

Dairy products and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies^{1–3}

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ABSTRACT

Background: The association between intake of dairy products and the risk of type 2 diabetes has been investigated in several studies, but the evidence is not conclusive.

Objective: We conducted an updated systematic review and dose-response meta-analysis of dairy product intake and the risk of type 2 diabetes.

Design: We searched the PubMed database for prospective cohort and nested case-control studies of dairy product intake and risk of type 2 diabetes up to 5 June 2013. Summary RRs were estimated by use of a random-effects model.

Results: Seventeen cohort studies were included in the meta-analysis. In the dose-response analysis, the summary RRs (95% CIs) were 0.93 (0.87, 0.99; $I^2 = 33%$) per 400 g total dairy products/d ($n = 12$), 0.98 (0.94, 1.03; $I^2 = 8%$) per 200 g high-fat dairy products/d ($n = 9$), 0.91 (0.86, 0.96; $I^2 = 40%$) per 200 g low-fat dairy products/d ($n = 9$), 0.87 (0.72, 1.04; $I^2 = 94%$) per 200 g milk/d ($n = 7$), 0.92 (0.86, 0.99; $I^2 = 0%$) per 50 g cheese/d ($n = 8$), and 0.78 (0.60, 1.02; $I^2 = 70%$) per 200 g yogurt/d ($n = 7$). Nonlinear inverse associations were observed for total dairy products (P -nonlinearity < 0.0001), low-fat dairy products (P -nonlinearity = 0.06), cheese (P -nonlinearity = 0.05), and yogurt (P -nonlinearity = 0.004), and there was a flattening of the curve at higher intakes.

Conclusions: This meta-analysis suggests that there is a significant inverse association between intakes of dairy products, low-fat dairy products, and cheese and risk of type 2 diabetes. Any additional studies should assess the association between other specific types of dairy products and the risk of type 2 diabetes and adjust for more confounding factors. *Am J Clin Nutr* 2013;98:1066–83.

INTRODUCTION

The prevalence of type 2 diabetes is increasing rapidly around the world, parallel to the increase in obesity, the reduction in physical activity, and dietary changes. It has been estimated that 366 million persons had diabetes (mostly type 2) in 2011, and the number has been projected to increase to 552 million by 2030 (1). Although diet is thought to be of major importance for the increased prevalence of type 2 diabetes, few dietary factors have been established as risk factors for type 2 diabetes (2–5).

Dairy products have been hypothesized to protect against type 2 diabetes because of their high content of calcium, magnesium, vitamin D, and whey proteins, which may reduce body fat and insulin resistance (6). However, some dairy products, such as cheese and cream, also have a high fat content that might offset any benefits of increased intake of calcium or other potentially

beneficial dairy components. Epidemiologic studies have yielded mixed results: some have suggested a decreased risk associated with higher intake of dairy products (7–14), whereas other studies suggested no association (15–23). Studies of specific types of dairy products have also shown mixed results: some have reported inverse associations for low-fat dairy products (7, 10, 13, 15, 19), milk (12, 16), low-fat or skim milk (7, 10, 14), cheese (10, 14, 21), and yogurt (7, 10, 19, 21), whereas other studies suggested no association (8, 17, 18, 20, 22–24). In contrast, most studies of high-fat dairy products reported no association (7, 8, 10, 13, 15, 20, 24), and only one study reported a reduced risk (23). The dose-response relation between dairy products and type 2 diabetes needs more detailed examination to establish whether there could be potential threshold effects. In addition, it is important to establish whether the associations may differ according to the type of dairy product consumed and by study characteristics such as geographic location and adjustment for confounding factors. To clarify the association between dairy product intake and risk of type 2 diabetes, we conducted a systematic review and meta-analysis of the available prospective studies, with specific aims of analyzing different types of dairy products, to clarify whether the association differed by study characteristics and to clarify any dose-response relation between dairy product intake and the risk of type 2 diabetes.

METHODS

Search strategy

We searched the PubMed database (<http://www.ncbi.nlm.nih.gov/pubmed>) up to 5 June 2013 for cohort studies of dairy intake and type 2 diabetes risk. As part of a larger systematic review of

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² Supported by the Liaison Committee between the Central Norway Regional Health Authority (RHA) and the Norwegian University of Science and Technology (NTNU).

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Received January 15, 2013. Accepted for publication July 22, 2013.

First published online August 14, 2013; doi: 10.3945/ajcn.113.059030.



dietary factors and type 2 diabetes risk we used broad search terms on a wide range of dietary factors and type 2 diabetes. The search terms included the following: (cereal OR grain OR grains OR rice OR bread OR roots OR tubers OR vegetable OR fruits OR pulse OR pulses OR bean OR beans OR lentil OR lentils OR legume OR legumes OR soy OR soya OR pea OR chickpeas OR chickpea OR nut OR seed OR peanut OR peanuts OR meat OR beef OR pork OR lamb OR poultry OR chicken OR fish OR egg OR eggs OR seafood OR shellfish OR dairy OR dairy products OR milk OR cheese OR yoghurt OR ice cream OR butter OR drink OR drinks OR beverage OR soda OR sodas OR juice OR juices OR punch OR foods) AND diabetes. We also searched the reference lists of previous reviews of the subject (25–28) and of the studies included in the analysis for any further studies.

Study selection

To be included, the study had to have a prospective cohort, a case-cohort, or a nested case-control design and to investigate the association between intake of dairy products and the risk of type 2 diabetes. Estimates of the RR (HR, risk ratio, OR) had to be available with the 95% CIs, and for the dose-response analysis a quantitative measure of intake and the total number of cases and person-years had to be available in the publication or on request from the authors. We identified 22 potentially relevant studies (7–24, 29–32). One study was excluded because of a cross-sectional design (31), 2 studies did not report any risk estimates for type 2 diabetes (29, 30), and one study was excluded because it reported on a combined outcome of impaired fasting blood glucose and type 2 diabetes (32). The European Investigation into Cancer and Nutrition (EPIC)–Potsdam Study (24) reported on different dairy food items than the EPIC-InterAct Study (21) and was therefore included despite the overlap between these studies.

Data extraction

We extracted the following data from each study: the first author's last name, publication year, country in which the study was conducted, study name, follow-up period, sample size, sex, age, number of cases, dietary assessment method (type, number of food items, and whether the method had been validated), exposure, quantity of intake, RRs and 95% CIs for the highest compared with the lowest intake, and variables adjusted for in the analysis.

Statistical methods

We used random-effects models to calculate summary RRs and 95% CIs for the highest compared with the lowest amount of dairy product intake and for the dose-response analysis (33). The average of the natural logarithm of the RRs was estimated, and the RR from each study was weighted by the inverse of its variance. A 2-tailed P value <0.05 was considered significant. For one study that reported results separately for men and women (18), but not combined, we combined the results by using a fixed-effects model to obtain an estimate for both sexes combined, which was used for the overall analysis.

We used the method described by Greenland and Longnecker (34) for the dose-response analysis and computed study-specific slopes (linear trends) and 95% CIs from the natural logs of the RRs and CIs across categories of dairy product intake. The

method requires that the distribution of cases and person-years or noncases and the RRs with the variance estimates for at least 3 quantitative exposure categories are known. We estimated the distribution of cases or person-years in studies that did not report these but reported the total number of cases/person-years (35). The median or mean amount of dairy product intake in each category of intake was assigned to the corresponding RR for each study. For studies that reported dairy product intake by ranges of intake we estimated the midpoint for each category by calculating the average of the lower and upper bound. When the highest or lowest category was open-ended, we assumed the open-ended interval length to be the same as the adjacent interval. In studies that reported the intakes by frequency, we used 43 g as a serving size for cheese, 177 g as a serving size for total dairy products, and 244 g as a serving size for milk and yogurt intake to recalculate the intakes to a common scale (g/d) (36). We examined a potential nonlinear dose-response relation between dairy intake and type 2 diabetes by using fractional polynomial models (37). We determined the best-fitting second-order fractional polynomial regression model, defined as the one with the lowest deviance. A likelihood ratio test was used to assess the difference between the nonlinear and linear models to test for nonlinearity (37). The intake in the reference category was subtracted from the intake in each category for the linear dose-response analysis but not for the nonlinear dose-response analysis. Supplementary information was requested from 3 studies (9, 14, 16) and was obtained from 2 of these studies (14, 16).

Heterogeneity between studies was assessed by the Q test and I^2 (38). I^2 is the amount of total variation that is explained by between-study variation. I^2 values of $\sim 25\%$, 50% , and 75% are considered to indicate low, moderate, and high heterogeneity, respectively. To investigate sources of heterogeneity, we conducted subgroup and meta-regression analyses stratified by study characteristics such as sex, duration of follow-up, number of cases, and adjustment for confounding factors.

Publication bias was assessed with Egger's test (39), and the results were considered to indicate publication bias when $P < 0.10$. We conducted sensitivity analyses excluding one study at a time to ensure that the results were not simply due to one large study or to a study with an extreme result. Results from these sensitivity analyses are presented excluding the 2 studies with the largest negative and positive impact on the summary estimates. The statistical analyses were conducted by using Stata, version 10.1 (StataCorp).

RESULTS

We identified 17 cohort studies (18 publications) (7–24) that could be included in the analysis. All the studies were included in the high compared with low meta-analysis (7–23), and 15 cohort studies (16 publications) (7, 8, 10, 12–24) could be included in the dose-response meta-analysis (Table 1 and Figure 1). Seven studies were from the United States, 6 studies were from Europe, 2 were from Asia, and 2 were from Australia (Table 1).

Total dairy products

Fourteen cohort studies (7, 9–11, 13–16, 18–23) investigated the association between total dairy product intake and type 2

TABLE 1
Prospective cohort studies of milk and dairy product intake and type 2 diabetes risk^a

First author, publication year, country/ region (ref)	Study name	Follow-up period	Study size, sex, age, number of cases	Dietary assessment	Exposure	Quantity	RR (95% CI)	Adjustment for confounders
Choi, 2005, USA (7)	Health Professionals Follow-Up Study	1986–1998, 12-y follow-up	41,254 men, age 40–75 y, 1243 cases	Validated FFQ, 131 food items	Total dairy intake Low-fat dairy foods High-fat dairy foods Skim, low-fat milk Whole milk	≥2.9 vs <0.9 servings/d Per 1 serving/d ≥1.58 vs <0.14 servings/d Per 1 serving/d ≥1.72 vs <0.38 servings/d Per 1 serving/d ≥2 servings/d vs <1 serving/mo ≥2 servings/wk vs <1 serving/mo	0.77 (0.62, 0.95) 0.91 (0.85, 0.97) 0.74 (0.60, 0.91) 0.88 (0.81, 0.94) 0.97 (0.78, 1.21) 0.99 (0.91, 1.07) 0.78 (0.63, 0.97) 1.19 (1.00, 1.43)	Age, total energy intake, FH of DM, smoking status, BMI, hypercholesterolemia, hypertension, physical activity, alcohol intake, cereal fiber, <i>trans</i> FAs, PUFA:SFA ratio, glycemic load
Montonen, 2005, Finland (8)	Finnish Mobile Clinic Health Examination Survey	1967–1990, 23-y follow-up	4304 men and women, age 40–69 y, 383 cases	Dietary history interview, >100 food items	Yogurt Sherbet Cottage, ricotta cheese Ice cream Other cheese Cream cheese Cream Sour cream	≥2 servings/wk vs <1 serving/mo ≥2 servings/wk vs <1 serving/mo ≥2 servings/wk vs <1 serving/mo ≥2 servings/wk vs <1 serving/mo ≥2 servings/wk vs <1 serving/mo ≥2 servings/wk vs <1 serving/mo ≥2 servings/wk vs <1 serving/mo ≥2 servings/wk vs <1 serving/mo	0.83 (0.66, 1.06) 0.85 (0.66, 1.09) 0.96 (0.80, 1.17) 0.78 (0.64, 0.95) 0.88 (0.67, 1.16) 1.06 (0.81, 1.39) 0.89 (0.72, 1.09) 1.04 (0.80, 1.36)	Age, sex, BMI, energy intake, smoking, FH of DM, geographic area
Pittas, 2006, USA (9)	Nurses' Health Study	1980–2000, 20-y follow-up	83,779 women, age 30–55 y, 4843 cases	Validated FFQ, 61–116 food items	Regular dairy products Reduced-fat dairy products Whole milk Butter Dairy foods	≥305 vs <39 g/d >0 vs 0 g/d ≥878 vs <326 g/d >59 vs <27 g/d ≥3 vs <1 serving/d	0.81 (0.62, 1.08) 0.90 (0.60, 1.36) 1.06 (0.75, 1.50) 1.15 (0.80, 1.67) 0.89 (0.81, 0.99)	Age, BMI, hypertension, FH of DM, smoking, physical activity, caffeine, alcohol, residence, SFAs, PUFAs, <i>trans</i> FAs, cereal fiber, Mg, GL, retinol, energy

(Continued)

TABLE 1 (Continued)

First author, publication year, country/ region (ref)	Study name	Follow-up period	Study size, sex, age, number of cases	Dietary assessment	Exposure	Quantity	RR (95% CI)	Adjustment for confounders
Liu, 2006, USA (10)	Women's Health Study	1993–2003, 10-y follow-up	37,183 women, age ≥45 y, 1603 cases	Validated FFQ, 131 food and beverage items	Total dairy intake Low-fat dairy foods High-fat dairy foods	>2.9 vs <0.85 servings/d Per 1 serving/d >2.00 vs 0.27 servings/d Per 1 serving/d >1.329 vs <0.20 servings/d	0.80 (0.67, 0.95) 0.97 (0.93, 1.01) 0.82 (0.68, 0.98) 0.95 (0.90, 1.01) 0.97 (0.80, 1.17)	Age, total energy intake, randomized treatment assignment, FH of DM, smoking status, BMI, hypercholesterolemia, hypertension, physical activity, hormones, alcohol, dietary fiber, total fat, GL
					Skim milk	Per 1 serving/d ≥2 servings/wk vs <1 serving/mo	1.00 (0.95, 1.04) 0.92 (0.78, 1.09)	
					Whole milk	≥2 servings/wk vs <1 serving/mo	1.04 (0.84, 1.30)	
					Yogurt	≥2 servings/wk vs <1 serving/mo	0.82 (0.70, 0.97)	
					Sherbet	≥2 servings/wk vs <1 serving/mo	0.92 (0.77, 1.05)	
					Cottage cheese	≥2 servings/wk vs <1 serving/mo	0.86 (0.71, 1.05)	
					Ice cream	≥2 servings/wk vs <1 serving/mo	0.88 (0.74, 1.05)	
					Other cheese	≥2 servings/wk vs <1 serving/mo	0.80 (0.64, 1.01)	
					Cream cheese	≥2 servings/wk vs <1 serving/mo	1.19 (0.97, 1.47)	
					Cream	≥2 servings/wk vs <1 serving/mo	1.03 (0.86, 1.25)	
					Sour cream	≥2 servings/wk vs <1 serving/mo	0.93 (0.74, 1.18)	
van Dam, 2006, USA (15)	Black Women's Health Study	1995–2003, 8-y follow-up	41,186 women, age 21–69 y, 1964 cases	Validated FFQ, 68 food items	Total dairy products Low-fat dairy products High-fat dairy products	2.53 vs 0.07 servings/d 1.33 vs 0.07 servings/d 1.33 vs 0.07 servings/d	0.93 (0.75, 1.15) 0.87 (0.76, 1.00) 1.03 (0.88, 1.20)	Age, total energy intake, alcohol, BMI, smoking status, strenuous physical activity, parental history of DM, education, coffee, sugar-sweetened soft drinks, processed meat, red meat, whole grains
Lecomte, 2007, France (11)	NA	1995/1997–2000/2002, 5-y follow-up	743 men with IFG, age 20–60 y, 127 cases	FFQ, 18 food items	Dairy products	Not daily vs daily	1.86 (1.21, 2.86)	FH of DM, BMI, TG, glucose at baseline

(Continued)

TABLE 1 (Continued)

First author, publication year, country/ region (ref)	Study name	Follow-up period	Study size, sex, age, number of cases	Dietary assessment	Exposure	Quantity	RR (95% CI)	Adjustment for confounders
Elwood, 2007, United Kingdom (16)	Caerphilly Prospective Study	1979/1983-NA, 20-y follow-up	640 men, age 45-59 y, 41 cases	7-d weighed records	Milk Dairy foods	396.8 vs 76.5 g/d ² 430.4 vs 107.0 g/d ²	0.57 (0.20, 1.63) 0.59 (0.21, 1.69) ²	Age, smoking, BMI, social class
Vang, 2008, USA (17)	Adventist Health Study	1960-1976, 17-y follow-up	8401 men and women, age 45-88 y, 543 cases	Validated FFQ	Cheese Milk	≥1 time/wk vs never ≥4 times/d vs never	0.90 (0.71, 1.15) 0.92 (0.65, 1.29)	Age, sex
Villegas, 2009, China (12)	Shanghai Women's Health Study	2000-2006, 6.9-y follow-up	64,191 women, age 40-70 y, 2270 cases (1514 confirmed cases)	Validated FFQ, 77 food items	Fresh milk, all participants Powdered milk Fresh milk, confirmed cases	250.0 vs 0 g/d Yes vs no 250.0 vs 0 g/d	0.46 (0.32, 0.64) 0.74 (0.67, 0.82) 0.60 (0.41, 0.88)	Age, energy intake, BMI, WHR, smoking status, alcohol, physical activity, income, education, occupation, hypertension
Kirri, 2009, Japan (18)	Japan Public Health Center-based Prospective Study	1995/1998-2000/2003, 5-y follow-up	59,796 men and women, age 40-59 y, 1114 cases	Validated FFQ, 147 food and beverage items	Powdered milk Dairy products, men Milk Cheese Yogurt Dairy products, women	Yes vs no ≥300 vs <50 g/d ≥200 vs <50 g/d ≥5 vs 0 g/d ≥60 vs 0 g/d ≥300 vs <50 g/d	0.85 (0.75, 0.96) 1.18 (0.90, 1.56) 1.02 (0.85, 1.24) 0.88 (0.64, 1.21) 1.01 (0.75, 1.36) 0.71 (0.51, 0.98)	Age, area, BMI, FH of DM, smoking status, alcohol intake, history of hypertension, exercise frequency, coffee consumption, energy-adjusted Mg, total energy intake
Malik, 2011, USA (13)	Nurses' Health Study II	1997-2005, 7-y follow-up	37,038 women, age 24-42 y, 550 cases	Validated FFQ, 133 food items	Total dairy Low-fat dairy foods High-fat dairy foods	2.14 vs 0.62 servings per 1000 kcal/d 1.44 vs 0.18 servings per 1000 kcal/d 1.14 vs 0.19 servings per 1000 kcal/d	0.75 (0.55, 1.02) 0.74 (0.54, 1.01) 0.72 (0.53, 0.99)	Age, BMI, total energy, FH of DM, smoking status, physical activity, alcohol use, OC use, HRT, PUFA; SFA ratio, GL, cereal fiber, <i>trans</i> fat, processed meat, carbonated soft drinks, fruit drinks, coffee; mutual adjustment; high- and low-fat dairy products

(Continued)

TABLE 1 (Continued)

First author, publication year, country/ region (ref)	Study name	Follow-up period	Study size, sex, age, number of cases	Dietary assessment	Exposure	Quantity	RR (95% CI)	Adjustment for confounders
Margolis, 2011, USA (19)	Women's Health Initiative	1994/1998–2005, 7.9-y follow-up	82,076 women, age 50–79 y, 3946 cases	FFQ, >300 foods and beverages	Low-fat dairy products Total dairy products Yogurt	2.8 vs 0.05 servings/d 3.4 vs 0.5 servings/d ≥2 servings/wk vs <1 serving/mo	0.65 (0.44, 0.96) 0.93 (0.83, 1.04) 0.46 (0.31, 0.68)	Age, race-ethnicity, total energy intake, income, education, BMI, smoking, alcohol intake, FH of DM, HRT, SBP, DBP, physical activity, interaction of low-fat dairy × BMI, interaction of yogurt × time
Stuijck, 2012, Europe (21)	EPIC-Interact Study	1991–2007, 11.7-y follow-up	24,475 men and women, mean age 52 y, 10,694 cases	Validated FFQ, 24-h recall	Total dairy products Milk Yogurt and thick, fermented milk Cheese Combined fermented dairy intake	628.9 vs 79.7 g/d 486.1 vs 0.3 g/d 190.4 vs 0 g/d 73.7 vs 3.2 g/d 220.7 vs 11.6 g/d	1.01 (0.89, 1.13) 1.10 (0.92, 1.31) 0.91 (0.81, 1.02) 0.88 (0.76, 1.02) 0.88 (0.78, 0.99)	Age; center; sex; BMI; education; smoking status; physical activity; intakes of alcohol, fruit and vegetables, red meat, processed meat, sugar-sweetened soft drinks, coffee, cereals, cereal products, energy
Struijk, 2012, Denmark (22)	The Inter99 Study	1999/2001–2006, 5-y follow-up	5953 men and women, age 30–60 y, 214 cases	Validated FFQ, 198 food items	Total dairy Low-fat dairy Full-fat dairy Milk and milk products Cheese Fermented dairy	578 vs 47 g/d Per 1 serving/d 536 vs 6 g/d Per 1 serving/d 89 vs 4 g/d Per 1 serving/d 546 vs 16 g/d Per 1 serving/d 49 vs 4 g/d Per 1 serving/d 260 vs 13 g/d Per 1 serving/d	0.96 (0.58, 1.58) 0.95 (0.86, 1.06) 0.85 (0.52, 1.40) 0.95 (0.85, 1.06) 0.94 (0.56, 1.58) 1.03 (0.77, 1.36) 0.95 (0.58, 1.57) 0.96 (0.86, 1.06) 0.78 (0.47, 1.29) 0.97 (0.82, 1.15) 0.86 (0.50, 1.47) 0.88 (0.69, 1.11)	Age; sex; intervention group; FH of DM; education; physical activity; smoking status; intakes of alcohol, whole-grain cereal, meat, fish, coffee, tea, fruit, vegetables, energy; change in diet from baseline to 5-y follow-up; waist circumference
Louié, 2012, Australia (23)	The Blue Mountains Eye Study	1992/1994–2002/2004, 10-y follow-up	1824 men and women, age ≥49 y, 145 cases	Validated FFQ, 145 food items	Total dairy Reduced/low-fat dairy Regular dairy	3.1 vs 0.5 servings/d 2.1 vs 0 servings/d 1.9 vs 0.1 servings/d	0.96 (0.54, 1.17) 1.00 (0.58, 1.71) 0.83 (0.47, 1.48)	Age, sex, smoking status, physical activity, GL, vegetable fiber, total energy, FH of DM2, SBP, BMI, HDL, total cholesterol, TG

(Continued)

TABLE 1 (Continued)

First author, publication year, country/ region (ref)	Study name	Follow-up period	Study size, sex, age, number of cases	Dietary assessment	Exposure	Quantity	RR (95% CI)	Adjustment for confounders
Grantham, 2013, Australia (14)	The Australian Diabetes and Obesity and Lifestyle Study	1999/2000–2004/2005, 5-y follow-up	5582 men and women, age ≥ 25 y, 209 cases	FFQ, 121 food items	Total dairy foods Low-fat milk Full-fat milk Yogurt Cheese	477 vs 205 g/d ² 375 vs 0 g/d ² 375 vs 0 g/d ² 114 vs 3 g/d ² 29 vs 4 g/d ²	0.71 (0.48, 1.05) 0.65 (0.44, 0.94) 1.18 (0.78, 1.79) 1.14 (0.78, 1.67) 0.78 (0.53, 1.15)	Age, sex, energy intake, FH DM, education, physical activity, smoking status, TG, HDL cholesterol, SBP, waist circumference, hip circumference
von Ruesten, 2013, Germany (24)	EPIC-Potsdam Study	1994/1998–NA, 8-y follow-up	23,531 men and women, age 35–65 y, 837 cases	Validated FFQ, 148 food items	Low-fat dairy products High-fat dairy products Low-fat cheese High-fat cheese	Per 100 g/d Per 100 g/d Per 30 g/d Per 30 g/d	1.02 (0.96, 1.09) 1.00 (0.92, 1.08) 0.98 (0.83, 1.15) 0.96 (0.85, 1.08)	Age, sex, smoking status, pack-years of smoking, alcohol, leisure-time physical activity, BMI, WHR, hypertension, high blood lipids, education, vitamin supplementation, total energy intake, other food groups
Soedamah-Muthu, 2013, UK (20)	The Whitehall II Prospective Study	1985/1988–2009, 10-y follow-up	4526 men and women, 35–55 y, 273 cases	FFQ, 114 food items	Total dairy High-fat dairy Low-fat dairy Total milk Fermented dairy Yogurt Cheese	575 vs 246 g/d 182 vs 27 g/d 458 vs 28 g/d 441 vs 147 g/d 105 vs 17 g/d 117 vs 0 g/d 31 vs 6 g/d	1.30 (0.95, 1.77) 1.23 (0.91, 1.67) 0.98 (0.73, 1.31) 0.97 (0.71, 1.32) 1.17 (0.87, 1.58) 1.04 (0.77, 1.42) 1.20 (0.88, 1.64)	Age; ethnicity; employment grade; smoking; BMI; physical activity; FH of CHD/hypertension; intakes of alcohol, fruit and vegetables, bread, meat, fish, coffee, tea, total energy

¹ CHD, coronary heart disease; DBP, diastolic blood pressure; DM, diabetes mellitus; EPIC, European Prospective Investigation into Cancer and Nutrition; FA, fatty acid; FFQ, food-frequency questionnaire; FH, family history; GL, glycemic load; HRT, hormone replacement therapy; IFG, impaired fasting glucose; NA, not available; OC, oral contraceptive; ref, reference; SBP, systolic blood pressure; TG, triacylglycerol; WHR, waist-to-hip ratio.

² Based on supplementary information provided by the authors.

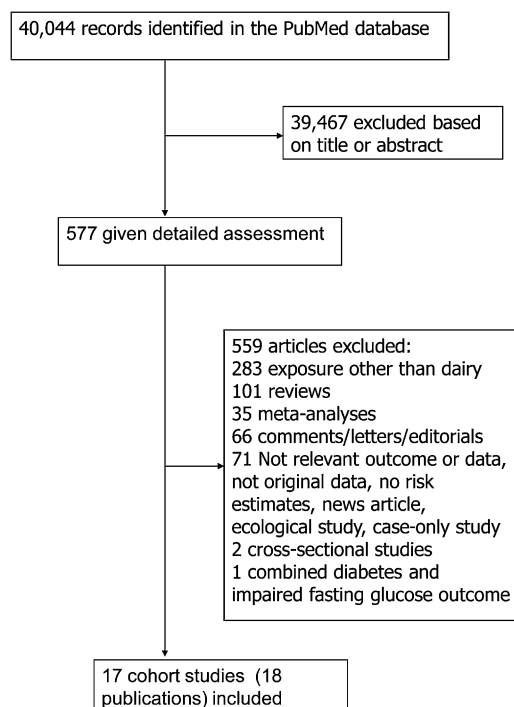


FIGURE 1. Flow chart of study selection. PubMed, <http://www.ncbi.nlm.nih.gov/pubmed>.

diabetes risk and included 26,976 cases among 426,055 participants. Twelve of these studies were included in the dose-response analysis (7, 9–11, 13–16, 18–23), and 2 studies were excluded because they only reported results for a high and low comparison (9, 11). The summary RR for high compared with low intake was 0.89 (95% CI: 0.82, 0.96), with moderate heterogeneity between studies ($I^2 = 42.1\%$ and P -heterogeneity = 0.05) (see Supplemental Figure S1 under “Supplemental data” in the online issue). The summary RR per 400 g/d was 0.93 (95% CI: 0.87, 0.99; $I^2 = 33.1\%$ and P -heterogeneity = 0.13) (Figure 2A). In sensitivity analyses excluding one study at a time from the analysis, the summary RRs for type 2 diabetes ranged from 0.91 (95% CI: 0.85, 0.97) when the EPIC-Interact Study (21) was excluded to 0.95 (95% CI: 0.90, 1.00) when the Health Professionals Follow-Up Study (7) was excluded. There was no indication of publication bias with Egger’s test ($P = 0.20$). There was evidence of a nonlinear association between dairy product intake and type 2 diabetes, and most of the benefit was observed when increasing the intake from low amounts (P -nonlinearity < 0.0001), and there was no further reduction in risk above an intake of 300–400 g/d (see Figure 2B and Supplemental Table S1 under “Supplemental data” in the online issue).

High-fat dairy products

Nine cohort studies (7, 8, 10, 13, 15, 20, 22–24) investigated the association between intake of high-fat dairy products and type 2 diabetes risk and included 7222 cases among 196,799 participants. One of these studies was only included in the dose-response analysis because it reported only a continuous result (24). The summary RR for high compared with low intake was 0.96 (95% CI: 0.87, 1.06; $I^2 = 15.8\%$ and P -heterogeneity = 0.31) (see Supplemental Figure S2 under “Supplemental data”

in the online issue). The summary RR per 200 g/d was 0.98 (95% CI: 0.94, 1.03; $I^2 = 7.6\%$ and P -heterogeneity = 0.37) (Figure 3A). The summary RRs ranged from 0.97 (95% CI: 0.91, 1.03) when the Women’s Health Study was excluded (10) to 0.99 (95% CI: 0.96, 1.03) when the Nurses’ Health Study II (13) was excluded. There was no evidence of publication bias ($P = 0.77$), and there was no evidence of a nonlinear association (P -nonlinearity = 0.57) (Figure 3B and Supplemental Table S2 under “Supplemental data” in the online issue).

Low-fat dairy products

Ten cohort studies (7, 8, 10, 13, 15, 19, 20, 22–24) were included in the analysis of low-fat dairy products and type 2 diabetes risk and included 11,168 cases among 278,875 participants. Nine of the studies were included in the dose-response analysis (7, 10, 13, 15, 19, 20, 22–24). One of the studies was excluded from the dose-response analysis because results were presented in only 2 categories (8), and one study was excluded from the high compared with low analysis because it presented only continuous results (24). The summary RR for high compared with low intake was 0.83 (95% CI: 0.76, 0.90; $I^2 = 0\%$ and P -heterogeneity = 0.67) (see Supplemental Figure S3 under “Supplemental data” in the online issue). The summary RR per 200 g/d was 0.91 (95% CI: 0.86, 0.96; $I^2 = 40.2\%$ and P -heterogeneity = 0.10) (Figure 3C). The summary RRs ranged from 0.90 (95% CI: 0.85, 0.94) when the EPIC-Potsdam Study was excluded (24) to 0.92 (95% CI: 0.87, 0.97) when the Women’s Health Initiative Observational Study (19) was excluded. There was no evidence of publication bias ($P = 0.49$). There was some indication of a nonlinear association between low-fat dairy products and type 2 diabetes (P -nonlinearity = 0.06), with no further reduction in risk above 300–400 g/d (see Figure 3D and Supplemental Table S3 under “Supplemental data” in the online issue).

Milk

Seven cohort studies (12, 16–18, 20–22) were included in the analysis of high compared with low milk intake and type 2 diabetes risk and included a total of 15,149 cases among 167,982 participants. The summary RR was 0.87 (95% CI: 0.70, 1.07), and there was high heterogeneity ($I^2 = 70.5\%$; P -heterogeneity = 0.002) (see Supplemental Figure S4 under “Supplemental data” in the online issue). The summary RR per 200 g/d was 0.87 (95% CI: 0.72, 1.04), and there was very high heterogeneity ($I^2 = 93.6\%$; P -heterogeneity < 0.0001) (Figure 4A). In a sensitivity analysis, the summary RRs of type 2 diabetes ranged from 0.84 (95% CI: 0.66, 1.06) when the EPIC-Interact Study (21) was excluded to 0.99 (95% CI: 0.95, 1.04) when the Shanghai Women’s Health Study (12) was excluded. The heterogeneity was also reduced when the latter study was excluded ($I^2 = 0\%$ and P -heterogeneity = 0.76). There was no indication of publication bias with Egger’s test ($P = 0.41$). There was evidence of a nonlinear inverse association between milk intake and type 2 diabetes (P -nonlinearity < 0.0001); however, the CIs were wide (see Figure 4B and Supplemental Table S4 under “Supplemental data” in the online issue). When the Shanghai Women’s Health Study (which seemed to be an outlier) was excluded, the test for nonlinearity was no longer significant (P -nonlinearity = 0.62)

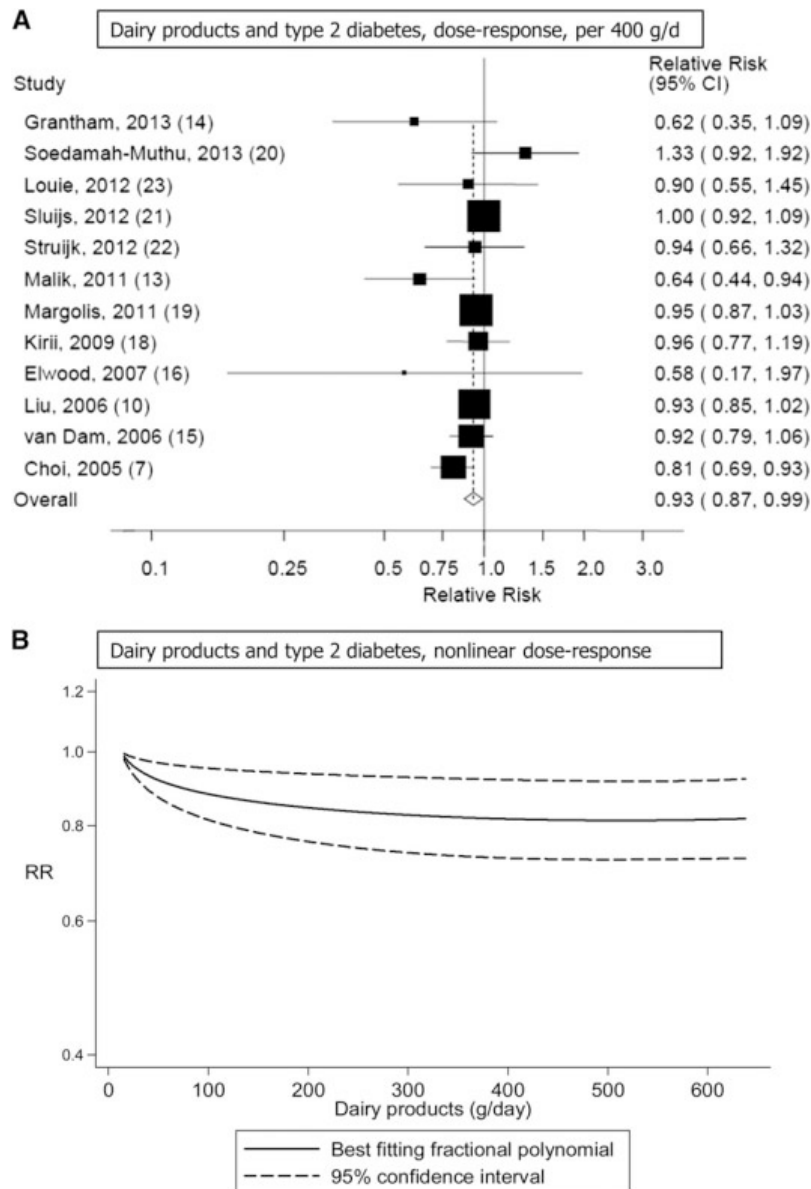


FIGURE 2. A, B: Intake of total dairy products and risk of type 2 diabetes. The summary RR per 400 g/d by using random-effects models was 0.93 (95% CI: 0.87, 0.99; $I^2 = 33.1\%$; P -heterogeneity = 0.13; $n = 341,533$). There was evidence of a nonlinear association between total dairy products and type 2 diabetes, P -nonlinearity < 0.0001.

and the association was null over the whole range of intake (results not shown).

Cheese

Eight cohort studies (7, 10, 14, 17, 18, 20–22) were included in the analysis of cheese intake and type 2 diabetes risk and included a total of 17,620 cases among 242,960 participants. The summary RR for high compared with low intake was 0.91 (95% CI: 0.84, 0.98), with no heterogeneity ($I^2 = 0\%$; P -heterogeneity = 0.57) (see Supplemental Figure S5 under “Supplemental data” in the online issue). The summary RR per 50 g/d was 0.92 (95% CI: 0.86, 0.99), with no heterogeneity ($I^2 = 0\%$; P -heterogeneity = 0.79) (Figure 5A). The summary RRs ranged from 0.91 (95% CI: 0.72, 1.14) when the EPIC-Interact Study (21) was excluded to 0.93 (95% CI: 0.86, 0.99) when the Australian Diabetes

Obesity and Lifestyle Study (14) was excluded. There was no evidence of publication bias with Egger’s test ($P = 0.74$). There was some indication of a nonlinear association between cheese intake and type 2 diabetes (P -nonlinearity = 0.05), with a reduction in risk up to an intake of ~ 50 g/d (see Figure 5B and Supplemental Table S5 under “Supplemental data” in the online issue); however, there were few data points above that value.

Yogurt

Seven cohort studies (7, 10, 14, 18–21) were included in the analysis of high compared with low yogurt intake and type 2 diabetes risk and included a total of 19,082 cases among 254,892 participants. The summary RR was 0.86 (95% CI: 0.75, 0.98), with moderate heterogeneity ($I^2 = 58.9\%$; P -heterogeneity

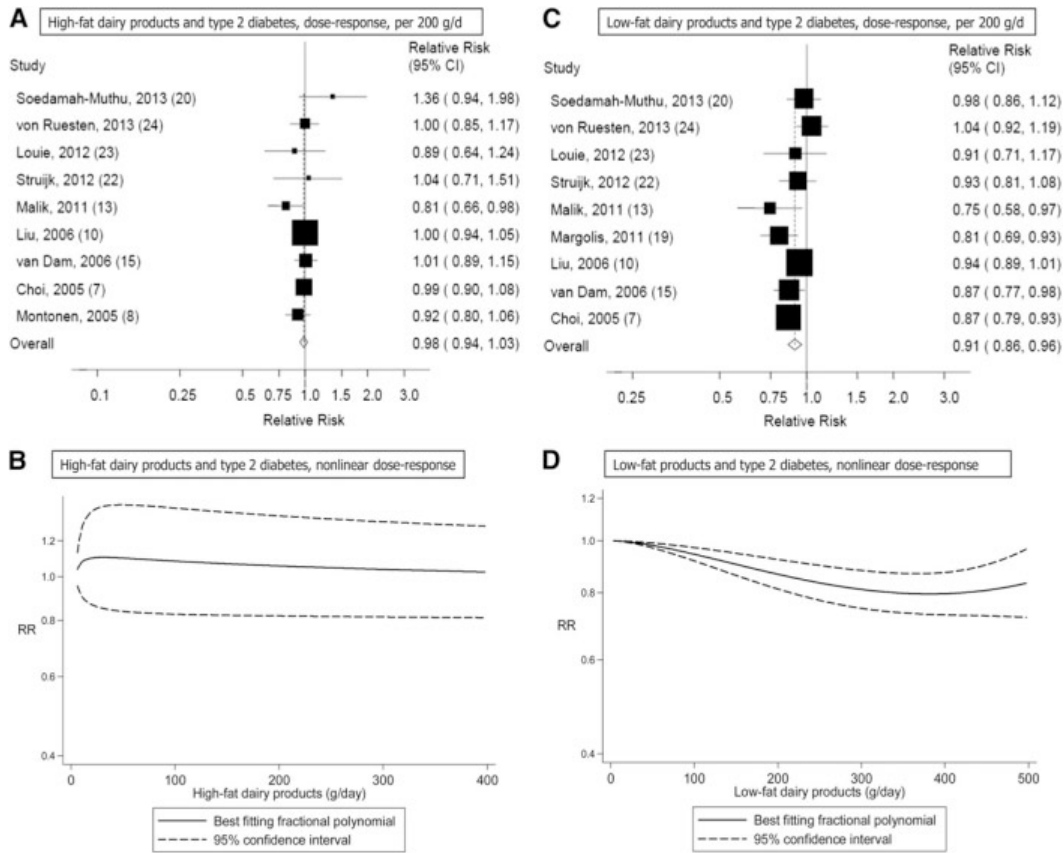


FIGURE 3. A–D: Intake of high- and low-fat dairy products and risk of type 2 diabetes. The summary RRs per 200 g/d by using random-effects models were 0.98 (95% CI: 0.94, 1.03; $I^2 = 7.6\%$; P -heterogeneity = 0.37; $n = 196,799$) for high-fat dairy products (A) and 0.91 (95% CI: 0.86, 0.96; $I^2 = 40.2\%$; P -heterogeneity = 0.10; $n = 274,571$) for low-fat dairy products (C). There was an indication of a nonlinear association between low-fat dairy products and type 2 diabetes (P -nonlinearity = 0.06) (D) but not between high-fat dairy products and type 2 diabetes (P -nonlinearity = 0.57) (B).

= 0.02) (see Supplemental Figure S6 under “Supplemental data” in the online issue). The summary RR per 200 g/d was 0.78 (95% CI: 0.60, 1.02), with high heterogeneity ($I^2 = 69.9\%$; P -heterogeneity = 0.003) (Figure 5C). The summary RRs ranged from 0.73 (95% CI: 0.55, 0.96) when the Australian Diabetes Obesity and Lifestyle Study (14) was excluded to 0.86 (95% CI: 0.72, 1.02) when the Women’s Health Initiative Observational Study (19) was excluded. Most of the heterogeneity was explained by the latter study as well and when excluded ($I^2 = 34.3\%$; P -heterogeneity = 0.18). There was no evidence of publication bias with Egger’s test ($P = 0.37$). There was evidence of a nonlinear association between yogurt intake and type 2 diabetes (P -nonlinearity = 0.004), and there was no further reduction in risk with an intake >120–140 g/d (see Figure 5D and Supplemental Table S6 under “Supplemental data” in the online issue).

Other dairy food items

Fewer studies reported results for other specific dairy food items. Inverse associations were observed for high compared with low intakes of low-fat or skim milk (summary RR = 0.82; 95% CI: 0.69, 0.97; $I^2 = 40.1\%$; P -heterogeneity = 0.19) (7, 10, 14), fermented dairy products (summary RR = 0.88; 95% CI: 0.79, 0.98; $I^2 = 0\%$; P -heterogeneity > 0.99) (21, 22), and ice cream (summary RR = 0.83; 95% CI: 0.73, 0.95; $I^2 = 0\%$; P -heterogeneity = 0.37) (7,

10), but there was no significant association with intake of whole milk (summary RR = 1.12; 95% CI: 0.99, 1.27; $I^2 = 0\%$; P -heterogeneity = 0.79) (7, 8, 10, 14), cottage cheese (summary RR = 0.91; 95% CI: 0.79, 1.04; $I^2 = 0\%$; P -heterogeneity = 0.43) (7, 10), cream (summary RR = 0.96; 95% CI: 0.84, 1.11; $I^2 = 4.9\%$; P -heterogeneity = 0.31) (7, 10), sour cream (summary RR = 0.98; 95% CI: 0.82, 1.16; $I^2 = 0\%$; P -heterogeneity = 0.54) (7, 10), or sherbet (summary RR = 0.90; 95% CI: 0.79, 1.03; $I^2 = 0\%$; P -heterogeneity = 0.60) (7, 10) (Table 2). The summary RRs were 1.06 (95% CI: 0.93, 1.20; $I^2 = 22.5\%$; P -heterogeneity = 0.28) per 200 g whole milk/d (see Supplemental Figure S7 under “Supplemental data” in the online issue) and 0.89 (95% CI: 0.84, 0.95; $I^2 = 0\%$; P -heterogeneity = 0.57) per 200 g low-fat or skim milk/d (see Supplemental Figure S8 under “Supplemental data” in the online issue). Because of the few studies we did not conduct a dose-response analysis for the remaining subtypes of dairy foods. There was a suggestion of a nonlinear positive association between whole milk (full-fat milk) intake and type 2 diabetes (P -nonlinearity = 0.01), with a rapid increase in risk when increasing intakes from low amounts to 40–50 g/d (see Figure 4C and Supplemental Table S7 under “Supplemental data” in the online issue), whereas the association between low-fat or skim milk and type 2 diabetes appeared to be linear (P -nonlinearity = 0.44) (see Figure 4D and Supplemental Table S8 under “Supplemental data” in the online issue).

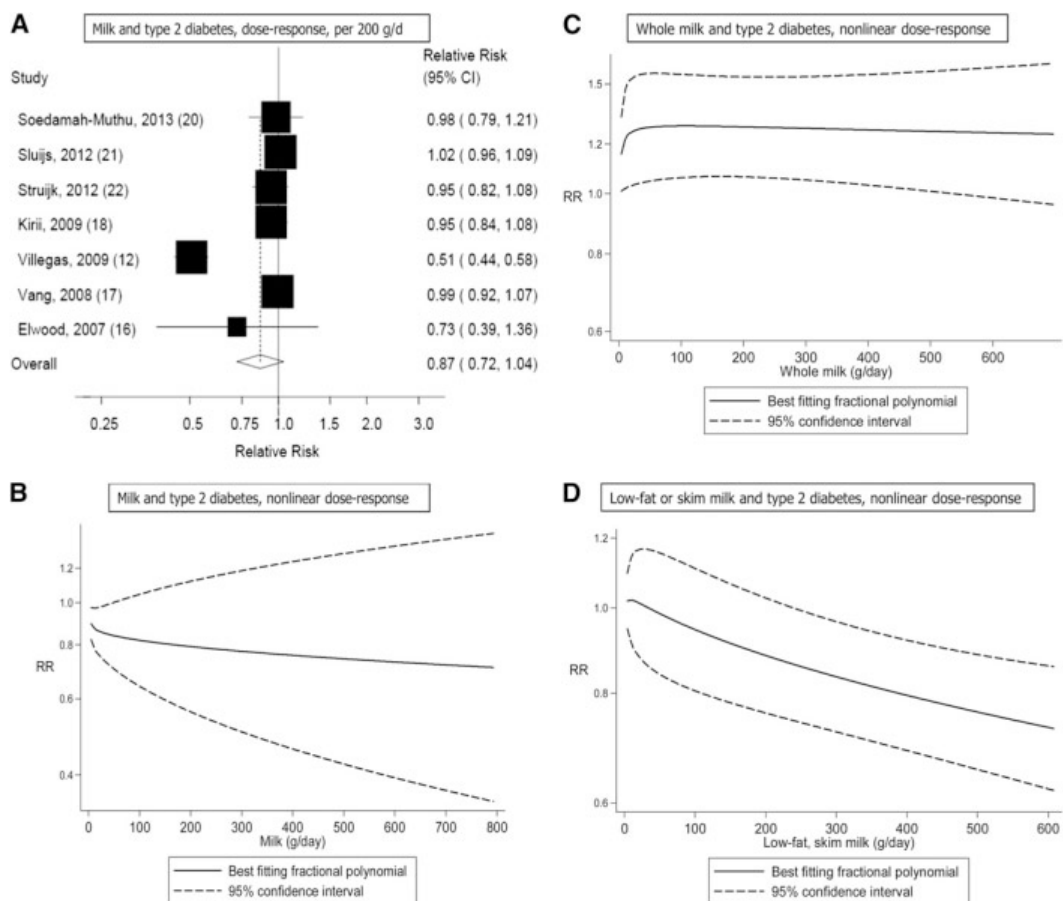


FIGURE 4. A–D: Intake of milk and types of milk and risk of type 2 diabetes. The summary RR per 200 g/d by using random-effects models was 0.87 (95% CI: 0.72, 1.04; $I^2 = 93.6\%$; P -heterogeneity < 0.0001; $n = 167,982$) (A). There was evidence of a nonlinear inverse association between milk intake and type 2 diabetes (P -nonlinearity < 0.0001) (B) and evidence of a nonlinear positive association between whole-milk intake and type 2 diabetes (P -nonlinearity = 0.01) (C), whereas the association between low-fat or skim milk and type 2 diabetes appeared to be linear (P -nonlinearity = 0.44) (D).

Subgroup, sensitivity, and meta-regression analyses

In subgroup and meta-regression analyses, we found no significant heterogeneity between subgroups when studies were stratified by sex, duration of follow-up, geographic location, or study size (Tables 3 and 4). There was some indication that the inverse association between total dairy products and yogurt and type 2 diabetes was restricted to the American but not the European studies; however, the tests for heterogeneity were not significant ($P = 0.10$ and 0.75 , respectively). Further subgroup analyses by whether studies had adjusted for confounding factors did not show significant heterogeneity between strata, although associations were not always significant. In a sensitivity analysis, we reconduted the analysis of total dairy, high-fat dairy products, and low-fat dairy products restricted to the 6 studies that were common for the 3 analyses (7, 10, 13, 15, 20, 22), and the summary RRs were 0.90 (95% CI: 0.80, 1.01; $I^2 = 49.7\%$; P -heterogeneity = 0.08) for total dairy products, 0.99 (95% CI: 0.93, 1.05; $I^2 = 30.9\%$; P -heterogeneity = 0.20) for high-fat dairy products, and 0.91 (95% CI: 0.86, 0.96; $I^2 = 24.2\%$; P -heterogeneity = 0.25) for low-fat dairy products, which was similar to the overall analysis.

DISCUSSION

In this meta-analysis, a high intake of dairy products was associated with a significant decrease in the risk of type 2 diabetes.

Significant inverse associations were also found for low-fat dairy products, low-fat or skim milk and cheese, and for yogurt in the high compared with low analysis, but no significant association was observed for high-fat dairy products or total milk.

The results from this meta-analysis support the hypothesis that intake of dairy products decreases the risk of type 2 diabetes and are consistent with 2 previous meta-analyses of cohort studies of dairy products and type 2 diabetes that also found inverse associations (26, 28). However, we further quantified the association between dairy product intakes and type 2 diabetes risk by conducting linear and nonlinear dose-response analyses and by analyzing specific types of dairy products. Dose-response analyses are important to guide recommendations for intake with regard to risk reduction. In addition, it is important to define potential threshold effects for assessments of benefits and risks, because there is some evidence of adverse effects of dairy consumption on certain diseases (40, 41).

Because this was a meta-analysis of observational studies, some limitations may have affected the results. It is possible that the observed inverse association between dairy product intake and risk of type 2 diabetes could be a result of unmeasured or residual confounding. Higher intake of dairy products, and perhaps in particular of low-fat dairy products, may be associated with other healthy behaviors including higher levels of physical activity and higher intakes of dietary fiber and whole grains,

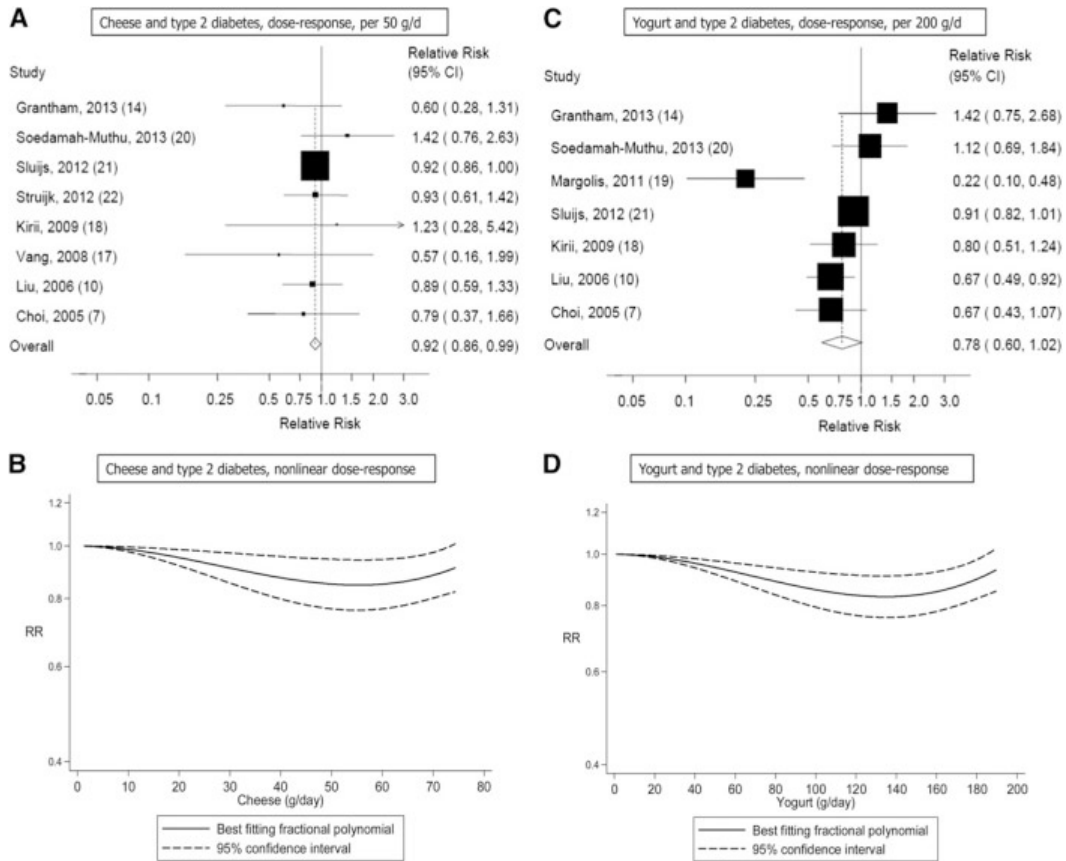


FIGURE 5. A–D: Intake of cheese and yogurt and risk of type 2 diabetes. The summary RRs by using random-effects models were 0.92 (95% CI: 0.86, 0.99; $I^2 = 0\%$; P -heterogeneity = 0.79; $n = 242,960$) per 50 g cheese/d (A, B) and 0.78 (95% CI: 0.60, 1.02; $I^2 = 69.9\%$; P -heterogeneity = 0.003; $n = 254,892$) per 200 g yogurt/d (C, D).

lower prevalence of smoking and overweight/obesity, and lower intakes of red and processed meat. However, many of the studies included in this meta-analysis adjusted for known confounding factors such as age, BMI, smoking, and fiber and energy intake. In the subgroup analyses for total dairy products, low-fat dairy products, and cheese, the associations persisted in several, although not all, subgroup analyses when stratified by whether confounding factors were adjusted for, possibly because of few studies in some subgroups. However, we found no evidence of heterogeneity between these subgroups with meta-regression analyses. In addition, it is possible that publication bias may have affected the results; however, we found no evidence of publication bias with the statistical tests, and there was no evidence of asymmetry in the funnel plots when inspected visually. Because

there were few studies reporting on the specific dairy items listed in Table 2, further studies are needed to clarify those findings.

Measurement errors in the assessment of dietary intake are known to bias effect estimates. Most of the studies included in our meta-analysis used validated food-frequency questionnaires, but only one study corrected for measurement error (21). Results were only slightly stronger with correction for measurement error with HRs of 1.03 (95% CI: 0.87, 1.22) and 0.84 (95% CI: 0.73, 0.97) for total dairy and cheese, respectively, compared with HRs of 1.01 (95% CI: 0.89, 1.13) and 0.88 (95% CI: 0.76, 1.02) without correction for measurement error.

The finding of an inverse association between dairy product intake and type 2 diabetes in this meta-analysis is consistent with previous research that showed a reduced risk or prevalence of the

TABLE 2

Other subtypes of dairy products and type 2 diabetes risk: high compared with low intake

Type of dairy product	<i>n</i>	RR (95% CI)	I^2	P -heterogeneity
Whole milk	4	1.12 (0.99, 1.27)	0	0.79
Low-fat/skim milk	3	0.82 (0.69, 0.97)	40.1	0.19
Fermented dairy products	2	0.88 (0.79, 0.98)	0	>0.99
Cottage cheese	2	0.91 (0.79, 1.04)	0	0.43
Cream	2	0.96 (0.84, 1.11)	0	0.31
Sour cream	2	0.98 (0.82, 1.16)	0	0.54
Ice cream	2	0.83 (0.73, 0.95)	0	0.37
Sherbet	2	0.90 (0.79, 1.03)	0	0.60

TABLE 3
Subgroup analyses of total dairy products, high-fat and low-fat dairy products, and type 2 diabetes risk: dose-response analysis¹

	Dairy products, per 400 g/d						High-fat dairy products, per 200 g/d						Low-fat dairy products, per 200 g/d					
	n	RR (95% CI)	I ²	P ²	P ³		n	RR (95% CI)	I ²	P ²	P ³		n	RR (95% CI)	I ²	P ²	P ³	
All studies	12	0.93 (0.87, 0.99)	33.1	0.13		%	9	0.98 (0.94, 1.03)	7.6	0.37		%	9	0.91 (0.86, 0.96)	40.2	0.10		
Duration of follow-up																		
<10 y	6	0.92 (0.84, 1.00)	15.3	0.32	0.63		4	0.96 (0.86, 1.07)	26.1	0.26	0.64		5	0.89 (0.80, 0.99)	58.7	0.05	0.65	
≥10 y	6	0.94 (0.85, 1.05)	50.7	0.07			5	0.99 (0.94, 1.04)	7.1	0.37			4	0.92 (0.87, 0.97)	12.6	0.33		
Sex																		
Men	4	0.85 (0.62, 1.18)	62.7	0.05	0.08/0.90 ^d		1	0.99 (0.90, 1.08)			0.87/0.85 ^d		1	0.87 (0.79, 0.93)			0.08/0.96 ^d	
Women	6	0.90 (0.82, 0.98)	39.0	0.15			3	0.97 (0.88, 1.07)	55.1	0.11			4	0.87 (0.79, 0.96)	53.7	0.09		
Men and women	4	1.01 (0.93, 1.09)	0	0.46			4	0.99 (0.84, 1.16)	25.4	0.26			4	0.98 (0.91, 1.06)	0	0.67		
Geographic location																		
Europe	4	1.01 (0.92, 1.11)	4.1	0.37	0.10		4	1.00 (0.88, 1.12)	22.2	0.28	0.83		3	0.99 (0.91, 1.07)	0	0.55	0.18	
America	5	0.90 (0.83, 0.97)	41.4	0.15			4	0.98 (0.93, 1.04)	32.2	0.22			5	0.87 (0.82, 0.94)	44.2	0.13		
Asia	1	0.96 (0.77, 1.19)					0						0					
Australia	2	0.77 (0.53, 1.11)	0	0.33			1	0.89 (0.64, 1.24)					1	0.91 (0.71, 1.17)				
Number of cases																		
<1000	6	0.86 (0.66, 1.12)	47.1	0.09	0.20		6	0.95 (0.85, 1.06)	29.6	0.21	0.28		5	0.95 (0.87, 1.04)	28.3	0.23	0.33	
1000 to <1500	2	0.86 (0.73, 1.02)	38.9	0.20			1	0.99 (0.90, 1.08)					1	0.87 (0.79, 0.93)				
≥1500	4	0.96 (0.91, 1.00)	0	0.60			2	1.00 (0.96, 1.05)	0	0.88			3	0.89 (0.81, 0.97)	53.3	0.12		
Adjustment for confounding factors																		
Alcohol																		
Yes	9	0.93 (0.88, 1.00)	41.5	0.09	0.30		7	0.99 (0.94, 1.04)	17.2	0.30	0.29		8	0.91 (0.86, 0.96)	47.7	0.06	0.98	
No	3	0.75 (0.53, 1.06)	0	0.57			2	0.92 (0.81, 1.04)	0	0.86			1	0.91 (0.71, 1.17)				
Smoking																		
Yes	12	0.93 (0.87, 0.99)	33.1	0.13	NC		9	0.98 (0.94, 1.03)	7.6	0.37	NC		9	0.91 (0.86, 0.96)	40.2	0.10	NC	
No	0						0						0					
BMI, waist circumference																		
Yes	12	0.93 (0.87, 0.99)	33.1	0.13	NC		9	0.98 (0.94, 1.03)	7.6	0.37	NC		9	0.91 (0.86, 0.96)	40.2	0.10	NC	
No	0						0						0					
Physical activity																		
Yes	11	0.93 (0.87, 0.99)	36.9	0.10	0.52		8	0.99 (0.95, 1.04)	8.4	0.37	0.37		9	0.91 (0.86, 0.96)	40.2	0.10	NC	
No	1	0.58 (0.17, 1.97)					1	0.92 (0.80, 1.06)					0					
Coffee, caffeine																		
Yes	6	0.96 (0.86, 1.07)	40.9	0.13	0.31		4	0.99 (0.83, 1.19)	57.5	0.07	0.93		5	0.93 (0.85, 1.02)	46.0	0.12	0.42	
No	6	0.91 (0.85, 0.97)	15.3	0.32			5	0.99 (0.87, 1.12)	43.8	0.13			4	0.89 (0.83, 0.96)	40.1	0.17		
Soft drinks																		
Yes	3	0.91 (0.78, 1.07)	64.7	0.06	0.66		3	0.95 (0.84, 1.08)	48.8	0.14	0.58		3	0.90 (0.76, 1.06)	71.0	0.03	0.90	
No	9	0.92 (0.86, 0.99)	18.5	0.28			6	0.99 (0.95, 1.04)	0	0.50			6	0.91 (0.86, 0.96)	21.8	0.27		
Meat																		
Yes	5	0.95 (0.83, 1.09)	52.6	0.08	0.33		4	0.99 (0.83, 1.19)	57.5	0.07	0.93		5	0.93 (0.85, 1.02)	46.0	0.12	0.42	
No	7	0.92 (0.87, 0.97)	1.2	0.42			5	0.99 (0.87, 1.12)	43.8	0.13			4	0.89 (0.83, 0.96)	40.1	0.17		

(Continued)

TABLE 3 (Continued)

	Dairy products, per 400 g/d				High-fat dairy products, per 200 g/d				Low-fat dairy products, per 200 g/d						
	<i>n</i>	RR (95% CI)	<i>I</i> ²	<i>P</i> ²	<i>P</i> ³	<i>n</i>	RR (95% CI)	<i>I</i> ²	<i>P</i> ²	<i>P</i> ³	<i>n</i>	RR (95% CI)	<i>I</i> ²	<i>P</i> ²	<i>P</i> ³
Fat															
Yes	3	0.84 (0.71, 0.99)	63.0	0.07	0.14	3	0.97 (0.89, 1.05)	53.5	0.12	0.98	3	0.89 (0.81, 0.97)	58.5	0.09	0.53
No	9	0.97 (0.92, 1.02)	0	0.48		6	0.99 (0.92, 1.07)	0	0.50		6	0.92 (0.86, 1.00)	39.5	0.14	
Grains, whole grains															
Yes	4	0.99 (0.90, 1.08)	17.6	0.30	0.15	4	1.03 (0.94, 1.13)	0	0.50	0.38	4	0.95 (0.88, 1.03)	27.8	0.25	0.19
No	8	0.90 (0.83, 0.97)	25.4	0.23		5	0.97 (0.91, 1.02)	26.6	0.24		5	0.88 (0.81, 0.95)	43.0	0.14	
Fiber															
Yes	4	0.85 (0.74, 0.97)	44.5	0.14	0.13	4	0.97 (0.90, 1.04)	35.5	0.20	0.87	4	0.89 (0.83, 0.97)	37.8	0.19	0.55
No	8	0.97 (0.91, 1.02)	5.6	0.39		5	0.99 (0.92, 1.07)	0	0.41		5	0.92 (0.85, 1.01)	51.5	0.08	
Glycemic load															
Yes	4	0.85 (0.74, 0.97)	44.5	0.14	0.13	4	0.97 (0.89, 1.04)	35.5	0.20	0.87	4	0.89 (0.83, 0.97)	37.8	0.19	0.55
No	8	0.97 (0.91, 1.02)	5.6	0.39		5	0.99 (0.92, 1.07)	0	0.41		5	0.92 (0.85, 1.01)	51.5	0.08	
Magnesium															
Yes	1	0.96 (0.77, 1.19)			0.83	0				NC	0				NC
No	11	0.92 (0.86, 0.99)	39.1	0.09		9	0.98 (0.94, 1.03)	7.6	0.37		9	0.91 (0.86, 0.96)	40.2	0.10	
Energy intake															
Yes	11	0.93 (0.87, 0.99)	36.9	0.10	0.52	9	0.98 (0.94, 1.03)	7.6	0.37	NC	9	0.91 (0.86, 0.96)	40.2	0.10	NC
No	1	0.58 (0.17, 1.97)				0					0				

¹ *n*, number of studies; NC, not calculable.

² *P* values for heterogeneity within each subgroup.

³ *P* values for heterogeneity between subgroups with meta-regression analysis.

⁴ *P* value for heterogeneity between men and women (studies with both sexes were excluded).

TABLE 4
Subgroup analyses of intake of milk, yogurt, and cheese and type 2 diabetes risk: dose-response analysis^a

	Milk, per 200 g/d						Yogurt, per 200 g/d						Cheese, per 50 g/d					
	n	RR (95% CI)	I ²	P ²	P ³	n	RR (95% CI)	I ²	P ²	P ³	n	RR (95% CI)	I ²	P ²	P ³			
All studies	7	0.87 (0.72, 1.04)	93.6	<0.0001		7	0.78 (0.60, 1.02)	69.9	0.003		8	0.92 (0.86, 0.99)	0	0.79				
Duration of follow-up																		
<10 y	3	0.77 (0.52, 1.16)	96.5	<0.0001	0.31	3	0.65 (0.26, 1.62)	85.3	0.001	0.66	3	0.86 (0.60, 1.23)	0	0.56	0.71			
≥10 y	4	1.01 (0.96, 1.05)	0	0.71		4	0.83 (0.68, 1.02)	43.6	0.15		5	0.92 (0.86, 0.99)	0	0.62				
Sex																		
Men	2	0.98 (0.84, 1.15)	0	0.33	0.46(0.47) ^d	3	0.86 (0.59, 1.27)	11.6	0.32	0.87(0.53) ^d	3	0.74 (0.41, 1.31)	0	0.57	0.47(0.62) ^d			
Women	2	0.66 (0.39, 1.14)	95.3	<0.0001		4	0.67 (0.38, 1.16)	76.9	0.005		3	0.89 (0.61, 1.29)	0	0.61				
Men and women	4	1.00 (0.96, 1.05)	0	0.80		2	0.92 (0.83, 1.02)	0	0.40		4	0.93 (0.86, 1.00)	0	0.49				
Geographic location																		
Europe	4	1.00 (0.95, 1.06)	0	0.58	0.22	2	0.92 (0.83, 1.02)	0	0.40	0.75	3	0.93 (0.86, 1.00)	0	0.40	0.33			
America	1	0.99 (0.92, 1.07)				3	0.52 (0.30, 0.88)	72.5	0.03		3	0.84 (0.60, 1.18)	0	0.79				
Asia	2	0.69 (0.37, 1.28)	97.8	<0.0001		1	0.80 (0.51, 1.24)				1	1.23 (0.28, 5.42)						
Australia	0					1	1.42 (0.75, 2.68)				1	0.60 (0.28, 1.31)						
Number of cases																		
<1000	4	0.98 (0.92, 1.04)	0	0.75	0.32	2	1.22 (0.83, 1.81)	0	0.58	0.16	3	0.96 (0.64, 1.44)	31.9	0.23	0.83			
1000 to <1500	1	0.95 (0.84, 1.08)				2	0.74 (0.54, 1.01)	0	0.60		2	0.86 (0.44, 1.68)	0	0.60				
≥1500	2	0.72 (0.36, 1.43)	98.9	<0.0001		3	0.60 (0.36, 1.00)	87.0	<0.0001		3	0.92 (0.86, 0.99)	0	0.74				
Adjustment for confounding factors																		
Alcohol																		
Yes	5	0.85 (0.66, 1.10)	95.5	<0.0001	0.84	6	0.73 (0.55, 0.96)	71.7	0.003	0.30	6	0.93 (0.86, 1.00)	0	0.82	0.24			
No	2	0.99 (0.92, 1.07)	0	0.33		1	1.42 (0.75, 2.68)				2	0.59 (0.31, 1.16)	0	0.94				
Smoking																		
Yes	6	0.84 (0.66, 1.07)	94.4	<0.0001	0.61	7	0.78 (0.60, 1.02)	69.9	0.003	NC	7	0.92 (0.86, 0.99)	0	0.76	0.48			
No	1	0.99 (0.92, 1.07)				0					1	0.57 (0.16, 1.99)						
BMI, waist circumference																		
Yes	6	0.84 (0.66, 1.07)	94.4	<0.0001	0.61	7	0.78 (0.60, 1.02)	69.9	0.003	NC	7	0.92 (0.86, 0.99)	0	0.76	0.48			
No	1	0.99 (0.92, 1.07)				0					1	0.57 (0.16, 1.99)						
Physical activity																		
Yes	5	0.85 (0.66, 1.10)	95.5	<0.0001	0.84	7	0.78 (0.60, 1.02)	69.9	0.003	NC	7	0.92 (0.86, 0.99)	0	0.76	0.48			
No	2	0.99 (0.92, 1.07)	0	0.33		0					1	0.57 (0.16, 1.99)						
Coffee, caffeine																		
Yes	4	1.00 (0.95, 1.05)	0	0.65	0.17	3	0.91 (0.82, 1.01)	0	0.59	0.39	4	0.93 (0.86, 1.00)	0	0.58	0.37			
No	3	0.71 (0.41, 1.24)	97.4	<0.0001		4	0.64 (0.37, 1.10)	77.4	0.004		4	0.79 (0.58, 1.09)	0	0.79				
Soft drinks																		
Yes	1	1.02 (0.96, 1.09)			0.54	1	0.91 (0.82, 1.01)			0.72	1	0.92 (0.86, 1.00)			0.91			
No	6	0.84 (0.66, 1.06)	93.8	<0.0001		6	0.74 (0.51, 1.06)	70.3	0.005		7	0.91 (0.72, 1.14)	0	0.69				
Meat																		
Yes	3	1.01 (0.95, 1.06)	0	0.62	0.30	2	0.92 (0.83, 1.02)	0	0.40	0.40	3	0.93 (0.86, 1.00)	0	0.40	0.42			
No	4	0.77 (0.54, 1.11)	96.2	<0.0001		5	0.68 (0.45, 1.02)	70.9	0.008		5	0.81 (0.60, 1.10)	0	0.85				
Fat																		
Yes	0				NC	2	0.67 (0.52, 0.87)	0	1.00	0.71	2	0.86 (0.61, 1.23)	0	0.78	0.73			
No	7	0.87 (0.72, 1.04)	93.6	<0.0001		5	0.82 (0.56, 1.20)	74.8	0.003		6	0.92 (0.86, 0.99)	0	0.59				
Grains, whole grains																		
Yes	3	1.01 (0.95, 1.06)	0	0.62	0.30	2	0.92 (0.83, 1.02)	0	0.40	0.40	3	0.93 (0.86, 1.00)	0	0.40	0.42			
No	4	0.77 (0.54, 1.11)	96.2	<0.0001		5	0.68 (0.45, 1.02)	70.9	0.008		5	0.81 (0.60, 1.10)	0	0.85				

(Continued)

TABLE 4 (Continued)

	Milk, per 200 g/d				Yogurt, per 200 g/d				Cheese, per 50 g/d						
	n	RR (95% CI)	I ²	P ²	P ³	n	RR (95% CI)	I ²	P ²	P ³	n	RR (95% CI)	I ²	P ²	P ³
Fiber															
Yes	0				NC	2	0.67 (0.52, 0.87)	0	1.00	0.71	2	0.86 (0.61, 1.23)	0	0.78	0.73
No	7	0.87 (0.72, 1.04)	93.6	<0.0001		5	0.82 (0.56, 1.20)	74.8	0.003		6	0.92 (0.86, 0.99)	0	0.59	
Glycemic load															
Yes	0				NC	2	0.67 (0.52, 0.87)	0	1.00	0.71	2	0.86 (0.61, 1.23)	0	0.78	0.73
No	7	0.87 (0.72, 1.04)	93.6	<0.0001		5	0.82 (0.56, 1.20)	74.8	0.003		6	0.92 (0.86, 0.99)	0	0.59	
Magnesium															
Yes	1	0.95 (0.84, 1.08)			0.74	1	0.80 (0.51, 1.24)			0.93	1	1.23 (0.28, 5.42)			0.72
No	6	0.85 (0.69, 1.06)	94.6	<0.0001		6	0.77 (0.57, 1.05)	74.8	0.001		7	0.92 (0.86, 0.99)	0	0.71	
Energy intake															
Yes	5	0.85 (0.66, 1.10)	95.5	<0.0001	0.84	7	0.78 (0.60, 1.02)	69.9	0.003	NC	7	0.92 (0.86, 0.99)	0	0.76	0.48
No	2	0.99 (0.92, 1.07)	0	0.33	0	0					1	0.57 (0.16, 1.99)			

¹ n, number of studies; NC, not calculable.

² P values for heterogeneity within each subgroup.

³ P values for heterogeneity between subgroups with meta-regression analysis.

⁴ P value for heterogeneity between men and women (studies with both sexes were excluded).

metabolic syndrome (16, 23, 42–46) and insulin resistance (47–49) in several epidemiologic studies, although some found no association (50, 51). Several potential mechanisms could explain an inverse association between dairy products and type 2 diabetes. Dairy products are an important source of dietary calcium, vitamin D, protein, and magnesium. It has been shown in both animal experiments and human studies that calcium increases insulin secretion and is essential for insulin-responsive tissues such as skeletal muscle and adipose tissue and may reduce insulin resistance (27). In addition, some dairy products may be fortified with vitamin D, which has been shown to be associated with reduced diabetes risk (52), possibly by influencing insulin secretion and reducing insulin resistance (27). However, the Women’s Health Initiative randomized trial found no association between supplementation with calcium and vitamin D on incident type 2 diabetes (53). Dairy products contain whey proteins, which have been shown to reduce gain in body weight and to increase insulin sensitivity in animal models (54). In addition, dairy products are a source of magnesium, which has been associated with reduced diabetes risk in epidemiologic studies (55), and with improved insulin sensitivity in some experimental studies, although the data are limited (56). The fat content of dairy products might also influence diabetes risk. We found no association between high-fat dairy products and risk of type 2 diabetes, but there was some evidence of an increased risk with intake of whole milk in the nonlinear analysis, which contrasted with the inverse associations with low-fat dairy products and with low-fat or skim milk. This suggests that the fat content of some dairy products might offset the beneficial effect of other nutrients in dairy foods. However, the results are in contrast with 2 recent studies that found inverse associations between plasma phospholipid concentrations of *trans*-palmitoleic acid, a biomarker of dairy fat, and type 2 diabetes risk (29, 57). It is not clear whether these differences are a result of measurement error in the intake of high-fat dairy products or whether the beneficial effect of *trans*-palmitoleic acid is driven by specific dairy foods such as cheese and yogurt, which we found were inversely associated with diabetes and which can be high in fat as well.

Our meta-analysis also has several strengths. Because we based our analyses on prospective studies, we effectively avoided recall bias and reduced the potential for selection bias. We conducted dose-response analyses to investigate whether specific amounts of dairy food intake were associated with type 2 diabetes risk. The interpretation of our results with regard to public health recommendations is, however, complicated by the fact that consumption of milk and dairy products and different subtypes of dairy products may have both beneficial (36, 58) and adverse effects (40, 41) with regard to other diseases. Additional studies of dairy products and other health outcomes, overall health, and mortality will be needed for a more detailed assessment of the costs-benefits of dairy product consumption.

In conclusion, our results suggest that intakes of dairy products, low-fat dairy products, and cheese are inversely associated with the risk of type 2 diabetes. Any additional studies should assess the association between other specific types of dairy products and the risk of type 2 diabetes and adjust for more confounding factors.

We thank Peter C Elwood and Janet Pickering for providing supplementary information from the Caerphilly cohort study and Dianna Magliano and Stephanie Tanamas for providing supplementary information from the Australian Diabetes Obesity and Lifestyle Study.

The authors' responsibilities were as follows—DA: designed the project, conducted the literature search and analyses, and wrote the first draft of the manuscript; and DA, TN, PR, and LJV: interpreted the data, revised the subsequent drafts for important intellectual content, and approved the final version of the manuscript to be published. The authors declared that there were no conflicts of interest associated with this article.

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