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Dairy consumption and CVD: a systematic review and meta-analysis

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Abstract

Inverse associations between dairy consumption and CVD have been reported in several epidemiological studies. Our objective was to conduct a meta-analysis of prospective cohort studies of dairy intake and CVD. A comprehensive literature search was conducted to identify studies that reported risk estimates for total dairy intake, individual dairy products, low/full-fat dairy intake, Ca from dairy sources and CVD, CHD and stroke. Random-effects meta-analyses were used to generate summary relative risk estimates (SRRE) for high *v.* low intake and stratified intake dose–response analyses. Additional dose–response analyses were performed. Heterogeneity was examined in sub-group and sensitivity analyses. In total, thirty-one unique cohort studies were identified and included in the meta-analysis. Several statistically significant SRRE below 1.0 were observed, namely for total dairy intake and stroke (SRRE = 0·91; 95 % CI 0·83, 0·99), cheese intake and CHD (SRRE = 0·82; 95 % CI 0·72, 0·93) and stroke (SRRE = 0·87; 95 % CI 0·77, 0·99), and Ca from dairy sources and stroke (SRRE = 0·69; 95 % CI 0·60, 0·81). However, there was little evidence for inverse dose–response relationships between the dairy variables and CHD and stroke after adjusting for within-study covariance. The results of this meta-analysis of prospective cohort studies have shown that dairy consumption may be associated with reduced risks of CVD, although additional data are needed to more comprehensively examine potential dose–response patterns.

Key words: **Meta-analyses: Epidemiology: Dairy products: Milk: CVD: Stroke: CHD**

The global health burden of CVD, including CHD and stroke, is immense, as CVD is the leading cause of mortality worldwide, accounting for approximately 30 % of all deaths[(1)]. CVD is the leading cause of death in Europe, accounting for over four million deaths each year[(2)]. In Europe, CHD and stroke account for the first and second most common causes of death, with an estimated 1·8 million and almost 1·1 million deaths each year, respectively, although both of these rates have been declining in most European countries from 1990 to 2010[(2)]. CVD is the leading cause of death in the USA, and it is responsible for approximately 600 000–800 000 deaths/annum, or one out of every three to four deaths[(3–6)]. In the USA, the relative rate of CVD and stroke declined significantly from 2000 to 2010, but each year approximately 795 000 people experience a new or recurrent stroke[(3,4)]. The most common type of heart disease in the USA is coronary artery disease, which is responsible for 380 000 deaths annually[(3,4,6)].

Several factors, including modifiable lifestyle factors, have been identified that increase or decrease the risk of CVD. In a recent paper regarding trends in CVD, the population attributable fraction was reported to be 40·6 % for high blood pressure on CVD mortality, and lower yet still meaningful attributable fractions were observed for smoking, poor diet, insufficient physical activity and abnormal blood glucose levels[(7)]. On the basis of a 2014 joint report from the American Heart Association and the Centers for Disease Control and Prevention, National Institutes of Health, and other governmental agencies, it was suggested that the declining trend in CVD and stroke rates are because of enhanced and proactive CVD risk factor control interventions, such as hypertension control efforts that were initiated over the past few decades[(3,4)]. Other interventions have included efforts to control diabetes mellitus and high cholesterol and smoking cessation programs[(3,4,8)]. Despite these successful efforts, CVD remains the most significant public health burden of disease in many countries, including Europe and the USA.

Several previous studies and meta-analyses have examined the relationship between dairy intake and CVD and related

Abbreviations: GLST, generalised least-squares trend; ICD, International Classification of Diseases; RR, relative risk; SRRE, summary relative risk estimate.

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outcomes, with inverse associations generally observed[9–13]. Most recently, Qin *et al.*[14] conducted a meta-analysis of dairy consumption and CVD and found statistically significant inverse associations for dairy consumption and total CVD and stroke, cheese intake and stroke and CHD, and low-fat dairy intake and stroke. However, the authors did not perform any dose–response analyses, and used broad categories of dairy variables and outcome variables in their analyses.

Given the accumulating epidemiological data on the relationship between dairy intake and CVD and CVD-related outcomes, the objective of the present study was to conduct a comprehensive meta-analysis of prospective cohort studies that updates the state of the epidemiological science. The specific aims were as follows: (i) to estimate summary associations between total dairy intake and specific dairy products and CVD, CHD and stroke; (ii) to conduct sub-group and sensitivity analyses by descriptive study characteristics to identify potential sources of heterogeneity and to evaluate patterns of associations; (iii) evaluate dose–response using categorical intake analyses and linear splines; and (iv) to evaluate the potential for publication bias.

Methods

We followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines for this systematic review and meta-analysis[15]. The PRISMA checklist has been submitted to the journal as an attachment to this manuscript. The twenty-seven checklist items pertain to the content of a systematic review and meta-analysis, which includes the title, abstract, methods, results, discussion and funding.

Literature search and study identification

A comprehensive literature search was conducted using PubMed to identify prospective cohort studies that investigated dairy consumption and CVD. Additional literature searches using Embase were performed as well. The exposures of interest included total dairy intake, specific dairy products (e.g. milk, cheese, yoghurt), Ca from dairy products (reported as an analytical variable in the individual studies) and low- and full-fat dairy intake. The outcomes of interest included CVD, CHD and stroke. Thus, a comprehensive literature search through March 2015, with no lower date limit, was conducted. The search included the following terms: ('dairy products' [MeSH] OR 'dairy calcium' OR milk OR yogurt OR cheese OR cream OR butter OR dairy) AND ('heart diseases' [MeSH] OR 'vascular diseases' [MeSH] OR 'death, sudden' [MeSH] OR 'heart disease' OR 'stroke' OR 'cerebrovascular accident' OR 'sudden death' OR 'cardiac arrest' OR 'cardiovascular disease' OR 'coronary artery disease' OR 'heart failure' OR 'cardiovascular mortality' OR 'coronary death' OR CHD OR CVD OR 'cardiac death' OR 'myocardial infarction' OR angina) AND ('randomized controlled trial' [PT] OR 'cohort studies' [MeSH] OR cohort OR RCT OR 'randomized controlled trial') NOT ('animal experimentation' [MeSH] OR 'case reports' [PT] OR 'cross-sectional studies' [MeSH] OR 'case-control studies' [MeSH] OR editorial [PT] OR letter [PT] OR 'in vitro' [PT] OR comment [PT] OR review [PT] OR 'review literature as topic' [MeSH]). Supplementary literature searches included screening of reference lists from all relevant studies, pertinent review articles and meta-analyses. All search results were screened by two authors.

To be included in the meta-analysis, a published study had to meet the following criteria: (1) prospective design; (2) adult human population; (3) English language; and (4) provide risk estimates and measures of variance for dairy intake and CVD. Total dairy intake, individual dairy products (e.g. yoghurt or milk) and dairy-derived Ca intakes were eligible exposure variables in each study. We did not include studies of dietary patterns, such as 'dairy product patterns' and CVD outcomes. Total CVD (fatal or non-fatal), CHD (fatal or non-fatal) and stroke (fatal or non-fatal, including specific types of stroke) were included as outcomes. The literature search flow diagram is shown in Fig. 1.

Data extraction and statistical analysis

The following data were extracted from each study: first author, publication year, cohort name, year of diet assessment, geographic location, sample size, years of follow-up, population demographic characteristics, diet assessment method, dairy exposure and definitions, CVD and related outcomes (including the author-based definitions and International Classification of Diseases (ICD) codes), median or range of intakes across quantiles, relative risk (RR) and 95 % CI in each quantile of intake and statistical adjustments. If more than one article from the same study population was published, data from the publication with the longest follow-up were extracted. If one cohort had more than one publication but each publication presented results from at least one unique analysis (e.g. the Japan Collaborative Cohort Study), data were extracted for all unique analyses. Two investigators ascertained individual study information independently.

Random-effects models were used to calculate summary relative risk estimates (SRRE), 95 % CI and corresponding *P* values for heterogeneity. The study weights were equal to the inverse of the variance of each study's effect estimate according to the methodology developed by DerSimonian and Laird[16]. Relative risks comparing the highest with the lowest category of intake were combined across all studies to produce the summary associations. When both crude and multivariate adjusted RR were provided, we extracted the most fully adjusted risk estimate. Primary meta-analysis models were created for total dairy consumption, specific dairy products (milk, cheese and yoghurt), full-fat and low-fat dairy intake, Ca from dairy sources and total CVD, CHD and stroke. We made an effort to not mix and match different dairy products together, and we harmonised our outcome classifications based on similar disease rubrics. To be included in the total dairy intake analyses, dairy intake had to be reported in the individual studies as a composite variable representing dairy intake from all sources. For example, if data for total milk only was reported in a study, these data would go into the milk only analyses. Similarly, total CVD was required to be reported as a composite of all CVD outcomes rather than specific outcomes, such as

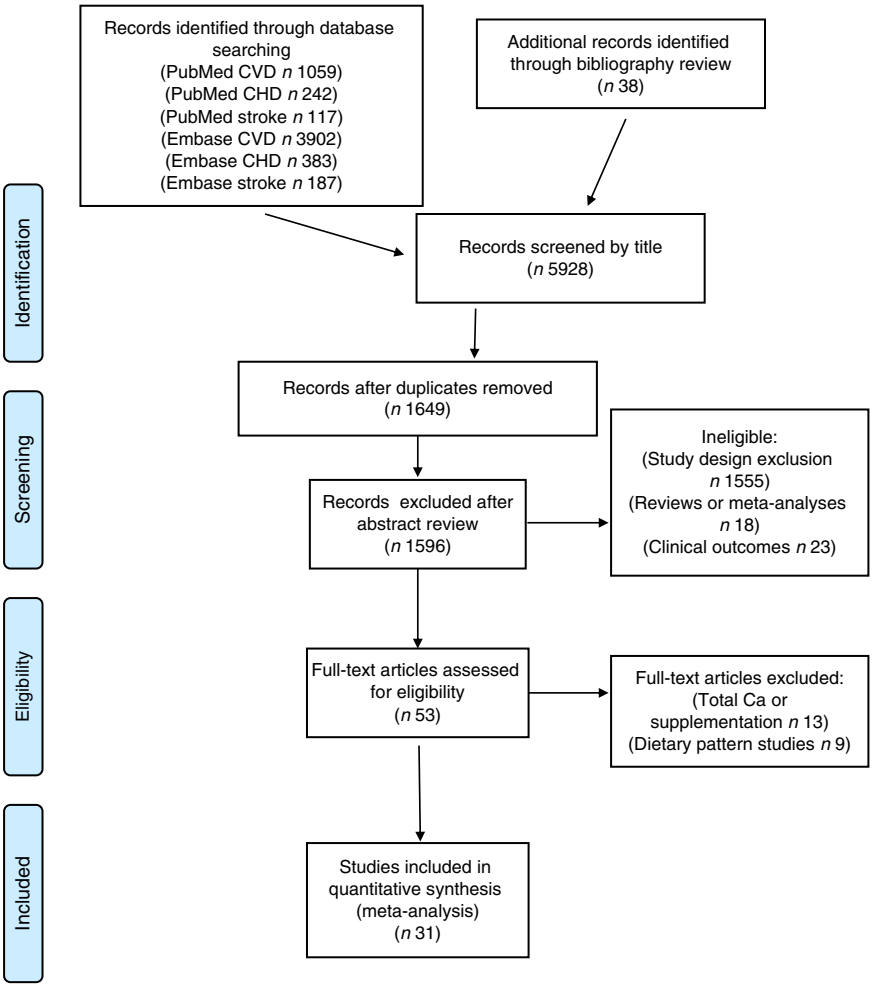

Fig. 1. Flow chart of the article screening process[15]. For more information, visit www.prisma-statement.org

stroke. Thus, we generated meta-analyses based on specific dairy products, such as milk, and specific outcomes, such as CHD or stroke. Sub-group and sensitivity analyses were conducted to evaluate variability by descriptive study factors and to identify potential sources of heterogeneity. Sub-group models were generated when three or more studies provided relevant data to be meta-analysed. One-study-removed sensitivity analyses were conducted to determine the relative influence each study had on the overall model.

We used two different approaches to estimate any possible dose–response patterns. First, we created meta-analysis models based on stratified categories of dairy intake. This involved extracting *all* available relative risk and 95 % CI data from *all* intake categories from *all* prospective cohort studies. Then, RR were combined and meta-analysed according to their intake category. Using this approach, no assumptions were made concerning linearity, and this method allows for the evaluation of risk based on varying levels of dairy consumption. However, this method does not account for within-study intake correlations. Thus, in our second dose–response approach, we conducted linear trend analyses that account for correlated intakes within studies. Specifically, when events and the number of person-years per category of dairy intake were available, or when they could be extrapolated using the methods described by Aune[17], they were used as input into the two-stage fixed-effects model described by Greenland and Longnecker[18] using the Stata command for generalised least-squares trend (GLST)[19,20] to estimate a summary risk ratio per dose of dairy intake. Linear splines were used to model dose effects where knots were placed at the same cut-off points for each dairy category described in this manuscript. Tests for linearity were conducted to determine whether splines improved GLST model fit. A limitation to this method is that the number of cases and person-years for each intake category are required for analytical inclusion, and not all studies reported this information. As a result, more data points were included in the stratified intake analyses, although the GLST analyses are able to account for within-study covariance. In addition, we ran restricted cubic spline GLST analyses; however, these models did not perform better than the linear GLST models. Thus, we reported results from the linear spline analyses.

Most studies reported results in terms of servings per d for total dairy intake, milk and cheese, although some studies

reported results based on g/d metrics. Therefore, we harmonised units by converting g/d to servings in these instances. To do this, we reviewed the distribution of intake in the individual studies and we also reviewed the United States Department of Agriculture National Nutrient Database[21]. A single serving of milk was considered as 244 g, and a serving of cheese was considered as 35 g. We were not able to convert grams of total dairy intake to servings because total dairy intake represents variable products (e.g. cheese, milk, yoghurt) with variable conversions. Some studies reported data for dairy intake and CVD/CHD/stroke per standard deviation of the mean in g/d or by unit increase in component score[22–24]; thus, data from these studies were used in our dose–response analyses only.

Statistical heterogeneity was assessed using the Cochran's Q test and I^2 statistic, which indicates the percentage of variation attributable to between-study heterogeneity[25]. The presence of publication bias was assessed visually by examining a funnel plot measuring the standard error as a function of effect size, as well as performing Egger's regression method and the Duval and Tweedie imputation method[26]. We generated forest plots for models of total dairy intake and CVD, CHD and stroke. All statistical analyses were performed using Comprehensive Meta-Analysis Software (version 3.3.070; Biostat) and Stata (version 14).

Results

A total of thirty-one unique prospective cohort studies were included in the meta-analysis (Table 1)[22–24,27–54]. Studies were published between 1996 and 2015 with baseline dietary assessment periods ranging between 1965 and 2001. Over one million participants were analysed for CVD or CVD-related outcomes across the studies. In the majority of studies, ICD codes for the CVD outcomes were provided. For CVD, ICD-9 codes 390–459 and ICD-10 codes 100–199 were reported; for CHD, ICD-9 codes 400–414, 427·5, 429·2, 798·1, 798·2, 798·9 and ICD-10 codes 120–125 were reported; and for stroke, ICD-9 codes 430–439 and ICD-10 codes 160–169 were reported. Follow-up periods ranged between 5 and 26 years, with most studies following up participants for 10–20 years. Studies were conducted in a variety of countries, including the USA, Europe, the Nordic countries, Australia and Japan. Dairy intake information was ascertained via FFQ, and while some studies reported results data for total dairy intake other studies reported data for specific products, such as milk, or specific constituents, such as dairy Ca. We made a concerted effort to make our analytical models as homogeneous as possible in terms of dairy exposure and CVD outcomes. Thus, if a study-specific variable was recorded as 'total milk', results data for this variable were not included in the meta-analysis model of individual study variable labelled as 'total dairy intake'. Midpoint values of dairy servings per d ranged between 0·1 and 9·3 for total dairy intake, 0·3 and 3·5 for milk and 0·3 and 6·0 for cheese. However, the greatest proportion of intake categories ranged between 1 and 3 servings/d for total dairy intake, and between 1 and 2 servings/d for milk and cheese.

Meta-analysis results

The meta-analysis results are summarised in Table 2.

Total dairy intake. Only four cohort studies reported a composite 'total dairy intake' variable with specific results data for a composite 'total CVD' variable[32,39,44,51]. Meta-analysis of these studies resulted in an SRRE of 0·88 (95 % CI 0·75, 1·04) with moderate heterogeneity ($P_H = 0·076$, $I^2 = 52·7$) (Fig. 2). There was no statistical evidence of publication bias in this model ($P = 0·39$).

The SRRE based on the meta-analysis of seven studies of total dairy intake and total CHD was 0·91 (95 % CI 0·80, 1·04) (Fig. 3)[30,33,36,39,44,48,50], with significant heterogeneity ($P_H = 0·038$, $I^2 = 52·8$) that was explained, in part, by descriptive study factors. Sub-group analysis of the three US studies showed no association between total dairy intake and risk of total CHD (SRRE = 0·99; 95 % CI 0·92, 1·07)[30,33,36]. The remaining four studies were all conducted among study participants from different countries. Four studies evaluated total dairy intake and CHD risk among women, resulting in an SRRE of 0·86 (95 % CI 0·71, 1·05)[30,33,39,48]. Only one study reported results data specifically for men. Meta-analysis of studies with follow-up periods of 15 years or less resulted in a statistically significant SRRE of 0·81 (95 % CI 0·71, 0·93) with little heterogeneity ($P_H = 0·549$, $I^2 = 0·0$)[33,44,48,50], but no association (SRRE = 1·00) was found in the analysis of studies with greater than 15 years of follow-up[30,36,39]. There was modest variability between full-fat dairy intake (SRRE = 1·05; 95 % CI 0·93, 1·19) and low-fat dairy intake (SRRE = 0·90; 95 % CI 0·82, 0·98) on CHD risk[30,36,44,50]. We stratified total dairy intake into three categories of intake but no patterns of associations based on levels of intake were apparent, with SRRE of 0·88, 0·93 and 0·86, based on <1·5 servings, 1·5–3 servings and >3 servings, respectively. Furthermore, the GLST procedure did not show a pattern of linear dose–response (RR per serving = 1·00; 95 % CI 0·98, 1·01), and the use of linear spline modelling did not provide evidence of a non-linear dose–response (χ^2 P value = 0·11). No evidence of publication bias was detected in the model of total dairy intake and CHD ($P = 0·41$).

Intake of total dairy intake was associated significantly and inversely with total stroke (SRRE = 0·91; 95 % CI 0·83, 0·99) with moderate heterogeneity ($P_H = 0·072$; $I^2 = 44·5$) (Fig. 4)[31,39–41,43,44,49]. The heterogeneity was explained, in part, by certain study characteristics, namely duration of follow-up, fat content and dose. Meta-analysis of studies that followed up participants longer than 15 years resulted in an SRRE of 0·88 (95 % CI 0·82, 0·95, $P_H = 0·492$, $I^2 = 0·0$). Adding Louie *et al.*[44] to this model (the mean follow-up in this study was 15 years) did not change the SRRE but made the model more homogeneous ($P_H = 0·614$, $I^2 = 0·00$). Both full-fat dairy intake (SRRE = 0·91; 95 % CI 0·84, 0·99) and low-fat dairy intake (SRRE = 0·90; 95 % CI 0·83, 0·96) were associated inversely and significantly with stroke, with no heterogeneity found in each model. Less than 1·5 servings and 1·5 or more servings of total dairy intake were associated inversely and statistically significantly with total stroke. We were unable to conduct GLST analyses because of lack of intake, cases per strata and person-year information in the articles.

Table 1. Descriptive study characteristics of prospective cohorts of dairy intake and CVD

First author, year	Study, country	Year baseline diet assessed	Follow-up	Number of subjects	Age (range) (years)	Dairy exposures analysed	Outcome	Statistical adjustments
Abbott, 1996	Honolulu Heart Program, USA	1965	22	3150	55–68	Dairy Ca	Thromboembolic stroke	Intakes of alcohol, K and Na, age, smoking, PA, BMI, SBP, total cholesterol, serum glucose, serum uric acid and haematocrit
Al-Delaimy, 2003	HPFS, USA	1986	12	39 800	40–75	Dairy Ca	Ischaemic heart disease	Age, time period, diabetes, hyperlipidaemia, fam hx of MI, smoking, aspirin intake, BMI, PA and intakes of energy and vit E
Avalos, 2013	Rancho Bernardo, USA	1984–1987	23	1759	≥40	Non-fat milk, yoghurt, ice cream, low-fat cheese, cheese, cottage cheese, cream, cream cheese, whole milk, milk chocolate, butter, hot chocolate	CHD incidence	Age, BMI, diabetes, HTN, LDL-cholesterol and current oestrogen use (women only)
Bernstein, 2010	NHS, USA	1980	26	84 136	30–55	High-fat dairy intake; low-fat dairy intake	CHD	Age, time period, BMI, smoking, menopausal status, fam hx of early MI, MVI use, vit E use, aspirin use, PA and intakes of energy, cereal fibre, alcohol and trans fat
Bernstein, 2012	NHS, USA	1980	26	84 010	30–55	Whole-fat dairy intake; low-fat dairy intake	Total stroke	Age, time period, BMI, smoking, menopausal status, fam hx of early MI, MVI use, vit E use, aspirin use, PA and intakes of energy, fruits and vegetables, cereal fibre, alcohol, other protein sources and trans fat
Bernstein, 2012	HPFS, USA	1986	22	43 150	40–75	Whole-fat dairy intake; low-fat dairy intake	Total stroke	Age, time period, BMI, smoking, fam hx of early MI, MVI use, vit E use, aspirin use, PA and intakes of energy, fruits and vegetables, cereal fibre, alcohol, other protein sources and trans fat
Bonthuis, 2010	Nambour, Australia	1992	16	1529	25–78	Total dairy intake, low-fat dairy intake, full-fat dairy intake, milk, yoghurt, full-fat cheese	CVD mortality	Age, sex, BMI, total energy intake, alcohol intake, school leaving age, PA level, pack-years of smoking, dietary supps use, β-carotene treatment during trial and using medications for HTN, diabetes mellitus or cardiac disorder and use of β-adrenergic blocking agents
Bostick, 1999	IWHS, USA	1986	8	34 486	55–69	Fat-containing dairy products; total dairy intake without butter	Ischaemic heart disease mortality	Age, intakes of energy, alcohol, dietary vit E and SFA, smoking, T2D, BMI, waist:hip ratio, post-menopausal oestrogen use, marital status and PA
Dalmeijer, 2013	EPIC-NL, Netherlands	1993	13	33 625	21–64	Cheese; high-fat dairy intake; low-fat dairy intake; total dairy intake	CHD events; stroke events	Sex, age, PA, education, smoking, BMI, intakes of energy, alcohol, coffee, fruits, vegetables, fish, meat and bread
Elwood, 2004	Caerphilly cohort, UK	1979	20	2403	44–63	Milk	Ischaemic stroke; fatal and non-fatal ischaemic heart disease	Age, smoking, social class, prior vascular disease, BMI, SBP, intakes of energy, alcohol and fat, and fasting cholesterol, HDL and TAG
Goldbohm, 2011	NLCS, Netherlands	1986	10	120 852	55–69	Milk products (non-fermented full-fat milk, non-fermented low-fat milk, fermented full-fat milk, fermented low-fat milk), cheese (fat cheese, low-fat cheese), butter, low-fat dairy intake, fat from dairy products	Ischaemic heart disease mortality, stroke mortality	Age, education, cigarette, cigar and pipe smoking, non-occupational PA, occupational PA, BMI, MVI use, alcohol, energy, energy-adjusted MUFA and PUFA intakes, and vegetable and fruit consumption

Table 1. *Continued*

First author, year	Study, country	Year baseline diet assessed	Follow-up	Number of subjects	Age (range) (years)	Dairy exposures analysed	Outcome	Statistical adjustments
Haring, 2014	ARIC, USA	1987–1989	22	12 066	45–64	Dairy intake, high-fat dairy intake, low-fat dairy intake	CHD incidence and mortality	Age, sex, race, study centre, total energy intake, smoking, education, systolic BP, use of antihypertensive medication, HDL-cholesterol, total cholesterol, use of lipid-lowering medication, BMI, waist:hip ratio, alcohol intake, sports-related PA, leisure-related PA, carbohydrate intake, fibre intake and Mg intake
Iso, 1999	NHS, USA	1980	14	85 764	30–55	Dairy Ca	Ischaemic stroke	Age, smoking, time interval, BMI, menopausal status, post-menopausal hormone use, PA, usual aspirin use, MVI use, vit E use, intakes of alcohol and *n*-3 fatty acids and histories of HTN, T2D and high cholesterol
Kinjo, 1999	Japanese Cohort, Japan	1965	15	233 170	40–69	Dairy milk	Death from cerebral haemorrhage; death from cerebral embolism or thrombosis; mortality from all cerebrovascular disease	Sex, age, follow-up period, prefecture, smoking, alcohol drinking and occupation
Kondo, 2013 (F)	NIPPON DATA80, Japan	1980	24	5198	≥30	Milk and dairy products	CHD death, CVD death, stroke death	Age, BMI, smoking, alcohol drinking habit, T2D, antihypertensive use, work category and energy intake
Kondo, 2013 (M)	NIPPON DATA80, Japan	1980	24	9243	≥30	Milk and dairy products	CHD death, CVD death, stroke death	Age, BMI, smoking, alcohol drinking habit, T2D, antihypertensive use, work category and energy intake
Larsson, 2009	ATBC, Finland	1985	13·6	26 556	50–69	Butter; cheese; cream; ice cream; low-fat milk; total dairy intake; whole milk; yoghurt	Intracerebral haemorrhage; cerebral infarction; subarachnoid haemorrhage; intercerebral haemorrhage;	Age, supplementation group, education, cigarettes smoked daily, BMI, serum cholesterol, serum HDL, T2D, heart disease, PA and intakes of energy, alcohol, caffeine, sugar, red meat, poultry, fish, fruit, fruit juices, vegetables, potatoes, whole grains and refined grains
Larsson, 2012	SMC and Cohort of Swedish Men, Sweden	1997	10·2	74 961	45–83	Cheese; cream and crème fraiche; full-fat dairy intake; low-fat dairy intake; total dairy intake; milk	Cerebral infarction; haemorrhagic stroke; stroke	Age, sex, smoking, pack-years smoking, education, BMI, PA, aspirin use, HTN, diabetes, fam hx MI and intakes of total energy, alcohol, coffee, fresh red meat, processed meat, fish, fruits, vegetables*
Li, 2012	EPIC-Heidelberg, Germany	1994	11	23 980	35–64	Dairy Ca	CVD mortality; MI; stroke	Sex, age, education, PA, BMI, smoking, lifetime alcohol intake, diabetes, use of Ca supps and intakes of vit D, SFA, protein and total energy
Lin, 2013	CVDFACTS, Taiwan	1989–1990	13	3326	≥17	Dairy products (milk of any kind, cheese, yoghurt)	Total stroke incidence, ischaemic stroke incidence	Sex, baseline age, urinary Na/creatinine, smoking status, drinking status, PA, BMI, SBP change, DBP change and HTN medication
Louie, 2013	BMES, Australia	1992	15	2900	49–97	Whole-fat dairy intake; low/reduced-fat dairy intake; total dairy intake	CHD death, CVD death, stroke death	Age, sex, BMI, change in weight during f/u, past MI, past stroke, smoking, stage II HTN, T2D, use of hypertensive medications and statins, change in dairy intake and intakes of total energy
Mann, 1997	Oxford Vegetarian Cohort, UK	1980	13·3	10 802	16–79	Cheese; milk	Ischaemic heart disease deaths	Age, sex, smoking and social class

Table 1. *Continued*

First author, year	Study, country	Year baseline diet assessed	Follow-up	Number of subjects	Age (range) (years)	Dairy exposures analysed	Outcome	Statistical adjustments
Ness, 2001	The Collaborative Study, UK	1970	25	5765	35–64	Pints of milk	Coronary heart disease mortality; CVD mortality; stroke mortality	Age, smoking, DBP, cholesterol, BMI, social class, father's social class, adjusted forced expiratory volume, education, deprivation category, siblings, car user, angina, ECG ischaemia, bronchitis and alcohol consumption
Panagiotakos, 2009	ATTICA, Greece	2001	5	2101	18–89	Dairy products (low-fat)	CVD incidence	Age, sex, PA, education, smoking, other components (dietary patterns), BMI, HTN, hypercholesterolaemia, diabetes, fam hx of CVD
Praagman, 2015	EPIC-NL, Netherlands	1993–1997	15	34 409	20–70	Total fermented dairy foods, yoghurt, cheese	CVD mortality, CHD mortality, stroke mortality	Age, sex, total energy intake, smoking habit, BMI, PA, education level, HTN at baseline, intakes of alcohol and energy-adjusted intakes of fruit and vegetables
Patterson, 2013	SMC, Sweden	1997	11·6	33 636	48–83	Cheese, cream/full-fat crème fraiche; total dairy intake; milk; cultured milk/yoghurt	MI	Age, smoking, PA, waist:hip ratio, alcohol, HTN, hypercholesterolaemia, fam hx of MI, education, aspirin, hormone therapy usage, and intakes of alcohol, total energy, fruits and vegetables and whole grains
Sauvaget, 2003	LSS, Japan	1979	16	37 130	34–103	Dairy products; total milk	Total stroke mortality	Sex, birth cohort, adjusted for city, radiation dose, self-reported BMI, smoking, alcohol habits, education, diabetes and HTN
Soedamah-Muthu, 2012	Whitehall II Study, UK	1997	10·8	4255	35–55	Total cheese; high-fat dairy intake; low-fat dairy intake; total dairy intake; total milk; yoghurt	Fatal and non-fatal CHD	Sex, age, ethnicity, employment grade, smoking, BMI, PA, fam hx of CHD or HTN and intakes of alcohol, fruit and vegetables, bread, meat, fish, coffee, tea and total energy
Sonestedt, 2011	MDC, Sweden	1991	12	26 445	44–74	Butter; cheese; cream; high-fat milk; low-fat milk; milk; fermented milk; total dairy intake	Incident CVD	Age, sex, season, diet method, BMI, smoking, PA, education, and intakes of energy, alcohol, vegetables, fruit and berries, fish and shellfish, meat, coffee and whole grains
Umesawa, 2006 (F)	JACC Study, Japan	1988	9·6	32 319	40–79	Dairy Ca	CHD mortality; CVD mortality; intraparenchymal haemorrhage mortality; ischaemic stroke mortality; stroke mortality; subarachnoid haemorrhage mortality; haemorrhagic stroke mortality	BMI, HTN, diabetes, smoking, intakes of ethanol, K and total energy
Umesawa, 2006 (M)	JACC Study, Japan	1988	9·6	21 068	40–79	Dairy Ca	CHD mortality; CVD mortality; intraparenchymal haemorrhage mortality; ischaemic stroke mortality; stroke mortality; subarachnoid haemorrhage mortality; haemorrhagic stroke mortality	BMI, HTN, diabetes, smoking, intakes of ethanol, K and total energy
Umesawa, 2008	JPHC Cohort, Japan	1990	12·9	41 526	40–59	Dairy Ca	Intraparenchymal haemorrhage; ischaemic stroke; subarachnoid haemorrhage; CHD; total stroke	Age, sex, BMI, diabetes, hypercholesterolaemia medications, menopause, smoking, public health centre, HTN and intakes of ethanol, Na, K, *n*-3 fatty acid intake
van Aerde, 2013	Hoorn Study, Netherlands	1989	12·4	1956	50–75	Cheese; high-fat dairy intake; low-fat dairy intake; total dairy intake; milk	Fatal CVD	Age, sex, BMI, smoking, education, PA, and intakes of alcohol, total energy, meat, fish, bread, vegetables, fruit, coffee and tea

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Table 1. *Continued*

First author, year	Study, country	Year baseline diet assessed	Follow-up	Number of subjects	Age (range) (years)	Dairy exposures analysed	Outcome	Statistical adjustments
Wang, 2015	JACC Study, Japan	1988	19	94 980	40–79	Milk	CVD mortality	Age categories, smoking status, drinking status, PA, sleeping duration, BMI, education level, participation in health checkups, green-leafy vegetable intake, and history of HTN, diabetes and liver disease

PA, physical activity; SBP, systolic blood pressure; HPFS, Health Professionals Follow-up Study; fam hx, family history; MI, myocardial infarction; vit, vitamin; HTN, hypertension; NHS, Nurses' Health Study; MVI, multivitamin; supps, supplements; IWHS, Iowa Women's Health Study; T2D, type 2 diabetes; EPIC-NL, Early Post-Menopausal Intervention Cohort Study; NLCS, Netherlands Cohort Study; ARIC, Atherosclerosis Risk in Communities Study; DBP, diastolic blood pressure; F, female; M, male; ATBC, Alpha-Tocopherol, Beta-Carotene Cancer Prevention; SMC, Swedish Mammography Cohort; CVDFACTS, CVD risk FACtor Two-township Study; BMES, Blue Mountain Eye Study; f/u, follow-up; ATTICA Study, study carried out in the Attica province of Greece; LSS, Life Span Study; MDC, Swedish Malmo Diet and Cancer Cohort; JACC, Japan Collaborative Cohort Study for the Evaluation of Cancer Risk; JPHC, Japan Public Health Center.

Milk. The summary association between total milk intake and total CVD was 0·94 (95 % CI 0·86, 1·03, $P_H = 0·167$, $I^2 = 38·1$), but it was based on only four studies[32,46,51,54]. Collectively, milk consumption was not associated with CHD, with summary associations observed slightly above and below the null value across sub-group analyses by country, sex, follow-up duration and dose. Meta-analysis of total milk and total stroke produced a non-statistically significant summary association of 0·90 (95 % CI 0·79, 1·02) with significant heterogeneity ($P_H < 0·001$, $I^2 = 79·6$). The study by Larsson *et al.*[40] appeared to be an outlier. Removal of this study in a sensitivity analyses resulted in an SRRE of 0·85 (95 % CI 0·79, 0·92) and made the model more homogeneous ($P_H = 0·163$, $I^2 = 34·7$). Although SRRE were similar and in the inverse direction, the model for total milk and total stroke among study participants followed up more than 15 years was homogeneous ($P_H = 0·780$, $I^2 = 0·0$). No dose–response relationship between total milk consumption and total stroke was apparent in our categorical intake analyses. Moreover, testing for dose–response using the GLST procedure resulted in no dose–response pattern (RR per serving = 1·0; 95 % CI 0·98, 1·02), and there was no evidence that using linear splines significantly improved model fit (χ^2 *P* value = 0·85).

Cheese. Cheese intake was associated inversely and non-statistically significantly with total CVD (SRRE = 0·89; 95 % CI 0·78, 1·01, $P_H = 0·317$, $I^2 = 13·0$), but only three studies reported results data for this relationship[23,47,51]. Consumption of cheese was associated with a statistically significant inverse SRRE of 0·82 (95 % CI 0·72, 0·93) with minimal heterogeneity ($P_H = 0·639$, $I^2 = 0·0$) for total CHD risk[29,35,47,48,50]. Analytical models based on intake categories were all homogeneous, and analyses based on 0–0·5 servings and >0·5–1·5 servings were not statistically significant, whereas >1·5 servings of cheese was associated with a statistically significant inverse SRRE of 0·86 (95 % CI 0·79, 0·94). In addition, analysis using the GLST procedure resulted in a 2 % (RR per serving = 0·98; 95 % CI 0·95, 1·01), albeit non-statistically significant, decrease in the RR of CHD for every serving increase of cheese intake after taking covariance into account. However, the use of linear splines did not significantly improve GLST model fit (χ^2 *P* value = 0·67). As with CHD, cheese intake was associated inversely and statistically significantly with total stroke (SRRE = 0·87; 95 % CI 0·77, 0·99, $P_H = 0·198$, $I^2 = 33·5$)[35,40,41,47]. Although a consistent pattern of intake response was not as clear, statistically significant inverse associations were found for >0·5–1·5 servings and for >1·5 servings of cheese and total stroke. GLST analyses did not support a significant pattern of association based on linear analyses (RR per serving = 0·99; 95 % CI 0·97, 1·01) or the use of linear splines (χ^2 *P* value = 0·485).

Yoghurt. Yoghurt consumption was not associated significantly with CVD or CHD. More studies are needed to evaluate the potential relationship between yoghurt intake and CVD and CVD-related outcomes.

Calcium from dairy products. Ca from dairy sources (as a reported variable in the individual studies) was not associated

significantly with total CHD (SRRE = 0·94; 95 % CI 0·82, 1·08)[28,42,52,53], but it was associated with a strong and statistically significant inverse SRRE for total stroke (SRRE = 0·69; 95 % CI 0·60, 0·81, $P_H = 0·274$, $I^2 = 21·2$)[27,37,42,52,53]. A non-linear pattern of inverse associations for total stroke based on 0–100, 100–300 and >300 mg of dairy Ca was observed. We were unable to complete a GLST analysis on Ca from dairy product because of a lack of intake, cases per strata and person-year information in the articles.

Discussion

Because of the significant public health burden of CVD, identifying modifiable factors that may decrease the risk of this disease is of great importance. Thus, we conducted a comprehensive meta-analysis to estimate associations between dairy intake and CVD, CHD and stroke by using all available data from prospective cohort studies. Although based on data from observational studies, our analyses indicate that dairy consumption may be associated inversely with CVD, CHD and stroke, based on extreme quantile comparisons. Collectively, the large majority of summary associations were <1·0, with many statistically significant inverse associations. Although the summary associations were not overly strong in magnitude (as is commonplace in nutritional epidemiology studies), many analyses produced 5–15 % reductions in CVD, CHD and stroke risk.

On the basis of data from the USDA, the average American consumes approximately 1·85 servings of dairy/d, with men and women over the age of 20 years consuming 1·95 and 1·50 servings, respectively[55]. However, the USDA currently recommends an equivalency of three cups of dairy per d, with a focus on fat-free or low-fat milk, yoghurt and cheese. We did not observe clear monotonic inverse trends based on increasing dairy intake and CVD outcomes, but the majority of our stratified intake analyses show that up to three (or above) servings of total dairy intake may be associated inversely with CHD and stroke risk. Similarly, cheese consumption was associated inversely with CHD and stroke risk at all levels of intake, with statistically significant SRRE at >1·5 servings. In contrast, no clear or consistent patterns of inverse associations based on frequency of milk intake were apparent, which was partly because of greater data inflection in the individual studies. Our GLST and linear spline analyses did not produce significant inverse dose–response trends based on increasing frequency of dairy intake. Such analyses require studies to report the number of cases and person-years in each intake strata using a proportional hazards modelling structure. As such, our GLST analyses included fewer studies based on limited reporting compared with the stratified intake analyses. However, the GLST modelling accounts for within-study covariance. Additional studies, with more complete data reporting for each dairy intake strata, are needed to more comprehensively examine potential dose–response patterns.

Our results are concordant with previously published meta-analyses of dairy consumption and CVD, CHD and stroke. The most recently published meta-analysis of prospective cohort studies of dairy consumption and CVD reported a summary RR of 0·88 (95 % CI 0·81, 0·96) for dairy consumption and overall risk of CVD[14], as well as a statistically significant inverse association for stroke (RR = 0·87; 95 % CI 0·77, 0·99). However, the authors did not perform any dose–responses analyses, and used broader categories of dairy variables and outcome variables in their analyses. Because broad categories of dairy variables were used (e.g. milk included with total dairy intake) in their analyses, a larger number of studies were included in their analytical models. In contrast, our analyses were rigorously specific to the type of dairy variable in that we did not combine different types of dairy products unless a composite dairy variable was reported in a study. Despite these methodological differences, our summary findings were relatively consistent.

There are several potential mechanisms by which dairy intake may beneficially have a role in CVD risk reduction. Dairy products are a rich source of (i) minerals, such as Ca, K and Mg; (ii) vitamins, such as riboflavin and vitamin B_{12}; and (iii) protein, such as whey and casein[56]. Individually, collectively or interactively, all of these nutrient sources may have a favourable effect on CVD. The potential role of Ca intake and supplementation on CVD risk is a controversial topic, with some studies suggesting an increased risk while other studies indicating a null or decreased risk[57–59]. However, the source of Ca may be important.

Although the epidemiological evidence appears to support a beneficial role of dairy intake on CVD and other chronic disease outcomes, some researchers have suggested that consumption of dairy products, a source of SFA, may contribute to an increase in heart disease. Experimental evidence from human studies have shown that high intake of SFA increases plasma levels of LDL-cholesterol[60,61], although milk and dairy products have also been associated with an increase in HDL-cholesterol and blood pressure reduction[11,61–64]. Indeed, the potential role of diets that are high in SFA on CVD risk is unclear and controversial, although emerging science suggests that a potential role of SFA on CVD risk may not be merited. Risk may depend on the substitutions for SFA that occur as different foods may affect risk in variable ways[56,65–68]. In a meta-analysis of prospective cohort studies, intake of SFA was not associated with an increased risk of CHD (RR = 1·07; 95 % CI 0·96, 1·19), stroke (RR = 0·81; 95 % CI 0·62, 1·05) or CVD (RR = 1·00; 95 % CI 0·89, 1·11) based on comparisons of extreme quintiles[68].

Although our analytical models were harmonised based on similar exposure and similar outcome classifications, the data used in this meta-analysis were generated from observational studies. Therefore, the validity of a meta-analysis is not immune to limitations, particularly in nutritional epidemiology where information bias is a predominant concern. In an effort to garner a better understanding of any potential relationships between dairy products and CVD, CHD and stroke, we conducted a variety of unique meta-analyses to discern any potential patterns of associations. Although most analyses produced inverse associations, it may be possible that those who consume dairy products, particularly low-fat dairy intake, may engage in other favourable dietary and lifestyle habits. However, our analyses of full-fat dairy intake and cheese were not associated with positive associations for CVD. Rather, inverse associations were

Table 2. Summary relative risk estimates (SRRE) for dairy intake and CVD, CHD and stroke (high *v.* low exposure unless otherwise noted)(SRRE and 95 % confidence intervals; *P* values for heterogeneity (P_H) and I^2)

Model	SRRE	95 % CI	P_H; I^2	Notes
Total dairy intake				
Total dairy intake and total CVD (*n* 4)	0·88	0·75, 1·04	0·076; 52·7 %	Studies required to report a composite variable for total dairy intake and a composite variable for total CVD
Total dairy intake and total CHD (*n* 7)	0·91	0·80, 1·04	0·038; 52·8 %	Studies required to report a composite variable for total dairy intake and a composite variable for total CHD
Sub-group analyses				
Total dairy intake and total CHD: studies conducted in the USA (*n* 3)	0·99	0·92, 1·07	0·872; 0·0 %	US study populations
Total dairy intake and total CHD: studies conducted among non-US populations (*n* 4)	0·83	0·67, 1·04	0·074; 53·1 %	Studies conducted in Japan, Australia, Sweden and the UK
Total dairy intake and total CHD: studies conducted among women (*n* 4)	0·86	0·71, 1·05	0·047; 62·18 %	Studies conducted among female participants
Total dairy intake and total CHD: average follow-up period ≤15 years (*n* 4)	0·81	0·71, 0·93	0·549; 0·0 %	Studies with an average follow-up time of 15 years or less
Total dairy intake and total CHD: average follow-up period >15 years (*n* 3)	1·00	0·83, 1·20	0·093; 53·2 %	Studies with an average follow-up time of more than 15 years
Full-fat dairy intake and total CHD (*n* 4)	1·05	0·93, 1·19	0·237; 29·3 %	Exposure reported as high-fat dairy intake or whole-fat dairy intake
Low-fat dairy intake and total CHD (*n* 4)	0·90	0·82, 0·98	0·991; 0·0 %	Exposure reported as low-fat dairy intake
Dose–response analyses				
<1·5 servings/d total dairy intake and total CHD (*n* 7 data points)	0·88	0·80, 0·96	0·013; 63·0 %	All RR meta-analysed for <1·5 servings/d of total dairy intake
1·5–3 servings/d total dairy intake and total CHD (*n* 9 data points)	0·93	0·85, 1·00	0·035; 51·6 %	All RR meta-analysed for 1·5–3 servings/d of total dairy intake
>3 servings/d total dairy intake and total CHD (*n* 5 data points)	0·86	0·79, 0·94	0·595; 0·0 %	All RR meta-analysed for >3 servings/d of total dairy intake
Total dairy intake and total stroke (*n* 7)	0·91	0·83, 0·99	0·072; 44·5 %	Studies required to report a composite variable for total dairy intake and a composite variable for total stroke
Sub-group analyses				
Total dairy intake and total stroke: studies conducted among women (*n* 2)	0·89	0·80, 0·98	0·324; 0·0 %	Studies conducted among female participants
Total dairy intake and total stroke: studies conducted among men (*n* 3)	1·00	0·84, 1·18	0·069; 62·6 %	Studies conducted among male participants
Total dairy intake and total stroke: average follow-up period ≤15 years (*n* 4)	0·97	0·81, 1·16	0·067; 58·0 %	Studies with an average follow-up time of 15 years or less
Total dairy intake and total stroke: average follow-up period >15 years (*n* 3)	0·88	0·82, 0·95	0·492; 0·0 %	Studies with an average follow-up time of more than 15 years
Total dairy intake and ischaemic stroke (*n* 3)	0·96	0·76, 1·20	0·024; 73·17 %	Results data reported for ischaemic stroke
Full-fat dairy intake and total stroke (*n* 3)	0·91	0·84, 0·99	0·882; 0·0 %	Exposure reported as high-fat dairy intake or whole-fat dairy intake
Low-fat dairy intake and total stroke (*n* 3)	0·90	0·83, 0·96	0·914; 0·0 %	Exposure reported as low-fat dairy intake
Dose–response analyses				
<1·5 servings/d total dairy intake and total stroke (*n* 15 data points)	0·92	0·89, 0·96	0·891; 0·0 %	All RR meta-analysed for <1·5 servings/d of total dairy intake
1·5+ servings/d total dairy intake and total stroke (*n* 10 data points)	0·91	0·88, 0·95	0·986; 0·0 %	All RR meta-analysed for 1·5 or more servings/d of total dairy intake
Milk				
Total milk and total CVD (*n* 4)	0·94	0·86, 1·03	0·167; 38·1 %	Studies required to report a composite variable for total CVD
Total milk and total CHD (*n* 6)	1·05	0·95, 1·16	0·392; 5·0 %	Studies required to report a composite variable for total CHD
Sub-group analyses				
Total milk and total CHD: studies conducted among UK populations (*n* 3)	0·84	0·67, 1·05	0·474; 0·0 %	UK study populations
Total milk and total CHD: studies conducted among women (*n* 3)	1·15	1·00, 1·33	0·849; 0·0 %	Studies conducted among female participants
Total milk and total CHD: studies conducted among men (*n* 4)	0·96	0·74, 1·25	0·130; 47·0 %	Studies conducted among male participants
Total milk and total CHD: average follow-up period ≤15 years (*n* 3)	1·07	0·94, 1·21	0·670; 0·0 %	Studies with an average follow-up time of 15 years or less
Total milk and total CHD: average follow-up period >15 years (*n* 3)	0·97	0·76, 1·25	0·129; 47·1 %	Studies with an average follow-up time of more than 15 years
Dose–response analyses				
0–1 servings of milk and total CHD (*n* 4 data points)	0·99	0·86, 1·13	0·645; 0·0 %	All RR meta-analysed for 0–1 serving/d of milk
>1 to <2 servings of milk and total CHD (*n* 9 data points)	1·02	0·93, 1·10	0·598; 0·0 %	All RR meta-analysed for >1 to <2 servings/d of milk
2+ servings of milk and total CHD (*n* 6 data points)	0·98	0·86, 1·12	0·215; 29·3 %	All RR meta-analysed for 2+ servings/d of milk
Total milk and total stroke (*n* 7)	0·90	0·79, 1·02	<0·001; 79·6 %	Studies required to report a composite variable for total stroke
Sub-group analyses				
Total milk and total stroke: studies conducted among men (*n* 4)	1·04	0·96, 1·14	0·476; 0·0 %	Studies conducted among male participants
Total milk and total stroke: average follow-up period ≤15 years (*n* 4)	0·90	0·77, 1·05	<0·001; 87·9 %	Studies with an average follow-up time of 15 years or less
Total milk and total stroke: average follow-up period >15 years (*n* 3)	0·93	0·78, 1·10	0·780; 0·0 %	Studies with an average follow-up time of more than 15 years

Table 2. *Continued*

Model	SRRE	95 % CI	P_H; I^2	Notes
Total milk and ischaemic stroke (*n* 4)	0·93	0·81, 1·06	0·006; 75·62 %	Results data reported for ischaemic stroke
Total milk and haemorrhagic stroke (*n* 3)	0·93	0·69, 1·25	0·001; 86·55 %	Results data reported for haemorrhagic stroke
Dose–response analyses				
0–1 servings of milk and total stroke (*n* 11 data points)	0·95	0·86, 1·04	< 0·001; 76·7 %	All RR meta-analysed for 0–1 serving/d of milk
>1 to <2 servings of milk and total stroke (*n* 9 data points)	0·98	0·90, 1·06	0·114; 38·2 %	All RR meta-analysed for >1 to <2 servings/d of milk
2+ servings of milk and total stroke (*n* 9 data points)	1·01	0·92, 1·11	0·069; 44·9 %	All RR meta-analysed for 2+ servings/d of milk
Cheese				
Total cheese and total CVD (*n* 3)	0·89	0·78, 1·01	0·317; 13·0 %	Studies required to report a composite variable for total CVD
Total cheese and total CHD (*n* 5)	0·82	0·72, 0·93	0·639; 0·0 %	Studies required to report a composite variable for total CHD
Dose–response analyses				
0–0·5 servings of cheese and total CHD (*n* 5 data points)	0·95	0·83, 1·08	0·942; 0·0 %	All RR meta-analysed for 0–0·5 serving/d of cheese
>0·5 to 1·5 servings of cheese and total CHD (*n* 6 data points)	0·91	0·79, 1·03	0·959; 0·0 %	All RR meta-analysed for 0·5–1·5 serving/d of cheese
>1·5 servings of cheese and total CHD (*n* 6 data points)	0·86	0·79, 0·94	0·591; 0·0 %	All RR meta-analysed for >1·5 serving/d of cheese
Total cheese and total stroke (*n* 4)	0·87	0·77, 0·99	0·198; 33·5 %	Studies required to report a composite variable for total stroke
Dose–response analyses				
0–0·5 servings of cheese and total stroke (*n* 6 data points)	1·00	0·92, 1·07	0·875; 0·0 %	All RR meta-analysed for 0–0·5 serving/d of cheese
>0·5–1·5 servings of cheese and total stroke (*n* 7 data points)	0·86	0·75, 0·97	0·059; 50·6 %	All RR meta-analysed for 0·5–1·5 servings/d of cheese
>1·5 servings of cheese and total stroke (*n* 6 data points)	0·92	0·87, 0·97	0·906; 0·0 %	All RR meta-analysed for >1·5 servings/d of cheese
Yoghurt				
Yoghurt and total CVD (*n* 3)	0·93	0·78, 1·12	0·171; 43·4 %	Studies required to report a composite variable for total CVD
Yoghurt and any CHD (*n* 4)	1·08	0·91, 1·28	0·144; 41·7 %	Studies required to report a composite variable for total CHD
Ca from dairy products				
Dairy Ca and total CHD (*n* 4)	0·94	0·82, 1·08	0·574; 0·0 %	Includes studies that reported a Ca from dairy sources variable
Dairy Ca and total stroke (*n* 5)	0·69	0·60, 0·81	0·274; 21·2 %	Includes studies that reported a Ca from dairy sources variable
Dose–response analyses				
0–100 mg/d of Ca from dairy products and total stroke (*n* 8 data points)	0·91	0·84, 1·00	0·941; 0·0 %	All RR meta-analysed for 0–100 mg/d of dairy Ca
100–300 mg/d of Ca from dairy product and total stroke (*n* 8 data points)	0·67	0·58, 0·77	0·256; 21·8 %	All RR meta-analysed for >100 to 300 mg/d of dairy Ca
>300 mg/d of Ca from dairy and total stroke (*n* 6 data points)	0·82	0·69, 0·97	0·185; 33·4 %	All RR meta-analysed for >300 mg/d of dairy Ca

RR, relative risk.

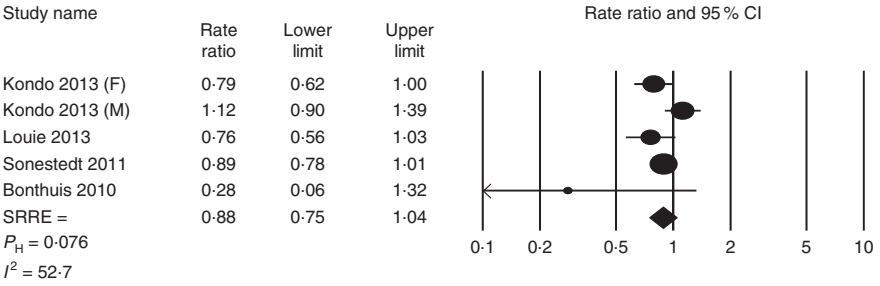

Fig. 2. Meta-analysis of total dairy intake and total CVD (high *v.* low intake analysis). SRRE, summary relative risk estimate. Individual studies required to report a composite total dairy variable and a compositive total CVD variable. F, female; M, male.

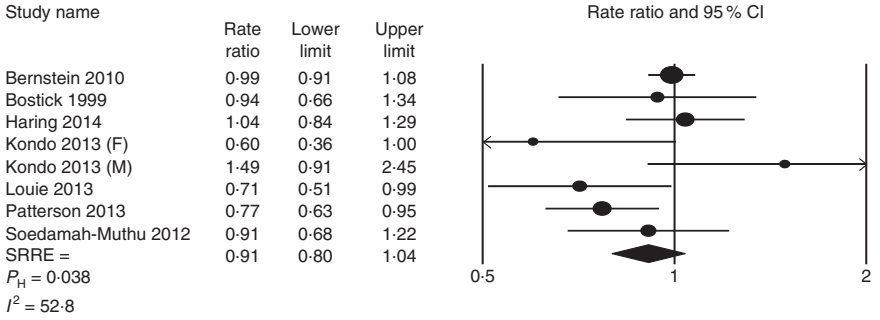

Fig. 3. Meta-analysis of total dairy intake and total CHD (high *v.* low intake analysis). SRRE, summary relative risk estimate. Individual studies required to report a composite total dairy variable and a compositive total CHD variable. F, female; M, male.

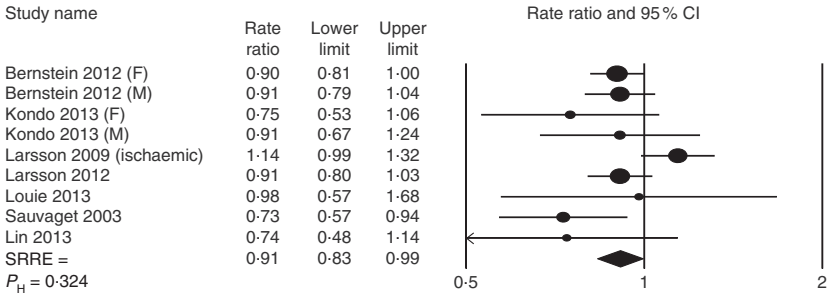

Fig. 4. Meta-analysis of total dairy intake and total stroke. SRRE, summary relative risk estimate. Individual studies required to report a composite total dairy variable and a compositive total stroke variable. F, female; M, male.

generally observed for these dietary variables. Furthermore, most of the observational studies included in this analysis adjusted for dietary and lifestyle factors, such as physical activity, sedentary lifestyle and hypertension.

Conclusions

Future prospective studies of dairy consumption and CVD should focus on isolating the independent effects of specific types of dairy products on specific CVD outcomes while clearly indicating the intake levels per stratum. In addition, reporting RR by varying levels of statistical adjustment may further elucidate the relevant potential confounding factors on dairy intake and CVD, and may help researchers estimate more accurately the independent effects of dairy intake. The current meta-analysis serves as an update and expansion to the existing body of literature on this topic. The results of this meta-analysis have shown that dairy consumption (high *v.* low intake) may be associated with reduced risks of CVD, CHD and stroke, although a dose–response relationship is not clear based on the existing evidence. Additional studies are needed that model dairy intake as a continuous variable to provide a better understanding of any potential dose–response patterns. As future studies are published, new meta-analyses may be warranted to continually refine our understanding of the relationship between dairy intake and CVD.

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The following authors contributed to this paper in the following ways.

D. D. A. conceptualised the analytical protocol, conducted the analyses and was the primary writer. A. J. V. conducted dose–response analyses, created figures and reviewed the content of the manuscript. L. C. B., P. E. M., S. R. I., and M. M. reviewed the content of the manuscript, provided editorial feedback, conducted the literature search, assisted with table and figure creation and extracted data. H. W. and A. D. reviewed the content of the manuscript and provided statistical support. S. S. C. and J. P. F. reviewed the content of the manuscript and provided editorial feedback.

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