



# Systematic Literature Review of Dairy Consumption and Cardiometabolic Outcomes

Naimisha Movva<sup>\*1</sup>, Mina Suh<sup>1</sup>, Susan T. Pastula<sup>1</sup>, Josie Gauthier<sup>1</sup>, Sarah S. Cohen<sup>2</sup>

## Abstract

**Background:** Current evidence is mixed regarding associations between dairy consumption and cardiometabolic outcomes, and limited synthesis has been conducted specifically regarding the type of dairy fat (e.g. full-fat, low-fat, no fat). Given the importance of nutrition for long-term health, we conducted a systematic literature review (SLR) to better understand associations between cardiometabolic outcomes and dairy consumption by type of dairy fat.

**Methods:** Literature searches were conducted in February 2025 to identify published randomized controlled trials, as well as cohort and case-control studies that included individuals older than 2 years of age and without dairy sensitivities. Studies of dairy (including milk, cheese, or yogurt) that specified the type of dairy fat and reported outcomes including cardiovascular disease (CVD), coronary heart disease (CHD), stroke, myocardial infarction (MI), hypertension, cholesterol, metabolic syndrome, and body mass index (BMI) were included.

**Results:** The SLR identified 137 studies specifying the fat type of dairy for inclusion; the majority were prospective cohorts (n=89, 65%) and conducted outside of the United States (US) (n=92, 67%). Adults were examined in 120 (88%) studies. Overall, the studies with significant associations were not consistent in direction of effect by type of dairy fat (no, low, or full-fat), specific dairy product (all dairy, milk, cheese, or yogurt), or specific outcome. For both CVD and CHD, higher quantities of low-fat dairy (but not high-fat or non-fat) trended in the direction of a protective effect, but risk estimates were heterogeneous across studies and often imprecise.

**Conclusions:** The results of this SLR indicate the potential for dairy exposure, and specifically the type of dairy fat, to impact cardiovascular health across global populations. However, interpretation is difficult given the heterogeneity in populations, outcome measures, dairy assessments, and study design and analysis across studies.

**Keywords:** Dairy, fat, cardiometabolic health, cardiovascular diseases, humans, nutrition, systematic literature review

## Introduction

Adequate nutrition plays a key role in the prevention of many illnesses including cardiometabolic conditions. Dairy products are an important source of protein and other nutrients including calcium, vitamin D, and potassium, and they are an integral part of a healthy dietary eating pattern (1). Consumption of dairy is part of the recommended dietary pattern by the United States

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**Citation:** Naimisha Movva, Mina Suh, Susan T. Pastula, Josie Gauthier, Sarah S. Cohen. Systematic Literature Review of Dairy Consumption and Cardiometabolic Outcomes. Fortune Journal of Health Sciences 8 (2025): 503-515.

**Received:** May 12, 2025

**Accepted:** May 22, 2025

**Published:** June 09, 2025

Department of Agriculture (USDA) with the 2020-2025 Dietary Guidelines for Americans recommending three cups of dairy per day (2). Dairy products more specifically deliver bioactive ingredients and nutrients that impact metabolic health (3).

Total dairy intake as well intake of specific dairy foods have not been linked with increased risk of adverse cardiometabolic outcomes overall – and in some cases have been linked to reduced risks - in numerous reviews and meta-analyses of collectively large and diverse study populations (4-8). However, evidence regarding the associations between the specific fat content of dairy products (e.g., no, low-, or full-fat) and cardiometabolic health outcomes has not been synthesized. Given the global burden of cardiometabolic conditions and the potential for nutritional interventions, the purpose of this systematic literature review (SLR) is to summarize the published literature examining associations between dairy exposures specifically by fat type and cardiometabolic outcomes.

## Methods

Prior to the start of this SLR, a study protocol was registered on PROSPERO (#CRD42023427990; [www.crd.york.ac.uk/PROSPERO](http://www.crd.york.ac.uk/PROSPERO)). The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (9) were followed in all aspects of this SLR. To identify relevant studies for this SLR, pre-defined study population, exposure, comparator, outcomes, and study design (PECOS) criteria were used. Studies of persons with a dairy sensitivity, aged <2 years, or stunted/malnourished populations were excluded; there were no other exclusions based on population. Studies examining consumption of dairy products, specifying the fat type of dairy e.g., full-fat, low-fat, etc., and including milk, cheese, and yogurt were considered. Studies examining ice cream, butter, whey protein, milk powders, or dairy as a supplement were not included.

Comparators were low or no exposure to the specified dairy product/s. Studies reporting mortality or incidence outcomes of cardiovascular disease (CVD), coronary heart disease (CHD), stroke, myocardial infarction (MI), hypertension, cholesterol, metabolic syndrome, body mass index (BMI), and related biomarkers (low-density lipoprotein [LDL], high-density lipoprotein [HDL], very low-density lipoprotein [VLDL], triglycerides, apolipoprotein B [ApoB], apolipoprotein A1 [ApoA1], C-reactive protein [CRP], IL-6, IL-B, IL-10, waist circumference, waist-to-hip ratio, and fat mass) were included. Included study designs were randomized controlled trials (RCTs) and observational study designs including cohort, case-control, and nested case-control while cross-sectional and ecologic studies as well as case series, case reports, and narrative reviews were excluded. Studies not published in English were excluded. Literature searches

were conducted in the PubMed and Embase databases to capture literature published through February 28, 2025. [Supplemental File 2, Table 1](#) describes the search strategy. DistillerSR software (10) was used for study de-duplication, article screening, and data abstraction. One reviewer screened the titles and abstracts according to the PECOS criteria. If an abstract was determined to be relevant, two independent reviewers examined the full text to determine if it met the PECOS criteria. For the studies that were included at the full-text stage, select data elements were abstracted, including study time period, location, age, health status, exposure including type of dairy, and reported outcomes.

Where papers reported multiple sets of results, the abstraction included only the results from the most fully adjusted statistical models presented (i.e., model with the most confounding variables). Reference lists of relevant reviews identified during the search were checked to identify any studies meeting the PECOS criteria that were not identified in the literature searches. Study quality of the included studies was assessed using the Newcastle-Ottawa Scale for Cohort and Case-Control studies (11) and the Cochrane risk of bias tool for RCTs (12). One reviewer abstracted the information, and another reviewer independently checked all the data elements; a senior reviewer resolved any conflicts.

## Results

### Article identification

The PRISMA flow diagram, shown in **Figure 1**, describes the study inclusion and exclusion at each stage of the review. See [Supplemental File 1](#) for the PRISMA checklist. The searches yielded 6,285 records after de-duplication across databases. These publications were screened at the title and abstract level. References cited in 71 relevant reviews were also assessed, resulting in 84 additional potentially relevant studies. A total of 603 studies were identified as eligible for full-text review.

Of these, 281 publications were excluded after full-text review (104 did not have any exposures of interest, 71 were relevant reviews, 35 had no outcomes of interest, 32 had no comparison group, 18 had no primary data, 12 were published earlier than 2000, and 9 were not eligible study design). Thus, 322 studies meeting the pre-defined PECOS criteria were considered eligible. Of these, 137 studies reported outcomes specifically by the type of fat in dairy products and these papers are the focus of this report. The remaining 185 studies examined relevant outcomes by general dairy exposure (not specifically by fat content); results from these studies were not evaluated further.

### Study and population characteristics

The characteristics of the 137 studies that described outcomes by type of dairy fat are provided in [Supplemental](#)

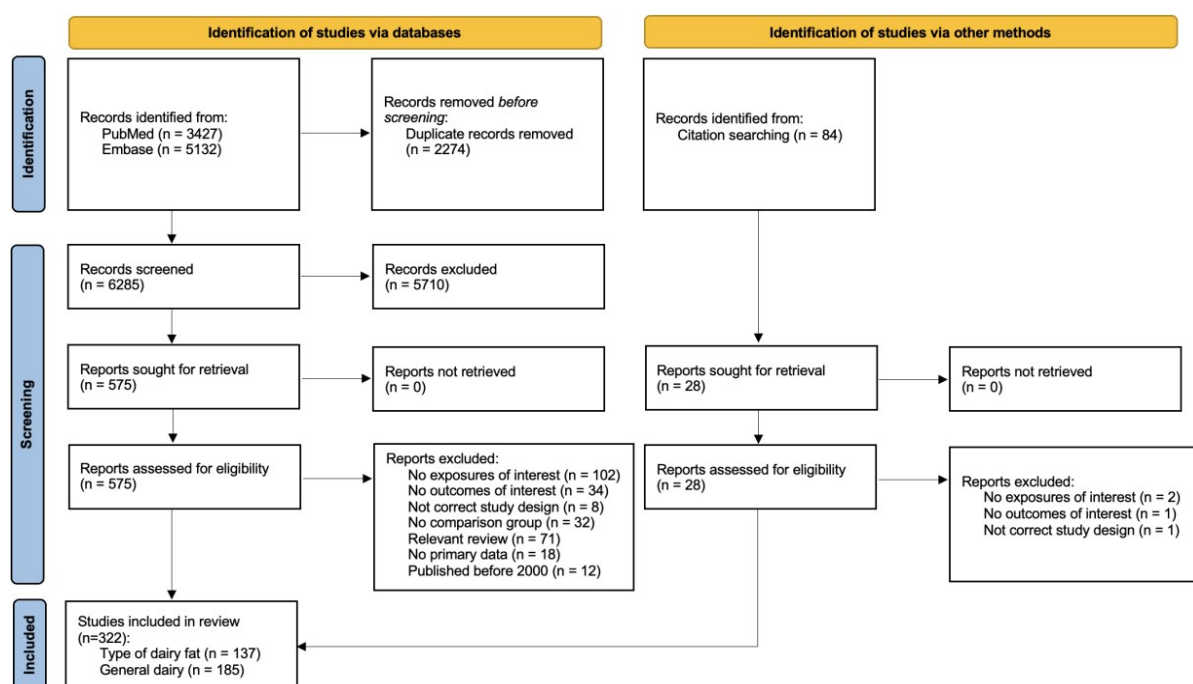


Figure 1: PRISMA study flow diagram

**File 2, Table 2.** Most of the studies were prospective cohorts (N=89, 65%) followed by clinical trials (N=33, 24%), case-control studies (N=11, 8%), and retrospective cohort studies (N=4, 3%). Ninety-two (67%) of the studies were conducted in countries outside of the US while 45 (33%) were conducted within the US. One hundred and twenty (88%) studies included adult populations while 16 (12%) included children, and one (<1%) included both adults and children.

Many of the studies (N=93, 68%) determined dairy product exposure through food frequency questionnaires (FFQ); other exposure assessment methods included documenting intake of specific foods (N=30, 22%), questionnaires besides FFQ (N=16, 12%), food logs (N=12, 9%), and 24-hour recalls (N=3, 2%). Most studies (N=116, 85%) reported incidence

as the outcome, but 15 (11%) of the studies reported on mortality and 6 (4%) reported both. Over three-quarters of the studies (N=103, 75%) used medical records/physician diagnosis to assess outcomes. Other outcome ascertainment methods included laboratory measurements (N=41, 30%), death certificates (N=28, 20%), and self-report (N=19, 14%). The evaluation of study quality found that ninety-six studies (70%) were deemed to be of good quality while 29 (21%) were graded as fair and 12 (9%) were graded as poor.

**Table 1** summarizes the 137 included studies by exposure type and outcome. Summaries of results for each outcome are included in the following sections. Results from only the most adjusted models (i.e., statistical model with the most confounding variables included) in each paper are discussed in this report.

Table 1: Studies with results presented by type of dairy exposure and outcome measured

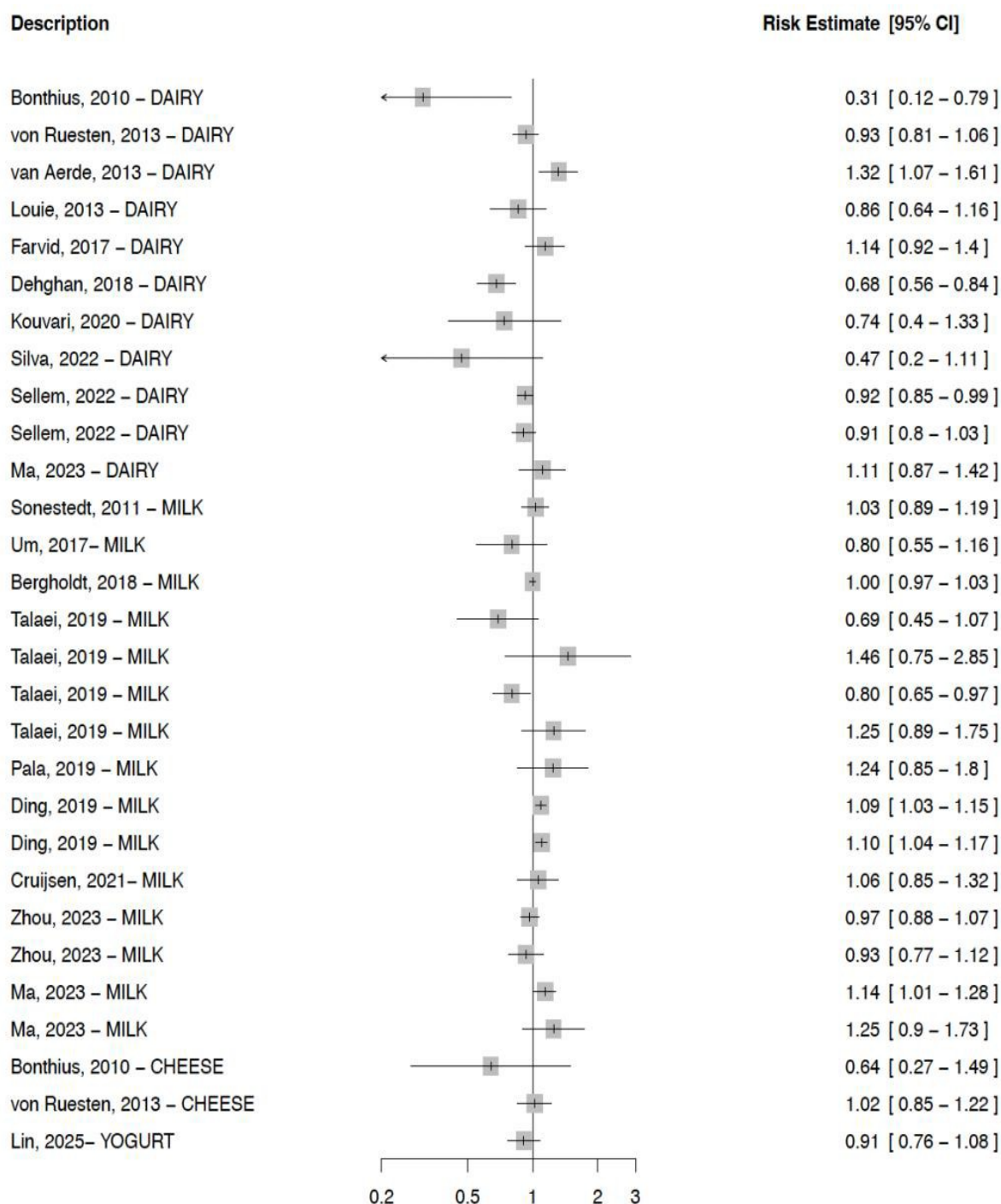
Study exposure / outcome	Dairy, grouped or unspecified	Milk	Yogurt	Cheese	Total number of studies <sup>1</sup>
CVD (composite or unspecified)	14	11	1	2	25
CHD	12	9	1	2	20
Stroke	9	10	0	2	19
Myocardial infarction	1	5	1	2	5
Metabolic syndrome	6	2	2	0	8
Cholesterol	20	16	4	8	39
Hypertension	27	15	5	9	42
Immunity markers	7	1	1	2	10
Body composition	30	25	9	9	58
Total number of studies <sup>1</sup>	78	58	15	17	137

<sup>1</sup>Column and row totals do not add up to 137 because many studies included multiple exposures and outcomes.

## CVD

Twenty-five observational studies (21 good and 4 fair quality), all conducted in adults, examined CVD including 9 studies examining incidence, 12 studies examining mortality, and 4 studies examining both incidence and mortality ([Supplemental File 2, Table 3](#)). Two dairy fat comparisons

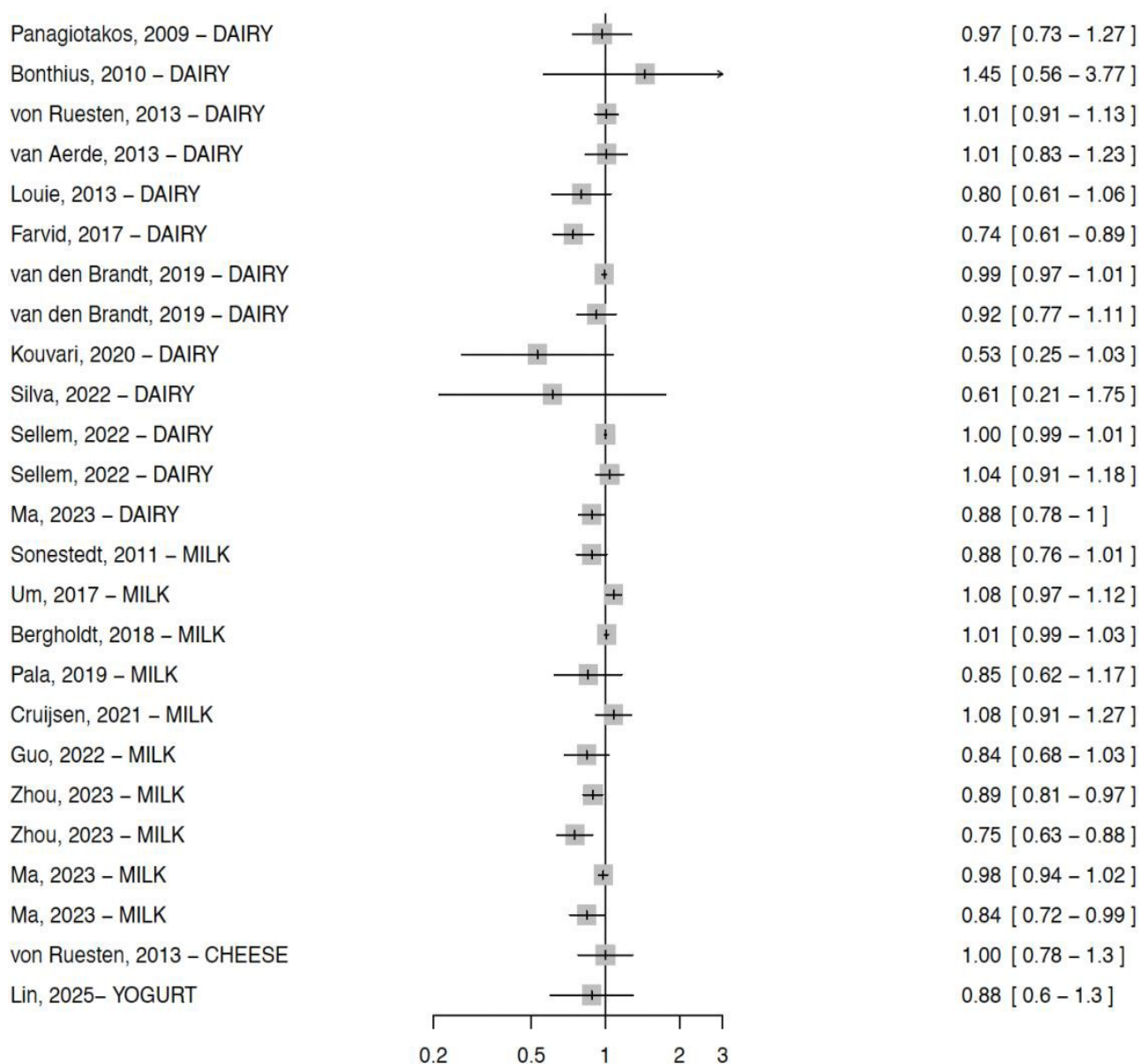
were common in the identified literature: those comparing higher versus lower intakes of full-fat dairy (**Figure 2a**) and those comparing higher versus lower intakes of low-fat dairy (**Figure 2b**). As seen in Figure 2a, for full-fat dairy, the results were quite heterogenous with effects in both the direction of CVD protection and elevated risk. Of note, many estimates were imprecise with wide confidence intervals.



**Figure 2A:** Risk estimates of CVD by higher versus lower/no consumption of full-fat dairy

Description

Risk Estimate [95% CI]



**Figure 2B:** Risk estimates of CVD by higher versus lower/no consumption of low-fat dairy

\*Kontogianni et al. 2008 estimate of 0.41 was not included this figure as it did not report 95% confidence intervals.

Patterns were not notably different between consumption of full-fat dairy (combined or unspecified) versus full-fat milk specifically versus cheese, although fewer studies of cheese consumption were found. As seen in Figure 2b, for low-fat dairy, the direction of effect was more towards a protective effect (i.e. relative risk estimates below 1). Few studies reported relative risks above the null. Similar to the full-fat dairy studies, precision was often low with wide confidence intervals observed in many studies. Patterns by type of dairy (all dairy versus milk versus cheese) were generally similar.

Other comparisons by dairy fat type were less common in the literature. Effect estimates for higher versus lower intakes of nonfat dairy were generally at or just below the null (13-15). One prospective cohort study of adults from 21 countries combined full and low-fat dairy and found a reduced risk of CVD with  $\geq 2$  servings per day versus no intake (RR=0.81, 95% CI: 0.62, 1.06) (16). In a study examining the highest versus the lowest consumption of daily intake of dietary fat among the Nurses' Health Study, Nurses' Health Study II, and the Health Professionals Follow-up cohorts, the

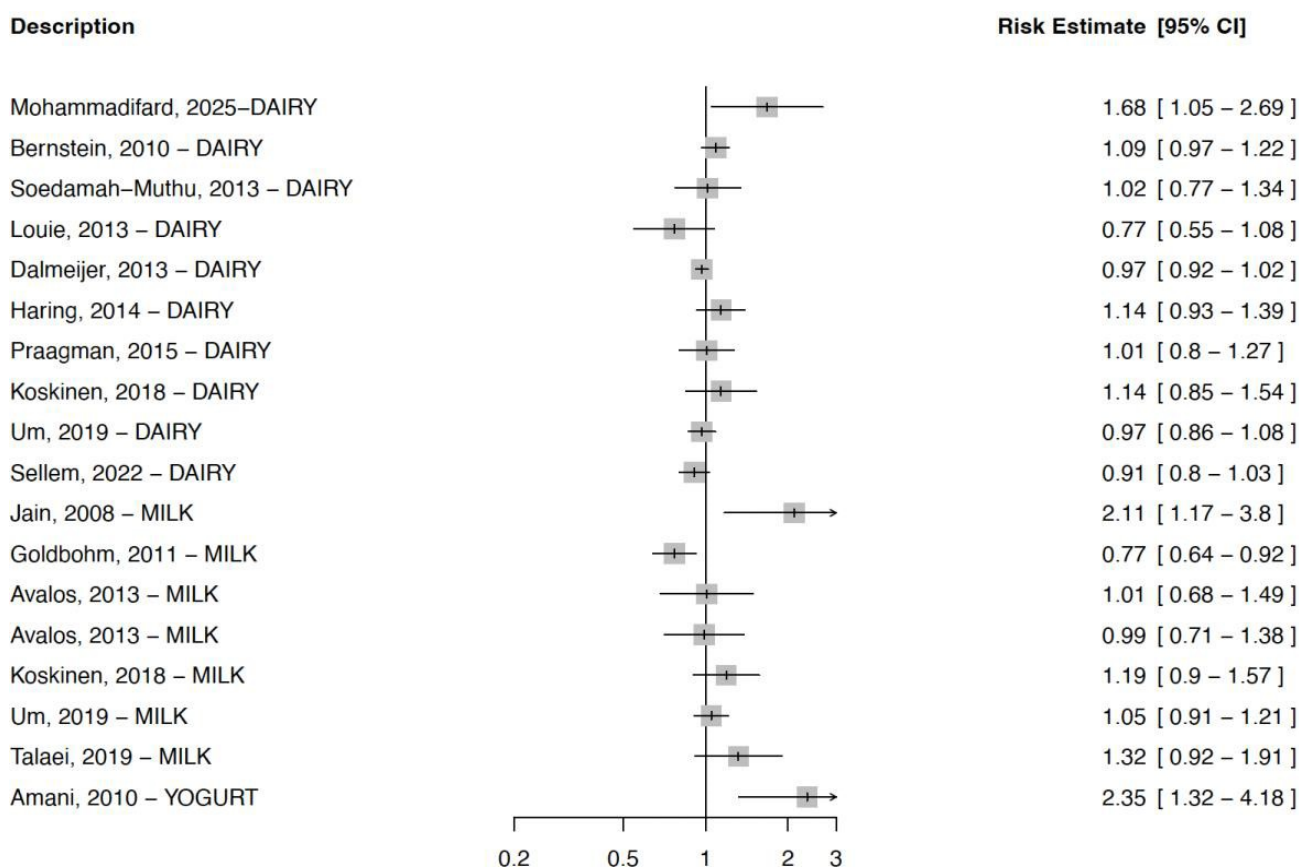
results for CVD were entirely null ( $RR=1.00$ , 95% CI: 0.95, 1.05) (17). Similarly, in another study consisting of these three cohorts, low-fat and no-fat dairy were combined, and the authors reported results very close to the null for CVD risk in relation to increasing amounts of this combination (18). Finally, one retrospective Australian study with a mean follow-up of 8.4 years compared full-fat milk consumption to both low-fat and no-fat milk consumption separately among males and females and found significant reductions in CVD risk for low-fat versus full-fat milk in both genders. No-fat milk versus full-fat milk was protective among males but not females but the precision of the estimates was low (19).

### Coronary Heart Disease

Twenty observational studies (17 good and 3 fair quality), all conducted in adults, examined CHD including 12 incidence, 5 mortality, and 3 incidence and mortality studies ([Supplemental File 2, Table 4](#)). Over half ( $N=11$ , 55%) of the studies reported no significant association between CHD and a specific type of dairy fat (17, 20-29). Comparisons of higher versus lower intakes of full-fat dairy are shown in **Figure 3a** and those comparing higher versus lower intakes of low-fat dairy are shown in **Figure 3b**. Like the results

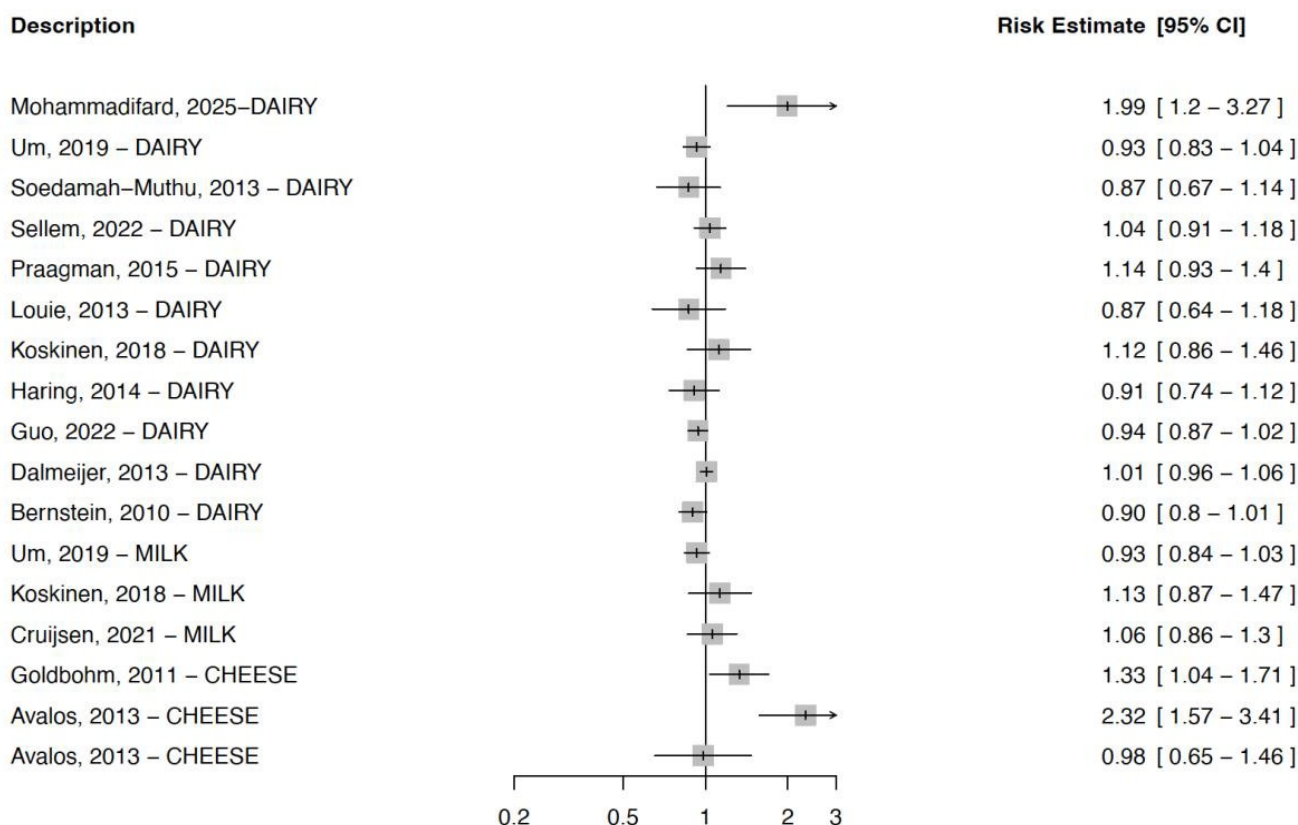
for full-fat dairy and CVD, measures of risk were quite heterogenous with effects in both the direction of protection and elevated risk with many estimates being imprecise with wide confidence intervals. As seen in Figure 3b, for low-fat dairy, more studies indicated a protective effect for CHD (i.e. relative risk estimates below 1) although heterogeneity across study results was still high.

Similar again to CVD, other comparisons of dairy fat were less common in the literature. One study of adults from a Southern California community examined intake levels of no-fat milk and found no association with CHD among men who consumed no-fat milk 'sometimes/often' compared with 'rarely/never' ( $RR=1.08$ , 95% CI: 0.78, 1.49) but an elevated CHD risk among women ( $RR=1.48$ , 95% CI: 1.02, 2.16) (30). A combined analysis of the Nurses' Health Study and Health Professionals Follow-up Study examined consumption levels of total dairy fat and found no association with CHD between the highest and lowest consumption groups ( $RR=1.03$ , 95% CI: 0.97, 1.10) (17). Comparing between different fat types, one case-control study of urban Indian middle-aged males reported an elevated, but imprecise, CHD risk with full-fat cream milk versus other milk ( $RR=1.66$ , 95% CI: 1.09, 2.54) (31). A large cohort study of adults from the National Health



**Figure 3A:** Risk estimates of CVD by higher versus lower/no consumption of full-fat dairy

\*Hamideh et. al 2007 estimate of 9.8 (95% CI: 7.9, 49.2) was not included this figure as it was an outlier.



**Figure 3B:** Risk estimates of CHD by higher versus lower/no consumption of low-fat dairy

and Nutrition Examination Survey similarly found the highest risk of CHD among consumers of full-fat milk compared to consumers of low-fat milk (32). In contrast, another large study conducted in the Netherlands reported no association when comparing across ratios of full- fat to low-fat dairy (RR=1.02, 95% CI: 0.98, 1.06) (22).

## Stroke

Nineteen observational studies (15 good, 2 fair, and 2 poor quality) evaluated stroke with 12 examining incidence, 5 mortality, and 2 both incidence and mortality, all of which were conducted in adults ([Supplemental File 2, Table 5](#)). Of note, the outcome measure is especially heterogeneous in this group as outcomes included all types of stroke grouped together as well as several stroke subtypes examined individually. As shown in **Figure 4a** (studies comparing higher versus lower intake of full-fat dairy) and **Figure 4b** (studies comparing higher versus lower intake of low-fat dairy), the majority of the results for stroke were non-significant, and the significant results that were observed were heterogeneous in terms of direction of association and often imprecise.

Other comparisons of dairy fat were less commonly found. A large cohort study from the UK Biobank observed a reduced risk of stroke among individuals who consumed semi-skimmed or skimmed milk compared to no milk intake but results for stroke mortality were not significant (13). A

combined analysis of the Nurses' Health Study and Health Professionals Follow-up Study examined consumption levels of total dairy fat and found no association with stroke between the highest and lowest consumption groups (RR=0.95, 95% CI: 0.88, 1.04) (17). Three cohort studies, which were conducted across the Netherlands, USA, and Denmark, compared different types of fat (combinations of full-fat versus low-fat versus no-fat) and all results were null (22, 32, 33).

## Myocardial Infarction (MI)

Five observational studies (4 good and one poor quality) examined MI as an outcome with 4 examining incidence and 1 examining mortality, all in adults ([Supplemental File 2, Table 6](#)). Four of the 5 studies reported associations close to the null that did not achieve statistical significance for a variety of dairy fat type comparisons (13, 34-36). In a fifth study conducted among women in Sweden, the risk of MI was significantly reduced in association with increased amounts of full-fat cheese (RR=0.83, 95% CI: 0.68, 1.01, p for trend=0.035). Similar results were seen for low-fat cheese (RR=0.84, 95% CI: 0.66, 1.06) while comparisons of the highest and lowest categories of consumption of full-fat and low-fat milk did not indicate any reduction in risk of MI (RR=1.10, 95% CI: 0.92, 1.31; RR=1.03, 95% CI: 0.89, 1.18, respectively) (37).

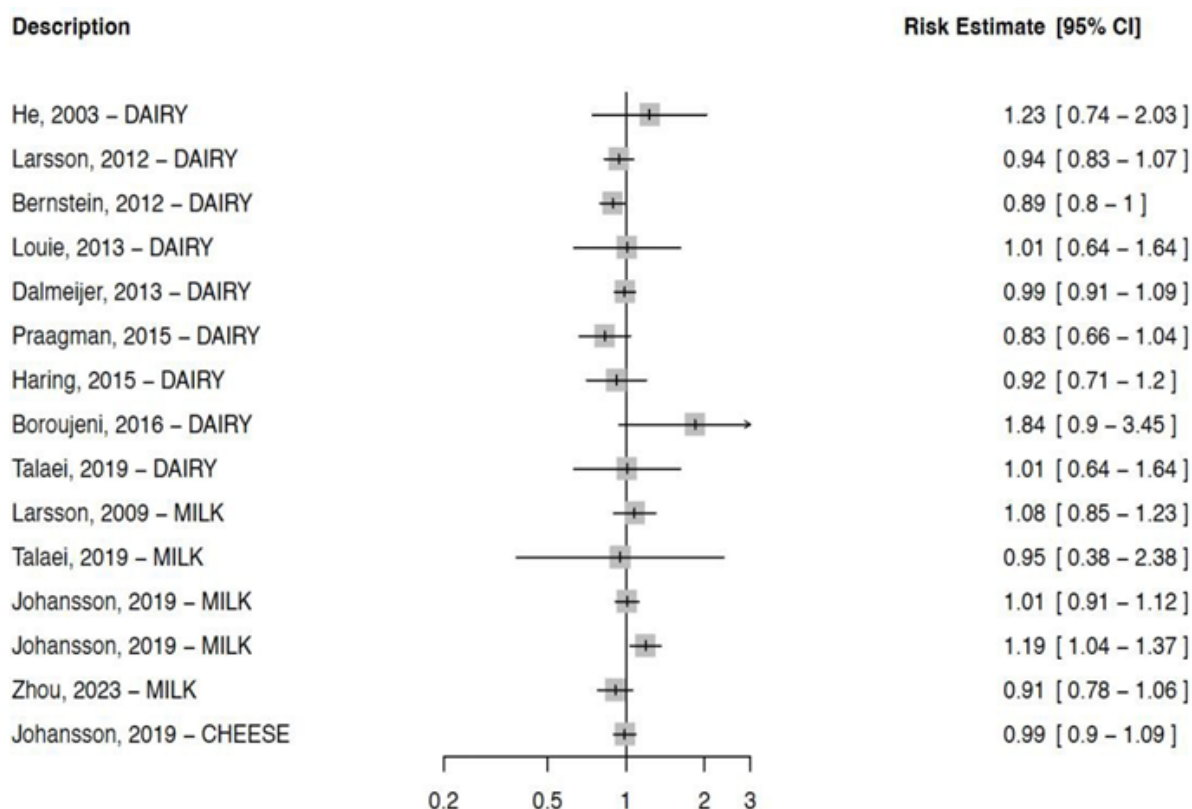


Figure 4A: Risk estimates of stroke by higher versus lower/no consumption of full-fat dairy

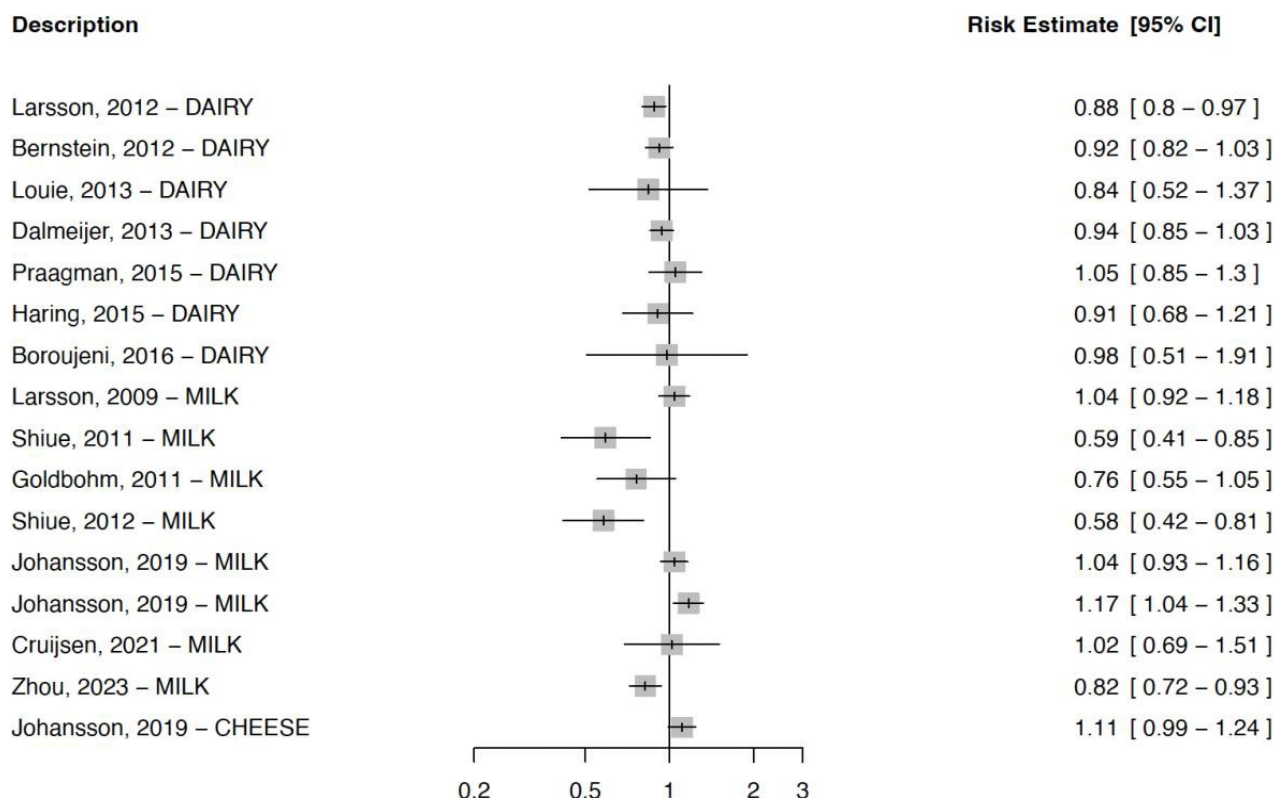


Figure 4B: Risk estimates of stroke by higher versus lower/no consumption of low-fat dairy

**Table 2:** Studies of cholesterol and body composition, by specific outcomes and population

Outcome	Total studies	Population: Adults (N)	Population: Children (N)	Population: Adults and Children (N)
Cholesterol outcomes				
LDL-C	30	26	3	1
HDL-C	35	30	4	1
Triglycerides	34	30	3	1
Total cholesterol	28	25	2	1
ApoA1	5	4	1	0
ApoB	7	6	1	0
Body Composition outcomes				
BMI	34	22	12	0
Waist circumference	26	23	3	0
Weight	25	23	2	0
Fat mass	12	8	4	0
Abdominal obesity	8	7	1	0
Lean mass	7	6	1	0
Percentage of fat	6	4	2	0
Hip circumference	5	4	1	0
Trunk mass	4	3	1	0
Waist: hip ratio	4	4	0	0
Waist: height ratio	1	0	1	0
Height	1	0	1	0
Neck circumference	1	0	1	0
Skinfold thickness	1	0	0	0

## Metabolic Syndrome

Eight observational studies (all good quality), all prospective cohorts, examined incidence of metabolic syndrome as an outcome, with 7 conducted in adults and one in children ([Supplemental File 2, Table 7](#)). Half of the studies did not observe a significant association between a specific type of dairy fat and metabolic syndrome although all measures of risk were in the protective direction (38-41). Both the Atherosclerosis Risk in Communities Study and the Brazilian Longitudinal Study of Adult Health reported a significantly reduced risk of metabolic syndrome in association with full-fat dairy but no significant associations with low-fat dairy (42, 43). Full-fat dairy was again associated with a reduced risk of metabolic syndrome in a third study conducted among Australian adults; this study, however, also observed that low-fat dairy was associated with an increased risk of metabolic syndrome (44). A Spanish study found that risk of metabolic syndrome was reduced in association with increased amounts of low-fat dairy products, low-fat yogurt, full-fat yogurt, and low-fat milk while there was no association with full-fat dairy products or full-fat milk (45).

## Immunity Markers

Ten studies (5 good, 4 fair, and one poor quality), including 6 randomized clinical trials and 4 prospective cohort studies, examined changes in concentrations of immune markers as an outcome, with 8 conducted in adults and one in children ([Supplemental File 2, Table 8](#)). Seven of the 9 studies examined CRP while one evaluated both CRP and IL-6 and the ninth examined low grade inflammation; no studies of IL-B and IL-10 were identified. The studies of CRP (including all 6 trials) reported estimates near the null with no significant associations observed between CRP and any specific type of dairy fat (39, 46-52). Increasing amounts of low-fat dairy foods were associated with reduced CRP in the Multiethnic Cohort study (partial Pearson correlation= -0.02,  $p<0.05$ ) (53). In the cross-over trial of IL-6, 4 weeks of receiving full-fat yogurt did not significantly increase IL-6 levels among the study population (change in mean=0.31, 95% CI: -1.44, 2.07) (52). In the Cohort on Diabetes and Atherosclerosis Maastricht study of low grade inflammation, non-significant increases in risk of inflammation were associated with both increased full-fat ( $\beta=0.040$ , 95% CI: -0.015, 0.095) and low-fat ( $\beta=0.003$ , 95% CI: -0.021, 0.027) dairy (54).

## Hypertension, Cholesterol, and Body Composition

A total of 42 studies (38 conducted in adults, 3 in children and 1 in both adults and children), including 22 randomized clinical trials and 20 observational studies, examined blood pressure outcomes ([Supplemental File 2, Table 9](#)). A total of 39 studies (33 conducted in adults, 5 in children, and 1 in both adults and children) examined changes in a range of measures of cholesterol ([Table 2](#)). Twenty-five studies were randomized clinical trials and the remaining 14 were cohort studies. [Supplemental File 2, Table 10](#) provides the reported outcome by each study. A total of 58 studies (44 conducted in adults and 14 in children) examined a range of body composition outcomes ([Table 2; Supplemental File 2, Table 11](#)). For all three of these outcomes, many different comparisons of dairy fat types were presented, and further complicating comparisons across studies, numerous measures were examined as outcomes. Collectively, the majority of the results for these 3 outcomes were non-significant, and the significant results observed were heterogeneous across specific measures of the outcome and direction of association.

## Discussion

The global burden of cardiometabolic diseases and disorders is significant, and thus potential protective effects of diet – a universal exposure with high potential to be modified – is of high interest. Reflecting this relevance, many studies have examined dietary factors in relation to such cardiometabolic outcomes, including a large body of evidence focused on dairy products. This SLR specifically identified 137 articles focused specifically on dairy fat type in relation to cardiometabolic outcomes including CVD, CHD, stroke, MI, metabolic syndrome, immune markers, cholesterol, hypertension, and body composition. Overall, there were many non-significant findings close to the null, and the significant results that were reported were heterogeneous in terms of direction of association, study quality, and by specific type of dairy food and type of fat. This observed heterogeneity could be due to study differences in person, place, time, dairy exposure assessment, and confounder adjustment and warrant further investigation. For both CVD and CHD, studies comparing higher and lower amounts of low-fat dairy tended in the direction of protective effects, but no quantitative analysis was conducted due to overall heterogeneity. Dairy foods are heterogeneous not only in terms of fat content (full, low, or no-fat) but also in the amount of saturated fat, presence or absence of specific fatty acids, and vitamin and mineral content, all of which may exert different effects on numerous pathways – including lipids, blood pressure, and inflammation – that ultimately influence cardiometabolic outcomes. Some studies have attempted to isolate specific aspects of dairy products such as the Chen et al. analysis in the Health Professionals Follow-up

Study and the Nurses Health Studies I and II which examined replacement of animal fats, including dairy fat, with vegetable sources of fats and polyunsaturated fatty acids (17). Further focused research on specific dairy foods with specific types of fat content on individual cardiometabolic outcomes is likely needed to untangle the complexities that are likely driving the heterogeneous results found in this body of literature.

Gaps in this research area include the lack of comparative trials for clinical outcomes such as CVD, CHD, MI, and stroke. Certainly, the feasibility of such studies is limited given the large sample size and long follow-up that would be required to have an adequately powered study, but the literature should be examined in this context, namely that residual confounding is a possible limitation of the observational studies. The study populations are largely made up of individuals from the US and Europe, and thus another gap in this body of literature is data collected among individuals from Asia, South America, and Africa. Additional gaps include the relatively limited number of studies of biomarkers other than cholesterol (such as ApoA1 or ApoB). Similarly, studies of immunity markers are largely limited to examinations of CRP with a lack of studies examining other markers including IL-6, IL-8, and IL-10. For body composition as well, measurements that are easily taken are well-represented but those that require specific equipment such as calipers or DEXA scans to provide more granular information are much less common and represent another gap. A future research direction might include meta-analysis or pooled analysis of specific CVD outcomes and dairy fat comparisons; such analyses could shed light on the direction of associations, but methodologic difficulties are an obstacle given differences in covariate assessment, measurement of specific dairy foods and fat types, and definitions in outcomes. Strengths of this SLR include the transparent and reproducible methodology including following PRISMA guidelines, 100% quality control of the data abstraction, inclusion of strong study designs including RCTs, cohorts, and case-control studies, examination of multiple outcomes with no geographical restrictions, and use of study quality rating tools which indicated largely good quality in this evidence pool. Limitations of this SLR start with the inherent difficulties in measuring dietary intakes in observational research. Numerous tools are used to collect self-reported dietary intake including food diaries, dietary histories, food frequency questionnaires, and 24-hour dietary recalls but all are prone to error due to their reliance on self-reported and often recalled information (55). The resultant data may not accurately reflect intake which may in turn result in misclassification of dairy consumption. Additionally, non-English language studies were excluded from the SLR. Further limitations related to the available literature more broadly are described above regarding research gaps which limit generalizability. The publications identified in this SLR collectively indicate potential for dairy exposure, and

specifically the fat content of dairy, to impact the risk of cardiovascular health across global populations, and highlight important areas for future research. This importance is underscored by the ubiquity of diet as a potential intervention target for a multitude of health outcomes. The evidence identified in this SLR may be relevant when evaluating current and proposed dietary recommendations to meet evolving health needs, but interpretation is difficult given the heterogeneity in populations, outcome measures, dairy assessments, and study design and analysis across this body of literature.

## Acknowledgements

This work was supported by a research grant from the National Dairy Council. The literature selection, methodological protocol development, interpretation of research findings, and manuscript writing, formatting, and submission were conducted solely by the authors.

**Competing interests:** The authors declare that they have no competing interests.

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