

# Consumption of dairy foods and diabetes incidence: a dose-response meta-analysis of observational studies<sup>1,2</sup>

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## ABSTRACT

**Background:** A growing number of cohort studies suggest a potential role of dairy consumption in type 2 diabetes (T2D) prevention. The strength of this association and the amount of dairy needed is not clear.

**Objective:** We performed a meta-analysis to quantify the associations of incident T2D with dairy foods at different levels of intake.

**Design:** A systematic literature search of the PubMed, Scopus, and Embase databases (from inception to 14 April 2015) was supplemented by hand searches of reference lists and correspondence with authors of prior studies. Included were prospective cohort studies that examined the association between dairy and incident T2D in healthy adults. Data were extracted with the use of a predefined protocol, with double data-entry and study quality assessments. Random-effects meta-analyses with summarized dose-response data were performed for total, low-fat, and high-fat dairy, (types of) milk, (types of) fermented dairy, cream, ice cream, and sherbet. Nonlinear associations were investigated, with data modeled with the use of spline knots and visualized via spaghetti plots.

**Results:** The analysis included 22 cohort studies comprised of 579,832 individuals and 43,118 T2D cases. Total dairy was inversely associated with T2D risk (RR: 0.97 per 200-g/d increment; 95% CI: 0.95, 1.00;  $P = 0.04$ ;  $I^2 = 66\%$ ), with a suggestive but similar linear inverse association noted for low-fat dairy (RR: 0.96 per 200 g/d; 95% CI: 0.92, 1.00;  $P = 0.072$ ;  $I^2 = 68\%$ ). Nonlinear inverse associations were found for yogurt intake (at 80 g/d, RR: 0.86 compared with 0 g/d; 95% CI: 0.83, 0.90;  $P < 0.001$ ;  $I^2 = 73\%$ ) and ice cream intake (at  $\sim 10$  g/d, RR: 0.81; 95% CI: 0.78, 0.85;  $P < 0.001$ ;  $I^2 = 86\%$ ), but no added incremental benefits were found at a higher intake. Other dairy types were not associated with T2D risk.

**Conclusion:** This dose-response meta-analysis of observational studies suggests a possible role for dairy foods, particularly yogurt, in the prevention of T2D. Results should be considered in the context of the observed heterogeneity. *Am J Clin Nutr* 2016;103:1111–24.

**Keywords:** dairy, milk, yogurt, cheese, type 2 diabetes, meta-analysis, prospective/observational studies, dose-response associations

## INTRODUCTION

The prevalence of type 2 diabetes (T2D) is increasing worldwide, from 8.3% in 2014 to an expected 10.1% ( $\sim 592$  million adults) in 2035 (1). T2D is considered to be a diet- and lifestyle-related disease. Large-scale intervention studies have demonstrated that a healthy diet and increased physical activity reduce the risk of progression to T2D by  $\sim 40\%$  (2). An increasing number of prospective cohort studies suggest a potential role of modest dairy consumption in T2D prevention. Although meta-analyses are typically meant to be conclusive, the widely conflicting conclusions from prior meta-analyses of dairy and T2D (3–9) show that a more comprehensive systematic review is necessary, especially taking into account the potential dose-dependent effects of dairy. Prior meta-analyses of observational studies showed (nonlinear) inverse associations of total dairy with T2D, which was mainly confined to the intake of low-fat dairy ( $\sim 10\%$  lower risk for a 200-g daily intake) (3, 7, 9). These older meta-analyses also showed inverse associations with intake of yogurt (3, 7, 9) and cheese (3, 7), but not all studies have agreed. On the other hand, a more recent meta-analysis of 14 prospective studies, which included 3 large US cohorts with 18–30 y of follow-up, conflictingly showed no association for total dairy and T2D risk (per daily serving, RR: 0.98; 95% CI: 0.96, 1.01) (4) and also no associations for low-fat or high-fat dairy in a separate analysis of the 3 US cohorts (4). The meta-analysis did show, however, a significant 18% lower risk per daily serving of yogurt (4). Recently, several new population-based cohorts on dairy consumption and T2D have been published (10–12). Therefore, to resolve conflicts and use all the available data (a total of 22 prospective cohort studies)

<sup>1</sup> This meta-analysis project on dairy products and incident diabetes was funded by Wageningen University.

<sup>2</sup> Supplemental Methods, Supplemental Figures 1–28, and Supplemental Tables 1–5 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://ajcn.nutrition.org>.

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(4, 10–28), we systematically examined a wide range of dairy foods in relation to risk of T2D in healthy adults by means of a comprehensive dose-response meta-analysis. This project used approaches similar to those gained from our previously published dairy meta-analyses with cardiovascular disease (29) and hypertension (30) as the outcome.

## METHODS

### Data sources and searches

This review was conducted and reported in accordance with the Meta-analysis Of Observational Studies in Epidemiology guidelines (31). Two analysts (LG and SSS-M) performed a systematic literature search based on the query syntax shown in the **Supplemental Methods** in the databases PubMed, Scopus, and Embase (from inception through 14 April 2015).

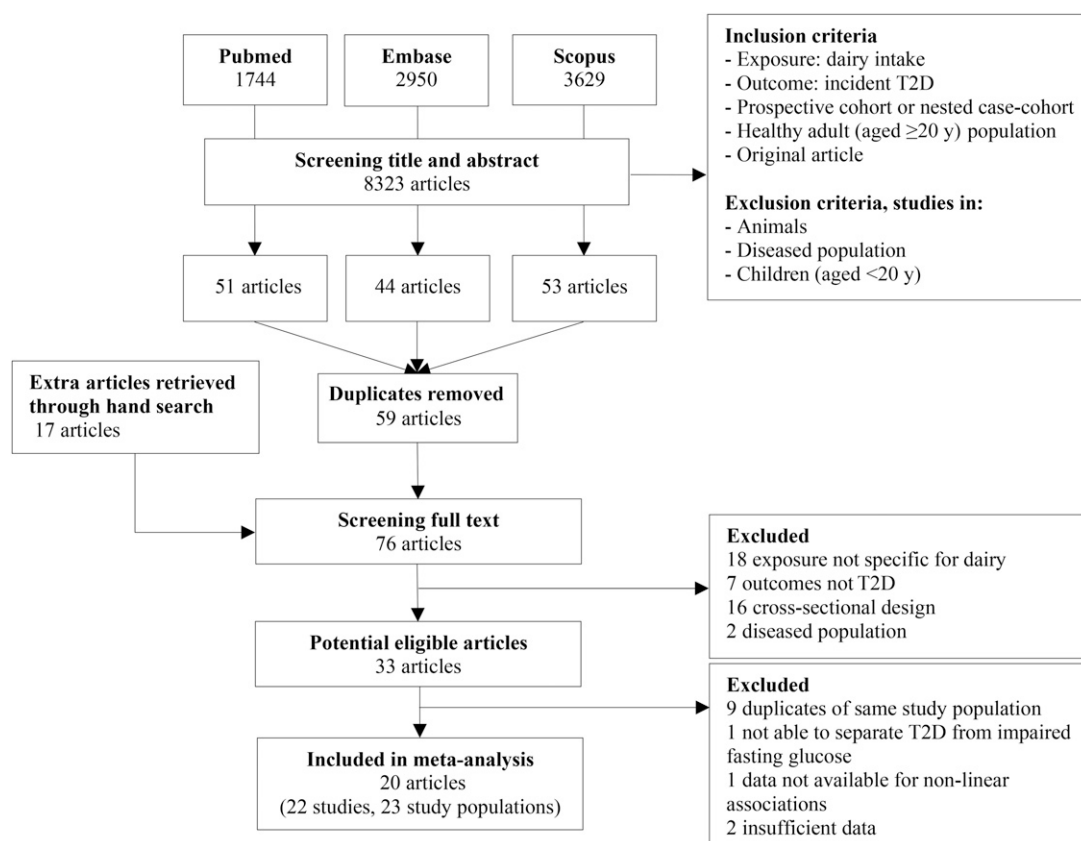
### Study selection

Titles, abstracts, and full texts of retrieved articles were screened for the following predefined inclusion criteria: dairy intake as main exposure, T2D as outcome, prospective cohort as design, healthy adults (baseline age of  $\geq 20$  y), original article, and English language. Excluded were studies in animals, children, and ill populations. In addition, we hand-searched reference lists of identified relevant studies and of previous reviews and meta-analyses. Of 76 fully reviewed articles, 33 articles (4, 10–28, 32–44) met the inclusion criteria (see **Figure 1**). Subsequently, 13 articles were excluded for the following reasons:

duplicate analysis of the same study population (32–35, 38–40, 42, 43), not able to separate T2D from impaired fasting glucose (37), data not suitable for nonlinear associations (44), and insufficient data (36, 41). Eventually, 20 articles based on 22 different cohorts (4, 10–28), of which 2 (12, 22) were case-cohort studies, were available for the meta-analysis. Kirii et al. (16) presented data for men and women separately, which were entered as 2 study populations in the meta-analysis.

### Data extraction and quality assessment

Data were extracted from published articles with the use of a predefined protocol, and double data-entry was performed. Apart from descriptive characteristics, we extracted the following data for each category of dairy intake: range of intake, median, number of subjects and T2D cases, person-years at risk, and RR with the corresponding 95% CI. For studies that presented several multivariable-adjusted RRs, the model with the largest number of covariates was taken. For studies not reporting the median of each category, we took the mean of the lower and the upper limit. When dairy intake was presented in servings or times 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, and high-fat dairy; 244 g for total, low-fat, and high-fat milk (585 g for 1 pint of milk); 244 g for yogurt; 43 g for cheese; and 25 g for cream (45, 46). When studies reported conversion factors, these factors were applied (14, 18, 19, 28). For several studies (13, 15, 19–22, 24) additional data were provided by the authors or coworkers.



**FIGURE 1** Flowchart of literature search for meta-analysis on dairy intake and incident T2D. T2D, type 2 diabetes.

There were overlapping data for 2 studies, namely, the European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct (22) and EPIC-Norfolk (12). When both studies reported on the same dairy food item, data from the EPIC-InterAct study (22) were extracted. For dairy items not analyzed in the EPIC-InterAct study (22), the EPIC-Norfolk (12) data were extracted.

Two reviewers (LG and SSS-M) independently evaluated the quality of the included studies with the use of the Newcastle-Ottawa quality assessment scale (47). The rating system scores studies from 0 (highest degree of bias) to 9 (lowest degree of bias), taking into account selection, comparability, and outcome assessment.

### Data synthesis and analysis

Meta-analysis was performed when  $\geq 3$  cohort studies/dairy type were available, which was the case for total dairy, low-fat dairy, high-fat dairy, total milk, low-fat milk, high-fat milk, cheese, yogurt, fermented dairy, cream, ice cream, and sherbet. Linearity of associations between dairy foods and risk of T2D were analyzed with the use of spline analysis and dose-response (generalized least-square trend) meta-regression. Splined variables were created with the use of MKSPLINE in Stata version 11.0. Goodness-of-fit tests and chi-square statistics were used to determine the most appropriate knot points and maximal goodness of fit, to determine the best dose-response inflection point of the nonlinear association. Linear and nonlinear associations were further analyzed with the use of dose-response generalized least-square trend meta-regression analysis. Random-effects meta-regression trend estimation of summarized dose-response data, described by Greenland and Longnecker (48), was used to derive the incremental dose-response RRs. For linear associations, the incremental dose-response RRs were expressed per serving size and fitted within the range of dairy intake of all studies. For nonlinear associations, the knot points defined these numbers. The shapes of the associations within individual studies were visualized by means of spaghetti plots, as described previously (49). Forest plots were made to visually assess the linear dose-response slopes and corresponding 95% CIs across studies (Supplemental Figures 1–12). We performed sensitivity analysis (based on linear dose-response slopes) by excluding one study at a time from the analyses.

To explore the presence of statistical heterogeneity, Cochran's Q test was conducted and the  $I^2$  statistic was calculated, representing the percentage of total variation attributable to between-study heterogeneity (50). Subgroup analyses were performed (based on linear dose-response slopes) by sex, age ( $\leq 50$ , 51–60, and  $> 60$  y), continent, follow-up duration ( $\leq 5$ , 6–10, and  $> 10$  y), and degree of adjustment. Subgroups for degree of adjustment were based on whether or not studies adjusted for the major confounders of age, sex, smoking, total energy intake, and BMI. We performed subgroup analyses by the Newcastle-Ottawa quality score ( $< 7$  or  $\geq 7$ ), but the subgroups were identical to the subgroups based on degree of adjustment; therefore, we only presented the results for the latter. Potential publication bias was assessed by the Egger's test (51) and by symmetry of individual study linear dose-response slopes of the funnel plot, if  $\geq 8$  cohort studies were available. Values reported in text and tables are

RRs and 95% CIs. Two-sided  $P$  values  $< 0.05$  were considered to be statistically significant.

## RESULTS

### Study characteristics

An overview of 22 prospective cohort studies based on 23 study populations (mean age  $> 36$  y), with a total of 579,832 individuals and 43,118 T2D cases, is provided in **Table 1**. The sample size of the cohorts ranged from 640 to 85,884, and the duration of follow-up ranged from 2.6 to 30 y. Nine studies were conducted in the United States (4, 14, 17, 19, 21, 25, 26), 8 in Europe (10–13, 20, 22–24), 3 in Asia (16, 27, 28), and 2 in Australia (15, 18). The dairy foods studied and definitions of dairy categories differed across studies, as described in **Supplemental Table 1**. Total dairy consumption (based on median intake amounts in populations) ranged from 111 to 400 g/d for all studies combined, and from 162 to 347 g/d in the United States, from 121 to 400 g/d in Europe, from 111 to 171 g/d in Asia and from 266 to 347 g/d in Australia. In studies reporting total dairy, milk made the largest contribution to total dairy intake (range: 62–331 g of milk/d), and more low-fat dairy (range: 65–294 g/d) than high-fat dairy (range: 17–135 g/d) was consumed. Study characteristics by dairy type are shown in **Supplemental Table 2**. The study-specific quality assessment ratings and scores are shown in **Supplemental Table 3**. Total scores ranged from 3 to 9, with 14 studies scoring  $\geq 7$ .

### Total, low-fat, and high-fat dairy and T2D

Total dairy intake (16 studies) (4, 10, 11, 13, 15–19, 22–25, 28) was linearly associated with a 3% lower T2D risk per 200 g/d (equal to 1.1 serving/d or 7.1 ounces/d) (RR: 0.97; 95% CI: 0.95, 1.00;  $P = 0.044$ ) (**Figure 2**). Significant heterogeneity was present ( $I^2 = 66\%$ ,  $P < 0.001$ ). Subgroup analyses (**Supplemental Table 4**) suggested a stronger inverse association in Asian populations (RR: 0.85 per 200 g/d; 95% CI: 0.65, 1.12), but no association in European populations. Also, in studies not adjusting for the major confounders, the association tended to be stronger (RR: 0.88 per 200 g/d; 95% CI: 0.76, 1.03). There was no evidence of publication bias, as indicated by the funnel plot (**Supplemental Figure 13**) and the Egger's test ( $P = 0.11$ ).

For low-fat dairy (13 studies) (4, 10–12, 17–19, 21, 23–25), a borderline significant linear inverse association with T2D risk was observed, with a 4% lower risk per 200 g/d (RR: 0.96; 95% CI: 0.92, 1.00;  $P = 0.072$ ) (**Figure 3**). Significant heterogeneity was present ( $I^2 = 68\%$ ,  $P < 0.001$ ). Subgroup analyses (**Supplemental Table 4**) indicated stronger inverse associations in populations aged  $> 60$  y (RR: 0.84 per 200 g/d; 95% CI: 0.77, 0.93) and in studies with a follow-up of 6–10 y (RR: 0.88 per 200 g/d; 95% CI: 0.82, 0.94). There was no evidence of publication bias (**Supplemental Figure 14**; Egger's test:  $P = 0.096$ ).

High-fat dairy intake (13 studies) (4, 10–12, 17, 18, 20, 21, 23–25) showed no association with T2D risk (RR: 0.98 per 200 g/d; 95% CI: 0.93, 1.04;  $P = 0.52$ ) (**Supplemental Figure 15**). There was significant heterogeneity ( $I^2 = 52\%$ ,  $P = 0.016$ ). In sensitivity analyses (**Supplemental Table 5**), excluding the study by Ericson et al. (11) reduced  $I^2$  to 2.6% ( $P = 0.42$ ), with results remaining similar (RR: 1.01 per 200 g/d; 95% CI: 0.97,



**TABLE 1**  
Prospective cohort studies reporting associations between dairy intake and type 2 diabetes risk<sup>1</sup>

Author, year	Cohort (follow-up duration) and baseline examination	Location	Men, %	Mean age, y	Mean BMI, kg/m <sup>2</sup>	Cases/total, n/n	Dairy type included in meta-analysis <sup>2</sup>	Dietary assessment	Diabetes ascertainment	Adjustments
Chen et al., 2014 (4)	Health Professionals Follow-Up Study (24 y) 1986	United States	100	53	24.9	3364/41,436	Total dairy Low-fat dairy High-fat dairy Low-fat milk High-fat milk Cheese Yogurt Cream Ice cream Sherbet	Updated validated FFQ	Self-report plus supplementary questionnaire about symptoms, diagnostic tests, and hypoglycemic therapy, validated by medical records	Age, BMI, total energy intake, race, smoking, physical activity, alcohol consumption, diabetes family history, hypertension, hypercholesterolemia, <i>trans</i> fat intake, glycemic load, red and processed meat intake, nut intake, sugar-sweetened beverage intake, and coffee intake
Chen et al., 2014 (4)	Nurses' Health Study (30 y) 1980	United States	0	46	24.2	7841/67,138	Total dairy Low-fat dairy High-fat dairy Low-fat milk High-fat milk Cheese Yogurt Cream Ice cream Sherbet	Updated validated FFQ	Self-report plus supplementary questionnaire about symptoms, diagnostic tests, and hypoglycemic therapy, validated by medical records	Age, BMI, total energy intake, race, smoking, physical activity, alcohol consumption, menopausal status and menopausal hormone use, diabetes family history, hypertension, hypercholesterolemia, <i>trans</i> fat intake, glycemic load, red and processed meat intake, nut intake, sugar-sweetened beverage intake, and coffee intake
Chen et al., 2014 (4)	Nurses' Health Study II (18 y) 1991	United States	0	36	24.5	3951/85,884	Total dairy Low-fat dairy High-fat dairy Low-fat milk High-fat milk Cheese Yogurt Cream Ice cream Sherbet	Updated validated FFQ	Self-report plus supplementary questionnaire about symptoms, diagnostic tests, and hypoglycemic therapy, validated by medical records	Age, BMI, total energy intake, race, smoking, physical activity, alcohol consumption, menopausal status and menopausal hormone use, oral contraceptive use, diabetes family history, hypertension, hypercholesterolemia, <i>trans</i> fat intake, glycemic load, red and processed meat intake, nut intake, sugar-sweetened beverage intake, and coffee intake

(Continued)

TABLE 1 (Continued)

Author, year	Cohort (follow-up duration) and baseline examination	Location	Men, %	Mean age, y	Mean BMI, kg/m <sup>2</sup>	Cases/total, n/h	Dairy type included in meta-analysis <sup>2</sup>	Dietary assessment	Diabetes ascertainment	Adjustments
Díaz-López et al., 2015 (10)	PREDIMED Study (4.1 y) 2003–2009	Spain	38	67	30.0	270/3454	Total dairy Low-fat dairy High-fat dairy Total milk Low-fat milk High-fat milk Fermented dairy Cheese Yogurt	Validated 137-item FFQ	Fasting plasma glucose $\geq 7$ mmol/L or 2-h plasma glucose $\geq 11.1$ mmol/L after a 75-g oral glucose load	Age, sex, BMI, dietary intervention group, leisure- time physical activity, education level, smoking, hypertension or antihypertensive use, fasting glucose, HDL cholesterol, triglycerides, and intake of vegetables, legumes, fruits, cereals, meat, fish, olive oil, nuts, alcohol and alcohol squared in g/d
Elwood et al., 2007 (13)	Caerphilly Cohort Study (20 y) 1979–1983	United Kingdom	100	52	26	41/640	Total dairy Total milk	7-d weighed dietary intake records	Self-report	For total dairy: age, smoking, social class, prevalent heart disease, total cholesterol, HDL cholesterol, alcohol, and total fat. Milk intake: Age, smoking, BMI, and social class
Ericson et al., 2015 (11)	Malmö Diet and Cancer Cohort (14 y) 1991–1996	Sweden	39	58	25.8	2860/26,930	Total dairy Low-fat dairy High-fat dairy Total milk Low-fat milk High-fat milk Low-fat and high-fat fermented dairy Cheese Yogurt Cream Ice cream Total milk	Validated 7-d menu book, 168-item FFQ, and interview	Registries with a physician diagnosis of fasting plasma glucose $\geq 7.0$ mmol/L or fasting whole-blood concentration $\geq 6.1$ mmol/L, measured at 2 different occasions, or $\geq 2$ glycated hemoglobin values $> 6.0\%$	Age, sex, method version, season, total energy intake, leisure-time physical activity, smoking, alcohol intake, education, and BMI
Fuhrman et al., 2009 (14)	Puerto Rico Heart Health Program (2.6 y) 1965–1968	Puerto Rico	100	54	25.2	519/4685	Total milk	24-h dietary recall	Self-report, medication, fasting blood glucose $> 126$ mg/dL	None

(Continued)



TABLE 1 (Continued)

Author, year	Cohort (follow-up duration) and baseline examination	Location	Men, %	Mean age, y	Mean BMI, kg/m <sup>2</sup>	Cases/total, n/n	Dairy type included in meta-analysis <sup>2</sup>	Dietary assessment	Diabetes ascertainment	Adjustments
Grantham et al., 2013 (15)	Australian Diabetes Obesity and Lifestyle Study (5 y) 1999–2000	Australia	45	51	NR	209/5582	Total dairy Total milk Low-fat milk High-fat milk Cheese Yogurt	121-item FFQ	Fasting plasma glucose $\geq 7.0$ mmol/L or 2-h postload plasma glucose $\geq 11.1$ mmol/L or treatment with insulin or oral hypoglycemic agents	Age, sex, energy intake, family history of diabetes, education level, level of physical activity, smoking status, triglycerides, HDL cholesterol, systolic blood pressure, waist circumference, and hip circumference
Kirri et al., 2009 (16)	Japan Public Health Center-Based Prospective Study (5 y) 1995 and 1998	Japan	100	57	23.6	634/25,877	Total dairy Total milk Cheese Yogurt	Validated 147-item FFQ	Self-report, validated by medical records or plasma glucose data	Age, area, BMI, family history of diabetes, smoking status, alcohol intake, history of hypertension, exercise frequency, coffee consumption, energy-adjusted magnesium, and total energy
Liu et al., 2006 (17)	Women's Health Study (10 y) 1992–1995	United States	0	55	25.9	1603/37,183	Total dairy Low-fat dairy High-fat dairy Low-fat milk High-fat milk Cheese Yogurt Cream Ice cream Sherbet	Validated 131-item FFQ	Self-report, validated by telephone interview, supplemental questionnaire, and medical record	Age, total energy intake, randomized treatment assignment, family history of diabetes, smoking, BMI, hypercholesterolemia, hypertension, physical activity, hormones, alcohol consumption, dietary glycemic load, dietary intake of fibers, total fat, calcium, vitamin D, and magnesium
Louie et al., 2013 (18)	Blue Mountains Eye Study (10 y) 1992–1994	Australia	42	64	26.2	145/1824	Total dairy Low-fat dairy High-fat dairy	Validated 145-item FFQ	Self-reported physician diagnosis plus taking type 2 diabetes medication or fasting blood glucose $\geq 7.0$ mmol/L	Age, sex, systolic blood pressure, baseline BMI status, HDL cholesterol, total cholesterol, triglycerides, and calcium

(Continued)



TABLE 1 (Continued)

Author, year	Cohort (follow-up duration) and baseline examination	Location	Men, %	Mean age, y	Mean BMI, kg/m <sup>2</sup>	Cases/total, n/h	Dairy type included in meta-analysis <sup>2</sup>	Dietary assessment	Diabetes ascertainment	Adjustments
Margolis et al., 2011 (19)	Women's Health Initiative Observational Study (8 y) 1994–1998	United States	0	63	27.0	3946/82,076	Total dairy Low-fat dairy Yogurt	122-item FFQ	Self-report, validated by medical records	Age, race/ethnicity, total energy intake, income, education, smoking, alcohol intake, family history of diabetes, use of postmenopausal hormone therapy, systolic blood pressure, diastolic blood pressure, BMI, physical activity, dietary glycemic load, dietary total fat, dietary total fiber, and total magnesium
Montonen et al., 2005 (20)	Finnish Mobile Clinic Health Examination Survey (23 y) 1967–1972	Finland	53	52	26.5	383/4304	High-fat dairy High-fat milk	Dietary history interview with the use of a 100-item questionnaire	Social Insurance Institution's nationwide register of persons receiving diabetic drug reimbursement	Age, sex, BMI, energy intake, smoking, family history of diabetes, and geographic area
Nettleton et al., 2008 (21)	Multi-Ethnic Study of Atherosclerosis (5 y) 2000–2002	United States	47	61.7	27.9	413/5011	Low-fat dairy High-fat dairy	Validated 120-item FFQ	Self-report, fasting glucose ≥126 mg/dL at any exam, or use of antidiabetes medication	Race, sex, age, study center, total energy intake, smoking status and pack- years, physical activity, alcohol, coffee, tea, meat (red and processed), fish, whole grains, and BMI
O'Connor et al., 2014 (12)	EPIC-Norfolk Study (11 y) 1993–1997	United Kingdom	44	59	26.3	753/4127	Low-fat dairy High-fat dairy	7-d food diary	Self-report confirmed by record linkage with several databases	Age, sex, BMI, family history of diabetes, smoking, alcohol, physical activity, social class, education level, energy, fiber, fruit, vegetables, red meat, processed meat, and coffee intake

(Continued)

TABLE 1 (Continued)

Author, year	Cohort (follow-up duration) and baseline examination	Location	Men, %	Mean age, y	Mean BMI, kg/m <sup>2</sup>	Cases/total, n/h	Dairy type included in meta-analysis <sup>2</sup>	Dietary assessment	Diabetes ascertainment	Adjustments
Stuijs et al., 2012 (22)	EPIC-InterAct Study (12 y) 1992–1998	8 countries in Europe	38	52	26.1	10,694/24,475	Total dairy Total milk Fermented dairy Cheese Yogurt	Validated quantitative dietary questionnaire or validated FFQ	Self-report, linkage to primary-care registers, secondary-care registers, medication use, hospital admissions, and mortality data, verified by review of medical records; in Denmark and Sweden, identified by diabetes and pharmaceutical registers	Center, age, sex, BMI, education level, smoking status, physical activity level, alcohol intake, energy intake, energy- adjusted intake of fruit plus vegetables, red meat, processed meat, sugar- sweetened drinks, coffee, cereals, cereal products, and dietary intake of calcium, magnesium, and vitamin D
Soedamah-Muthu et al., 2013 (23)	Whitehall II study (10 y) 1985–1988	United Kingdom	72	56	25.9	273/4186	Total dairy Low-fat dairy High-fat dairy Total milk Fermented dairy Cheese Yogurt	Validated 114-item FFQ	Self-report of doctor's diagnosis, initiation of antidiabetic medication, and a 2-h 75-g oral-glucose- tolerance test	Age, sex, ethnicity, employment grade, smoking, alcohol intake, BMI, physical activity, family history of coronary heart disease/hypertension, fruit and vegetables, bread, meat, fish, coffee, tea, and total energy intake
Struijk et al., 2013 (24)	Inter99 Study (5 y) 1999–2001	Denmark	48	46	26.1	214/5232	Total dairy Low-fat dairy High-fat dairy Total milk Fermented dairy Cheese	Validated 198-item FFQ	Fasting plasma glucose $\geq 7.0$ mmol/L and/or 2-h plasma glucose $\geq 11.1$ mmol/L based on 1 oral-glucose- tolerance test	Age, sex, intervention group, diabetes family history, education level, physical activity, smoking status, intake of alcohol, whole- grain cereal, meat, fish, coffee, tea, fruit, vegetables, and energy, change in diet form baseline to 5-y follow-up, and waist circumference

(Continued)





TABLE 1 (Continued)

Author, year	Cohort (follow-up duration) and baseline examination	Location	Men, %	Mean age, y	Mean BMI, kg/m <sup>2</sup>	Cases/total, <i>n/h</i>	Dairy type included in meta-analysis <sup>2</sup>	Dietary assessment	Diabetes ascertainment	Adjustments
van Dam et al., 2006 (25)	Black Women's Health Study (8 y) 1995	United States	0	39	27.6	1964/41,186	Total dairy Low-fat dairy High-fat dairy	Validated 68-item FFQ	Self-report, validated by questionnaires filled out by physicians	Age, total energy intake, BMI, smoking, strenuous physical activity, alcohol consumption, parental history of diabetes, education level, coffee consumption, sugar-sweetened soft drink intake, processed meat and other red meat, and whole grain
Vang et al., 2008 (26)	Adventist Mortality Study and Adventist Health Study (17 y) Adventist Mortality Study: 1960 Adventist Health Study: 1976	United States	62	65	24.5	543/8401	Total milk Cheese	FFQ	Self-report	Age and sex
Villegas et al., 2009 (27)	Shanghai Women's Health Study (6.9 y) 1996–2000	China	0	50	23.8	1514/64,169	High-fat milk	In-person interviews using a validated 77-item FFQ	Self-report and fasting glucose concentration ≥7 mmol/L on ≥2 separate occasions, or an oral-glucose- tolerance test ≥11.1 mmol/L, and/or use of hypoglycemic medication	Age, energy intake, BMI, waist:hip ratio, smoking status, alcohol consumption, physical activity, income level, education level, occupation, and hypertension

(Continued)

TABLE 1 (Continued)

Author, year	Cohort (follow-up duration) and baseline examination	Location	Men, %	Mean age, y	Mean BMI, kg/m <sup>2</sup>	Cases/total, n/h	Dairy type included in meta-analysis <sup>2</sup>	Dietary assessment	Diabetes ascertainment	Adjustments
Zong et al., 2014 (28)	Nutrition and Health of Aging Population in China Study (6 y) 2005	China	41	59	24.3	504/2091	Total dairy Total milk	74-item FFQ	Self-report, use of any oral hypoglycemic medication or insulin, or fasting glucose $\geq 7.0$ mmol/L	Age, sex, region, and residence, smoking (current, past, or never), family history of diabetes, BMI, and dietary fiber intake, further adjusted for changes in BMI and waistline

<sup>1</sup>EPIC, European Prospective Investigation into Cancer and Nutrition; FFQ, food-frequency questionnaire; NR, not reported; PREDIMED, Prevención con Dieta Mediterránea.

<sup>2</sup>Dairy types were interpreted by LG and SSS-M and defined into uniform categories. The original definitions are found in Supplemental Table 1.

1.04). There was no evidence of publication bias (Supplemental Figure 16; Egger's test:  $P = 0.93$ ).

## Milk and T2D

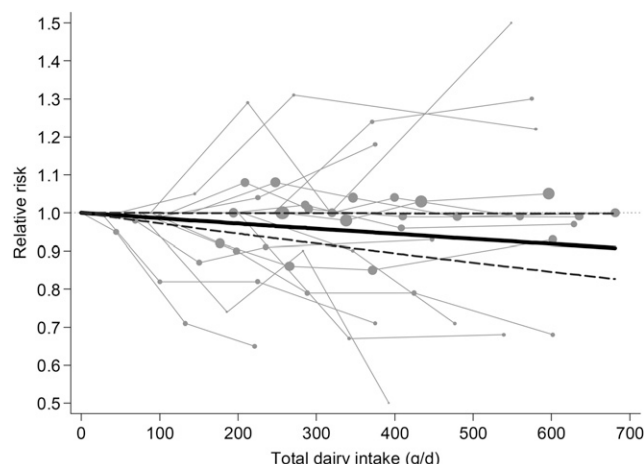
Total milk intake (11 studies) (10, 11, 13–16, 22–24, 26, 28) was not associated with T2D risk (RR: 0.97 per 200 g/d; 95% CI: 0.93, 1.02;  $P = 0.25$ ) (Supplemental Figure 17). Significant heterogeneity was present ( $I^2 = 57\%$ ,  $P = 0.007$ ). Subgroup analyses (Supplemental Table 4) suggested a direct association (RR: 1.03 per 200 g/d; 95% CI: 1.00, 1.06) in European populations, and an inverse association (RR: 0.87 per 200 g/d; 95% CI: 0.72, 1.05) in Asian populations. Also, a direct association was suggested for studies adjusting for the major confounders (RR: 1.03 per 200 g/d; 95% CI: 1.00, 1.06), and an inverse association for studies not adjusting for these major confounders (RR: 0.94 per 200 g/d; 95% CI: 0.88, 1.01). There was no evidence of publication bias (Supplemental Figure 18; Egger's test,  $P = 0.071$ ).

Low-fat milk (7 studies) (4, 10, 11, 15, 17) showed no association with T2D risk (RR: 1.01; 95% CI: 0.97, 1.05;  $P = 0.55$ ) (Supplemental Figure 19). There was significant heterogeneity ( $I^2 = 72\%$ ,  $P = 0.002$ ). Subgroup analyses indicated a direct association for studies with a long-term ( $>10$  y) follow-up duration (RR: 1.03 per 200 g/d; 95% CI: 1.01, 1.06) and for studies adjusted for major confounders (RR: 1.03 per 200 g/d; 95% CI: 1.00, 1.06). An inverse association was seen for studies not adjusting for these major confounders (RR: 0.81 per 200 g/d; 95% CI: 0.71, 0.93), although this subgroup was only based on 2 studies, and these had a short-term ( $\leq 5$  y) follow-up duration.

High-fat milk intake (9 studies) (4, 10, 11, 15, 17, 20, 27) was not associated with T2D risk (RR: 0.99 per 200 g/d; 95% CI: 0.88, 1.11;  $P = 0.85$ ) (Supplemental Figure 20). There was significant heterogeneity ( $I^2 = 84\%$ ,  $P < 0.001$ ). In sensitivity analyses (Supplemental Table 5), excluding the Asian study by Villegas et al. (27) reduced  $I^2$  to 44% ( $P = 0.08$ ), with results remaining similar (RR: 1.04 per 200 g/d; 95% CI: 0.97, 1.10). Subgroup analyses indicated a direct association for studies in American populations (RR: 1.11 per 200 g/d; 95% CI: 1.03, 1.20), and based on 2 studies in younger ( $\leq 50$  y) populations (RR: 1.10 per 200 g/d; 95% CI: 1.00, 1.22). There was no evidence of publication bias (Supplemental Figure 21; Egger's test,  $P = 0.78$ ).

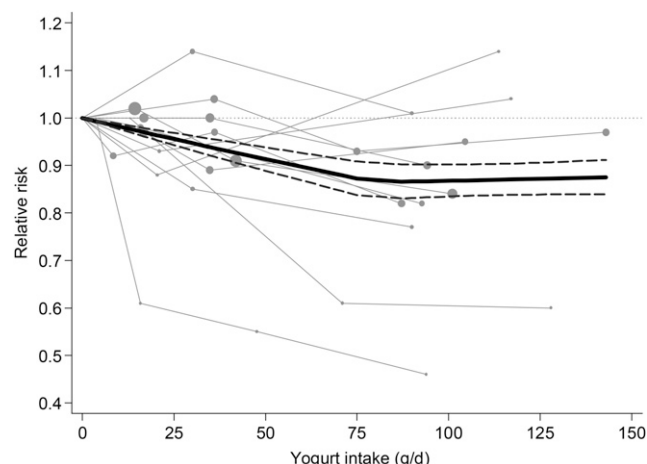
## Fermented dairy and T2D

Ericson et al. (11) reported no risk estimates for total fermented dairy, but for low-fat and high-fat fermented dairy separately. A meta-analysis (5 studies) (10, 11, 22–24), including the low-fat estimate by Ericson et al. (11), showed no association with T2D (Supplemental Figure 22A), but when the high-fat estimate was included, a significant 12% lower risk for an intake of 40 g/d was observed, with no further decreases at a higher intake (Supplemental Figure 22B). Cheese (12 studies) (4, 10, 11, 15–17, 22–24, 26) was not associated with T2D risk (RR: 1.00 per 10 g/d; Supplemental Figure 23). Significant heterogeneity was present ( $I^2 = 62\%$ ,  $P = 0.002$ ). In men (Supplemental Table 4), based on 2 studies, cheese intake was associated with a 5% higher T2D risk per 10 g/d (RR: 1.05; 95% CI: 1.02, 1.09).



**FIGURE 2** Spaghetti plot for the linear association between total dairy intake and diabetes risk (RR: 0.97 per 200 g/d; 95% CI: 0.95, 1.00;  $P = 0.044$ ), including 16 studies (17 study populations;  $n = 489,113$  individuals). Linearity of association was analyzed with the use of spline analysis. The association was further analyzed with the use of random-effects dose-response generalized least-square trend meta-regression analysis. Each solid gray line represents a study population. The circles are placed at the study-specific RRs that are related to the corresponding quantity of intake. The area of the circle is proportional to the study-specific weight. The solid black line represents the pooled RR at each quantity of intake, and the dashed black line is the corresponding 95% CI. The dotted gray line represents the reference line.

Yogurt (11 studies) (4, 10, 11, 15–17, 19, 22, 23) was nonlinearly inversely related to T2D, showing a 14% lower risk for an intake of 80 g/d (RR: 0.86 compared with 0 g/d; 95% CI: 0.83, 0.90;  $P < 0.001$ ). The risk did not further decrease at higher intake amounts of yogurt  $>80$  g/d (**Figure 4**). There was significant heterogeneity ( $I^2 = 73\%$ ,  $P < 0.001$ ). Subgroup analyses (Supplemental Table 4) indicated a stronger inverse association



**FIGURE 4** Spaghetti plot for the nonlinear association ( $P$ -nonlinearity:  $<0.001$ ) between yogurt intake and diabetes risk (RR: 0.86 at 80 g/d compared with 0 g/d; 95% CI: 0.83, 0.90;  $P < 0.001$ ), including 11 studies (12 study populations;  $n = 438,140$  individuals). Linearity of association was analyzed with the use of spline analysis. The association was further analyzed with the use of random-effects dose-response generalized least-square trend meta-regression analysis. Each solid gray line represents a study population. The circles are placed at the study-specific RRs that are related to the corresponding quantity of intake. The area of the circle is proportional to the study-specific weight. The solid black line represents the pooled RR at each quantity of intake, and the dashed black line is the corresponding 95% CI. The dotted gray line represents the reference line.

for studies in women (RR: 0.89 per 50 g/d; 95% CI: 0.83, 0.95), and based on 2 studies in older ( $>60$  y) populations (RR: 0.74 per 50 g/d; 95% CI: 0.60, 0.90). There was no evidence of publication bias in the meta-analyses of cheese and yogurt (**Supplemental Figures 24 and 25**; Egger's test: both  $P > 0.15$ ).

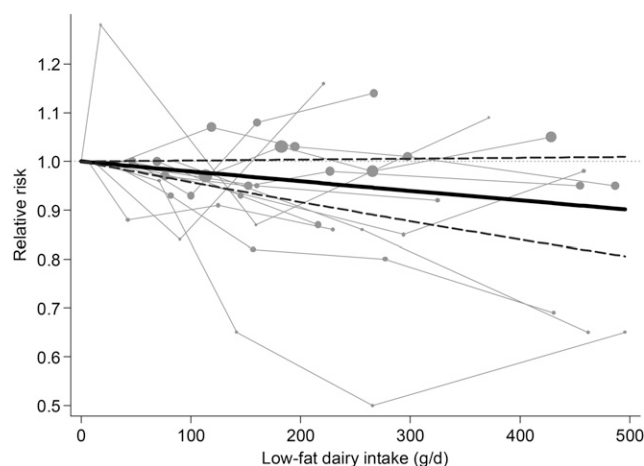
### Other dairy foods and T2D

Cream (5 studies) (4, 11, 17) was not associated with T2D risk (RR: 0.99 per 5 g/d) and there was no significant heterogeneity (**Supplemental Figure 26**). Ice cream (5 studies) (4, 11, 17) was significantly associated with a 19% lower T2D risk at an intake of 10 g/d (RR: 0.81 compared with 0 g/d, 95% CI: 0.78, 0.85;  $P < 0.001$ ), with no further decrease at a higher intake (**Supplemental Figure 27**). Significant heterogeneity ( $I^2 = 86\%$ ,  $P < 0.001$ ) was present but could not be explored because of the limited number of studies. Sherbet intake (4 studies) (4, 17) was not associated with T2D risk (RR: 1.00 per 5 g/d; **Supplemental Figure 28**), and there was no heterogeneity.

### DISCUSSION

This dose-response meta-analysis combining data from 22 prospective cohort studies showed nonlinear inverse associations for yogurt and ice cream intake and suggestive linear inverse associations for total and low-fat dairy with incident T2D. Given the considerable heterogeneity, results should be interpreted cautiously. For high-fat dairy, milk (total, low-fat and high-fat), cheese, cream, and sherbet intake, no significant associations were observed.

The role of dairy foods in the prevention of diabetes received considerable attention in meta-analyses of observational (3–9) and intervention studies (52, 53). In our meta-analysis, a 3%



**FIGURE 3** Spaghetti plot for the linear association between low-fat dairy intake and diabetes risk (RR: 0.96 per 200 g/d; 95% CI: 0.92, 1.00;  $P = 0.072$ ), including 13 studies ( $n = 405,667$  individuals). Linearity of association was analyzed with the use of spline analysis. The association was further analyzed with the use of random-effects dose-response generalized least-square trend meta-regression analysis. Each solid gray line represents a study population. The circles are placed at the study-specific RRs that are related to the corresponding quantity of intake. The area of the circle is proportional to the study-specific weight. The solid black line represents the pooled RR at each quantity of intake, and the dashed black line is the corresponding 95% CI. The dotted gray line represents the reference line.

lower T2D risk was observed per 200 g total dairy/d, which likely was attributable to low-fat dairy (4% lower risk per 200 g/d). Chen et al. (4) showed in their meta-analysis of 14 prospective cohort studies no significant association for total dairy (RR:  $0.98 \cdot \text{serving}^{-1} \cdot \text{d}^{-1}$ ; 95% CI: 0.96, 1.01), and, in a separate analysis of 3 large US cohorts, no association for low-fat dairy (RR:  $1.00 \cdot \text{serving}^{-1} \cdot \text{d}^{-1}$ ; 95% CI: 0.98, 1.02). Earlier meta-analyses showed strong inverse associations for total and low-fat dairy (3, 7). Aune et al. (3) reported a significant 19% lower T2D risk at a total dairy intake of 400 g/d, based on 12 studies, with no additional benefit at a higher intake. For low-fat dairy, based on 9 studies, a 9% lower risk per 200 g/d was found. The lack of association in the study by Chen et al. (4) may be explained at least partly, as acknowledged by the authors, by the longer follow-up of the 3 large US cohorts (4). In our subgroup analysis of studies of longer duration ( $>10$  y) we also found no associations with total or low-fat dairy intake.

Consistent with previous meta-analyses (3, 4, 7), yogurt intake was strongly inversely associated with incident T2D. The association appeared to be nonlinear, with an intake of 80–125 g/d related to a 14% lower T2D risk, which is in line with the results from Aune et al. (3). Yogurt may have contributed to our findings for total dairy and low-fat dairy intake. In our meta-analysis we had no data on the contribution of yogurt to total or low-fat dairy, which may vary considerably across countries. In the United States, the contribution of yogurt to total dairy based on the NHANES study was only 3%, of which 76% was low-fat or skimmed yogurt (54), whereas in the Spanish Prevención con Dieta Mediterránea study, it was 24% (70% skimmed) (10). The Prevención con Dieta Mediterránea study showed inverse associations for both low-fat and high-fat yogurt with T2D (10). Yogurt may exert beneficial metabolic effects because of probiotic bacteria, which have been reported to lower blood cholesterol (55). Yogurt also contains vitamin K-2 (menaquinone), which was inversely associated with the risk of T2D in a large prospective cohort (56). Cheese, however, is also rich in vitamin K-2 but was not related to the risk of T2D in our meta-analysis. We could not distinguish between plain and sugar-sweetened yogurt, for which intake may vary considerably across countries. The latter could adversely affect the cardiometabolic risk profile, and our findings may not be generalizable to all types of yogurt.

Ice cream intake was inversely associated with T2D risk, a finding comparable with other studies (3, 4, 7). In the US cohorts analyzed by Chen et al. (4), however, the strong inverse association for ice cream was attenuated when dietary information was no longer updated after hypertension or hypercholesterolemia had been diagnosed, implying that reverse causation may have influenced these findings. We could not examine this source of bias in our meta-analysis. Also, the narrow variations in ice cream intake (0–30 g/d) and the possibility of misreporting of ice cream intake are reasons to interpret these results with caution.

We observed no association with milk and T2DM. Findings of previous meta-analyses (3, 7) also showed no significant association between milk intake and the risk of T2D. In line with our results, a very recent publication not included in our meta-analysis that reported on a Mendelian randomization study indicated no evidence of an association between milk and T2D (57).

Dairy is a heterogeneous food group with products differing in water content, amount of fermentation, and nutrients such as fat and sodium. A major strength of this meta-analysis is that we examined a wide range of well-specified dairy foods in relation to T2D risk, making use of data from 22 prospective studies. We were able to examine dose-response relations and nonlinearity of the associations, which could be important for setting dietary guidelines. A limitation of this meta-analysis is that, for fermented dairy, ice cream, and several other dairy products, the variation in intake and the number of studies was small. These results, as well as the findings from subgroup analyses, therefore should be interpreted with caution. When evaluating data from stratified analysis, it should be noted that factors other than the stratifying variable may be responsible for differences across subgroups. To illustrate, the larger risk reductions observed in Asian populations may also be due to different amounts or types of dairy consumed, or the confounders adjusted for in the analysis. For our study, we extracted risk estimates from the papers that were adjusted for the largest number of covariates. However, a limitation of observational studies, including the present meta-analysis, is that residual confounding (for example by social economic status), selection bias, and information bias cannot be ruled out.

In conclusion, this dose-response meta-analysis of prospective cohort studies suggested an inverse association of dairy foods, in particular yogurt, with T2D. Associations for yogurt were supported with potential biological mechanisms, and were in line with previously published meta-analyses. However, the results should be considered in the context of the observed heterogeneity. The results from our updated meta-analysis imply a possible role of dairy foods in the prevention of T2D, but this needs confirmation by randomized controlled trials.

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The authors' responsibilities were as follows—LG: generated the design of the study, acquired and analyzed the data, and contributed to the statistical planning, interpretation of the data and writing of the manuscript; ELD: contributed to the design of the study, statistical analysis and interpretation of the data, and writing of the manuscript; VSM and JdG: contributed to the design of the study, interpretation of the data, and writing of the manuscript; JMG: generated the idea and design for the study and contributed to the statistical planning and interpretation of the data and writing of the manuscript; SSS-M: generated the idea and design for the study, acquired the data, and contributed to the statistical planning, interpretation of the data, and writing of the manuscript; and all authors: had full access to all study data, take full responsibility for the accuracy of the data analysis, have authority over submission preparation and decisions to submit for publication, and read and approved the final manuscript. SSS-M previously received funding





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## REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 6th edn [Internet]. Brussels, Belgium: International Diabetes Federation, 2013 [cited 2015 Feb 18]. Available from: <http://www.idf.org/diabetesatlas>.
2. Stevens JW, Khunti K, Harvey R, Johnson M, Preston L, Woods HB, Davies M, Goyder E. Preventing the progression to type 2 diabetes mellitus in adults at high risk: a systematic review and network meta-analysis of lifestyle, pharmacological and surgical interventions. *Diabetes Res Clin Pract* 2015;107:320–31.
3. Aune D, Norat T, Romundstad P, Vatten LJ. Dairy products and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. *Am J Clin Nutr* 2013;98:1066–83.
4. Chen M, Sun Q, Giovannucci E, Mozaffarian D, Manson JE, Willett WC, Hu FB. Dairy consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. *BMC Med* 2014;12:215.
5. Elwood PC, Givens DI, Beswick AD, Fehily AM, Pickering JE, Gallacher J. The survival advantage of milk and dairy consumption: an overview of evidence from cohort studies of vascular diseases, diabetes and cancer. *J Am Coll Nutr* 2008;27:723S–34S.
6. Elwood PC, Pickering JE, Givens DI, Gallacher JE. The consumption of milk and dairy foods and the incidence of vascular disease and diabetes: an overview of the evidence. *Lipids* 2010;45:925–39.
7. Gao D, Ning N, Wang C, Wang Y, Li Q, Meng Z, Liu Y, Li Q. Dairy products consumption and risk of type 2 diabetes: systematic review and dose-response meta-analysis. *PLoS One* 2013;8:e73965.
8. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab* 2007;92:2017–29.
9. Tong X, Dong JY, Wu ZW, Li W, Qin LQ. Dairy consumption and risk of type 2 diabetes mellitus: a meta-analysis of cohort studies. *Eur J Clin Nutr* 2011;65:1027–31.
10. Díaz-López A, Bullo M, Martínez-González MA, Corella D, Estruch R, Fito M, Gómez-Gracia E, Fiol M, García de la Corte FJ, Ros E, et al. Dairy product consumption and risk of type 2 diabetes in an elderly Spanish Mediterranean population at high cardiovascular risk. *Eur J Nutr* 2015 Feb 7 (Epub ahead of print; DOI 10.1007/s00394-015-0855-8).
11. Ericson U, Hellstrand S, Brunkwall L, Schulz C-A, Sonestedt E, Wallstrom P, Gullberg B, Wirfalt E, Orho-Melander M. Food sources of fat may clarify the inconsistent role of dietary fat intake for incidence of type 2 diabetes. *Am J Clin Nutr* 2015;101:1065–80.
12. O'Connor LM, Lentjes MAH, Luben RN, Khaw K-T, Wareham NJ, Forouhi NG. Dietary dairy product intake and incident type 2 diabetes: a prospective study using dietary data from a 7-day food diary. *Diabetologia* 2014;57:909–17.
13. Elwood PC, Pickering JE, Fehily AM. Milk and dairy consumption, diabetes and the metabolic syndrome: the Caerphilly prospective study. *J Epidemiol Community Health* 2007;61:695–8.
14. Fuhrman BJ, Smit E, Crespo CJ, Garcia-Palmieri MR. Coffee intake and risk of incident diabetes in Puerto Rican men: results from the Puerto Rico Heart Health Program. *Public Health Nutr* 2009;12:842–8.
15. Grantham NM, Magliano DJ, Hodge A, Jowett J, Meikle P, Shaw JE. The association between dairy food intake and the incidence of diabetes in Australia: the Australian Diabetes Obesity and Lifestyle Study (AusDiab). *Public Health Nutr* 2013;16:339–45.
16. Kirii K, Mizoue T, Iso H, Takahashi Y, Kato M, Inoue M, Noda M, Tsugane S. Calcium, vitamin D and dairy intake in relation to type 2 diabetes risk in a Japanese cohort. *Diabetologia* 2009;52:2542–50.
17. Liu S, Choi HK, Ford E, Song Y, Klevak A, Buring JE, Manson JE. A prospective study of dairy intake and the risk of type 2 diabetes in women. *Diabetes Care* 2006;29:1579–84.
18. Louie JCY, Flood VM, Rangan AM, Burlutsky G, Gill TP, Gopinath B, Mitchell P. Higher regular fat dairy consumption is associated with lower incidence of metabolic syndrome but not type 2 diabetes. *Nutr Metab Cardiovasc Dis* 2013;23:816–21.
19. Margolis KL, Wei F, de Boer IH, Howard BV, Liu S, Manson JE, Mossavar-Rahmani Y, Phillips LS, Shikany JM, Tinker LF. A diet high in low-fat dairy products lowers diabetes risk in postmenopausal women. *J Nutr* 2011;141:1969–74.
20. Montonen J, Jarvinen R, Heliövaara M, Reunanen A, Aromaa A, Knekt P. Food consumption and the incidence of type II diabetes mellitus. *Eur J Clin Nutr* 2005;59:441–8.
21. Nettleton JA, Steffen LM, Ni H, Liu K, Jacobs DR Jr. Dietary patterns and risk of incident type 2 diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes Care* 2008;31:1777–82.
22. Sluijs I, Forouhi NG, Beulens JWJ, van der Schouw YT, Agnoli C, Arriola L, Balkau B, Barricarte A, Boeing H, Bueno-de-Mesquita HB, et al. The amount and type of dairy product intake and incident type 2 diabetes: results from the EPIC-InterAct Study. *Am J Clin Nutr* 2012;96:382–90.
23. Soedamah-Muthu SS, Masset G, Verberne L, Geleijnse JM, Brunner EJ. Consumption of dairy products and associations with incident diabetes, CHD and mortality in the Whitehall II study. *Br J Nutr* 2013;109:718–26.
24. Struijk EA, Heraclides A, Witte DR, Soedamah-Muthu SS, Geleijnse JM, Toft U, Lau CJ. Dairy product intake in relation to glucose regulation indices and risk of type 2 diabetes. *Nutr Metab Cardiovasc Dis* 2013;23:822–8.
25. van Dam RM, Hu FB, Rosenberg L, Krishnan S, Palmer JR. Dietary calcium and magnesium, major food sources, and risk of type 2 diabetes in U.S. black women. *Diabetes Care* 2006;29:2238–43.
26. Vang A, Singh PN, Lee JW, Haddad EH, Brinegar CH. Meats, processed meats, obesity, weight gain and occurrence of diabetes among adults: findings from Adventist Health Studies. *Ann Nutr Metab* 2008;52:96–104.
27. Villegas R, Gao Y-T, Dai Q, Yang G, Cai H, Li H, Zheng W, Shu XO. Dietary calcium and magnesium intakes and the risk of type 2 diabetes: the Shanghai Women's Health Study. *Am J Clin Nutr* 2009;89:1059–67.
28. Zong G, Sun Q, Yu D, Zhu J, Sun L, Ye X, Li H, Jin Q, Zheng H, Hu FB, et al. Dairy consumption, type 2 diabetes, and changes in cardiometabolic traits: a prospective cohort study of middle-aged and older Chinese in Beijing and Shanghai. *Diabetes Care* 2014;37:56–63.
29. Soedamah-Muthu SS, Ding EL, Al-Delaimy WK, Hu FB, Engberink MF, Willett WC, Geleijnse JM. Milk and dairy consumption and incidence of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. *Am J Clin Nutr* 2011;93:158–71.
30. Soedamah-Muthu SS, Verberne LDM, Ding EL, Engberink MF, Geleijnse JM. Dairy consumption and incidence of hypertension: a dose-response meta-analysis of prospective cohort studies. *Hypertension* 2012;60:1131–7.
31. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.
32. Buijsse B, Boeing H, Drogan D, Schulze MB, Feskens EJ, Amiano P, Barricarte A, Clavel-Chapelon F, de Lauzon-Guillain B, Fagherazzi G, et al. Consumption of fatty foods and incident type 2 diabetes in populations from eight European countries. *Eur J Clin Nutr* 2015;69:455–61.
33. Choi HK, Willett WC, Stampfer MJ, Rimm E, Hu FB. Dairy consumption and risk of type 2 diabetes mellitus in men: a prospective study. *Arch Intern Med* 2005;165:997–1003.
34. Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE. Diet and risk of clinical diabetes in women. *Am J Clin Nutr* 1992;55:1018–23.
35. Ericson U, Sonestedt E, Gullberg B, Hellstrand S, Hindy G, Wirfalt E, Orho-Melander M. High intakes of protein and processed meat associate with increased incidence of type 2 diabetes. *Br J Nutr* 2013;109:1143–53.
36. Fumeron F, Lamri A, Abi Khalil C, Jaziri R, Porchay-Balderelli I, Lantieri O, Vol S, Balkau B, Marre M. Dairy consumption and the incidence of hyperglycemia and the metabolic syndrome: results from a French prospective study, Data from the Epidemiological Study on the Insulin Resistance Syndrome (DESIR). *Diabetes Care* 2011;34:813–7.

37. Fumeron F, Lamri A, Emery N, Bellili N, Jaziri R, Porchay-Balderelli I, Lantieri O, Balkau B, Marre M. Dairy products and the metabolic syndrome in a prospective study, DESIR. *J Am Coll Nutr* 2011;30(5 Suppl 1):454S-63S.
38. Malik VS, Sun Q, van Dam RM, Rimm EB, Willett WC, Rosner B, Hu FB. Adolescent dairy product consumption and risk of type 2 diabetes in middle-aged women. *Am J Clin Nutr* 2011;94:854-61.
39. Mozaffarian D, Cao H, King IB, Lemaitre RN, Song X, Siscovick DS, Hotamisligil GS. Trans-palmitoleic acid, metabolic risk factors, and new-onset diabetes in U.S. adults: a cohort study. *Ann Intern Med* 2010;153:790-9.
40. Pittas AG, Dawson-Hughes B, Li T, Van Dam RM, Willett WC, Manson JE, Hu FB. Vitamin D and calcium intake in relation to type 2 diabetes in women. *Diabetes Care* 2006;29:650-6.
41. Sugimori H, Miyakawa M, Yoshida K, Izuno T, Takahashi E, Tanaka C, Nakamura K, Hinohara S. Health risk assessment for diabetes mellitus based on longitudinal analysis of MHTS database. *J Med Syst* 1998;22:27-32.
42. van Dam RM, Rimm EB, Willett WC, Stampfer MJ, Hu FB. Dietary patterns and risk for type 2 diabetes mellitus in U.S. men. *Ann Intern Med* 2002;136:201-9.
43. van Dam RM, Willett WC, Rimm EB, Stampfer MJ, Hu FB. Dietary fat and meat intake in relation to risk of type 2 diabetes in men. *Diabetes Care* 2002;25:417-24.
44. von Ruesten A, Feller S, Bergmann MM, Boeing H. Diet and risk of chronic diseases: results from the first 8 years of follow-up in the EPIC-Potsdam study. *Eur J Clin Nutr* 2013;67:412-9.
45. Bodner-Montville J, Ahuja JKC, Ingwersen LA, Haggerty ES, Enns CW, Perloff BP. USDA food and nutrient database for dietary studies: released on the web. *J Food Compos Anal* 2006;19:S100-7.
46. Food Standards Agency. Food portion sizes, 3rd ed. Norwich, London: TSO; 2005.
47. Wells GASB, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses [Internet]. [cited 2015 Jun 8]. Available from: [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp).
48. Greenland S, Longnecker MP. Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. *Am J Epidemiol* 1992;135:1301-9.
49. Bauer SR, Hankinson SE, Bertone-Johnson ER, Ding EL. Plasma vitamin D levels, menopause, and risk of breast cancer: dose-response meta-analysis of prospective studies. *Medicine (Baltimore)* 2013;92:123-31.
50. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539-58.
51. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629-34.
52. Benatar JR, Sidhu K, Stewart RAH. Effects of high and low fat dairy food on cardio-metabolic risk factors: a meta-analysis of randomized studies. *PLoS One* 2013;8:e76480.
53. Turner KM, Keogh JB, Clifton PM. Dairy consumption and insulin sensitivity: A systematic review of short- and long-term intervention studies. *Nutr Metab Cardiovasc Dis* 2015;25:3-8.
54. National Dairy Council. NHANES 2009-2010. Centers for Disease Control and Prevention, National Center for Health Statistics, National Health and Nutrition Examination Survey data [Internet]. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, [2009-2010] [cited 2015 Jun 4]. Available from: <http://www.cdc.gov/nchs/nhanes.htm>.
55. Parvez S, Malik KA, Ah Kang S, Kim HY. Probiotics and their fermented food products are beneficial for health. *J Appl Microbiol* 2006;100:1171-85.
56. Beulens JWJ, van der A DL, Grobbee DE, Sluijs I, Spijkerman AMW, van der Schouw YT. Dietary phylloquinone and menaquinones intakes and risk of type 2 diabetes. *Diabetes Care* 2010;33:1699-705.
57. Bergholdt HK, Nordestgaard BG, Ellervik C. Milk intake is not associated with low risk of diabetes or overweight-obesity: a Mendelian randomization study in 97,811 Danish individuals. *Am J Clin Nutr* 2015;102:487-96.

