessed the associations between dairy product consumption (total dairy, low-fat dairy, high-fat dairy, fermented dairy, milk, yogurt, and cheese) and risk of 3 health outcomes (overweight or obesity, hypertension, and T2DM) by examining study-specific risks and conducting linear or nonlinear dose–response analyses. For overweight or obesity, restricted cubic spline modeling was performed only for total dairy, milk, and yogurt. Although limited to a small number of included studies, a linear dose–response association was found for them. The risk of overweight or obesity decreased by 25%, 7%, and 12% per 200-g/d intake increase for total dairy, high-fat dairy, and milk, respectively, while the risk decreased by 13% per 50-g/d increment of yogurt intake. For hypertension, the nonlinear association was observed only in total dairy. Inverse significant associations with hypertension were found for low-fat dairy and milk, both decreasing by 6% per 200-g/d intake increase. For T2DM, all types of dairy food consumption except for milk and low-fat dairy products showed nonlinear associations, whereas the associations were not significant for milk and low-fat dairy, and total dairy and yogurt intakes were inversely associated with risk of T2DM.

For overweight or obesity, our meta-analysis suggested that risk of overweight or obesity for total dairy, high-fat dairy, and milk decreased by 27%, 7%, and 12% with per 200-g/d intake increase, respectively, with yogurt decreasing risk by 13% per 50-g/d increment. A previous meta-analysis (21) only explored the association by comparing the highest with the lowest category of dairy product consumption, reporting that total dairy showed a significant association (RR: 0.73; 95% CI: 0.61, 0.87) with yogurt (0.81; 0.71, 0.92), low-fat dairy (1.00; 0.92, 1.09), and whole-fat dairy (0.83; 0.64, 1.07) combining high-fat dairy, butter, and whipping cream together. Given the variation in level of dairy product consumption across different populations and the differing definitions of low and high consumption in different studies, the dichotomous analysis would not be sufficiently informative.

In comparing the previous 4 meta-analyses focusing on hypertension (22–25), our results were in line with the first 2 meta-analyses (22, 23). Nine cohort studies (17, 18, 65–69) additionally included in our meta-analysis showed that total dairy, low-fat dairy, and milk but not high-fat dairy, yogurt, and cheese could decrease the incidence of hypertension. At the same time, a similar linear dose–response relation was found for low-fat dairy and milk. Although total dairy in our meta-analysis was nonlinear but reported as linear by Soedamah-Muthu et al. (22), the protective trend for hypertension was generally consistent. Two recently updated meta-analyses (24, 25) showed inconsistent results, however, with subgroup and dose–response analyses based on the type of dairy products not performed. Considering that various types of dairy products may have different effects on health outcomes, additional analyses based on various types of dairy products are necessary (75, 76).

Although previous meta-analyses (46, 77–79) investigated the relation of dairy products and T2DM, 10 additional cohort studies (13, 19, 20, 26–31) were included in our meta-analysis. We found that total dairy, low-fat dairy, and yogurt showed a positive association with T2DM incidence, which was consistent with recent meta-analyses (79, 80). The nonlinear dose–response observed for total dairy in our research, however, contradicted the work of Gijsbers et al. (79). The discrepancy might be attributed to our present analysis including more comprehensive data and a wider range in total dairy consumption (0–1700 g/d).

A significant inverse association was found between total dairy and overweight or obesity, hypertension, and T2DM. Consistent with our findings, there was evidence that dairy products containing specific components, such as calcium, vitamin D, magnesium, potassium, and whey protein, have a favorable impact on the prevention of excess body weight, hypertension, and glucose accumulation, according to several studies (74, 81–86). These specific components may increase insulin secretion and insulin sensitivity and reduce insulin resistance (87–90). In addition, they also enhance renal sodium excretion (91), block calcium channels, reduce intracellular calcium concentrations (12), and increase nitric oxide synthesis (92). Conversely, there was no significant relation of high-fat dairy with hypertension and T2DM or of cheese with overweight or obesity, hypertension, and T2DM. The possible reason is that the high saturated fatty acid content in high-fat dairy products and salt in cheese can impede calcium and magnesium absorption (60, 93), counteracting their favorable effects; however, because a limited number of studies were included (70, 74), the positive relation between high-fat dairy and overweight or obesity may be a chance finding.

For yogurt consumption, our results are consistent with many studies that report that yogurt has a protective effect on overweight or obesity (71, 73), hypertension (66, 69, 74), and T2DM (46, 77, 78, 94–96). Several mechanisms

may explain the inverse association. The nutrients in yogurt may be more bioavailable than in other dairy products (97). Calcium in yogurt can reduce lipogenesis and increase lipolysis by the suppression of the formation of 1,25-dihydroxyvitamin D and by the secretion of parathyroid hormone, and it can promote the formation of calcium soaps in the intestine, resulting in increased fat excretion and reduced fat absorption (98, 99). Yogurt may exert beneficial effects because of probiotic bacteria, which have been shown to improve the lipid profile and antioxidant status in patients with T2DM (100, 101), have been reported to lower cholesterol concentrations (102), and have been found to inhibit angiotensin-converting enzyme and thus reduce blood pressure (23). Yogurt also contains vitamin K-2, which was shown to be inversely associated with the risk of T2DM (103). In addition, yogurt is made through fermentation, a process in which biologically active peptides such as isoleucine–proline–proline (IPP) and valine–proline–proline (VPP) are formed when milk proteins are catalyzed by proteolytic lactic acid bacteria (104). IPP and VPP have been shown to promote antihypertensive effects by inhibiting angiotensin-converting enzyme (105). Of note, BMI may be a potential source of heterogeneity in the relation between yogurt consumption and hypertension, with a lower heterogeneity ($I^2 = 6.8\%$) in the studies with adjustment for BMI. A previous study reported that obesity may increase the activity of the adipose renin–angiotensin system, which further enhances the synthesis of angiotensin II and results in vasoconstriction (106). In addition, geographical location may influence the associations between yogurt and T2DM, with an inverse association reported in US populations but not in other regions. The inherent differences in study populations in terms of general characteristics, other dietary and lifestyle factors, or their variable consumption of substitutes for dairy products, for instance, may affect the reported associations.

For low-fat dairy consumption, our meta-analysis found an inverse association with hypertension and a borderline inverse association with T2DM, which was in line with most previous studies (22, 77, 78, 94, 107). People who consume low-fat dairy may be more health conscious and have healthier eating and lifestyle patterns. Surprisingly, a stronger inverse association was found in studies with a follow-up of $\leq$10 y. Our finding, suggesting that the potential benefits of low-fat dairy were less evident with longer follow-up periods, was supported by previous studies (46, 74, 79). As for overweight or obesity, the association of low-fat dairy is not significant, possibly because only 2 studies were included in the analysis (70, 74). Future studies should therefore focus on low-fat dairy products and obesity to confirm the association.

A significant inverse association was found between milk and overweight or obesity and hypertension. These results are consistent with previous findings (17, 18, 66, 69). The underlying mechanism may be calcium in milk products combining with fatty acids and bile acids in the gut, thereby increasing fecal fat excretion and/or inhibiting fat reabsorption (108, 109). Calcium in milk also reduces blood pressure via suppression of 1,25-dihydroxyvitamin D, which increases intercellular calcium in vascular smooth muscle cells (110). Although we observed no association with milk and T2DM, consistent with previous meta-analyses (77, 94) and a study of Mendelian randomization (111), restricted cubic spline modeling showed that the risk of T2DM decreased as milk intake increased. The mechanism behind the relation between milk and T2DM is not clear at present, and more related studies are expected in the future. In addition, our subgroup analysis showed that geography may affect the relation between milk and T2DM, with a positive association found in Europe. The possible reason for this difference may be that the composition of milk is different between regions. For fermented dairy, the variation in intake and the number of studies were too small for subgroup analysis. These results, therefore, should be interpreted with caution.

A major strength of the current meta-analysis is that we examined a wide range of well-specified dairy foods in relation to overweight or obesity, hypertension, and T2DM risk based on cohort studies, making use of data from 42 articles. We were able to examine dose–response relations and linear/nonlinear associations, which may provide further scientific evidence for developing dietary guidelines for dairy product consumption. According to NUQUEST, >80% of the included studies were neutral, indicating that the overall quality of this meta-analysis is good with a high level of credibility. The current study was also subject to several limitations. First, the included studies were conducted in different populations, with different follow-up periods and baseline ages, and were adjusted for different factors. Although a statistical model that takes the diverse nature of these studies into account was used, some of their characteristics might have influenced the results. Second, although possible publication bias existed in the meta-analysis assessing the associations of low-fat dairy and yogurt consumption with T2DM risk, the trim-and-fill adjustment did not substantially change the results. Third, consumption of dairy products was self-reported and assessed by FFQ, possibly introducing recall and measurement biases, although FFQ is a proven dietary assessment tool. Fourth, standard servings of 177 g for total, high-fat, low-fat, and fermented dairy; 244 g for milk and yogurt; and 43 g for cheese were assumed for studies that did not define serving size, which may have over- or underestimated the empirical intake levels of dairy intake. Fifth, because of the limited number of original articles for overweight or obesity, we did not conduct subgroup analyses or explore publication bias. We therefore look forward to more related studies published in the future to strengthen the reliability of our results. Finally, the results should be interpreted cautiously because the present analyses were based only on cohort rather than intervention studies.

In conclusion, the present meta-analysis of 52 cohort studies indicated that total dairy, milk, and yogurt intakes were associated with a lower risk of overweight or obesity, with similar results for total dairy, low-fat dairy, and milk

intakes for hypertension and total dairy and yogurt intakes for T2DM. Our results suggest that total dairy intake, including any other type of dairy product, is protective for overweight or obesity, hypertension, and T2DM, although the separate effects of various types of dairy products on these 3 outcomes are inconsistent. In addition, the current results are based on cohort studies and need to be confirmed in randomized controlled trials in the future.

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