



# Funding sources and outcomes of dairy consumption research – A meta-analysis of cohort studies: The case of type-2 diabetes and cardiovascular diseases

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## ABSTRACT

Despite requirements to disclose funding sources and contributors involved with published research, industry-funded research is frequently viewed as inherently biased. A meta-analysis (29 cohort studies) was conducted to investigate the association between dairy consumption and the risk of type-2 diabetes (T2D) and cardiovascular diseases (CVD), comparing findings from industry-funded versus non-industry-funded research. Pooled results indicated an inverse association between dairy intake and the risk of T2D and CVD (RR = 0.923; 95% CI: 0.884–0.964;  $p < 0.001$ ). Studies funded by neutral organisations (21) indicated that dairy consumption is significantly associated with decreased risk of developing T2D and CVD (RR = 0.920; 95% CI: 0.875–0.967;  $p < 0.01$ ), whereas for studies funded by the food industry (8), the results were not significant (RR = 0.932; 95% CI: 0.854–1.017;  $p = 0.115$ ). Subgroup analysis showed that there were no significant differences between industry-funded and neutral, non-industry-funded research studies.

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## 1. Introduction

### 1.1. Sponsorship influences on research results

The radicalised discourse that emerged in recent years sees industry-funded research as inherently biased due to the obvious vested interests of any industry that initiates and funds certain studies. While such suspicion is of concern in the case of the Pharmaceutical Industry, for which several cases showed an inclination to shelve or bury studies whose results cast doubt on the efficacy of the drugs they manufactured (Lexchin, 2012; Lexchin, Bero, Djulbegovic, & Clark, 2003), we sought to check if the suspicion is warranted when it comes to the dairy industry. We examined the hypothesis that industry sponsorship affected the results of studies in a way that made them more favourable to the sponsor (Bekelman, Li, & Gross, 2003; Bes-Rastrollo, Schulze, Ruiz-Canela, & Martinez-Gonzalez, 2013; Chartres, Fabbri, & Bero, 2016; Lundh, Lexchin, Mintzes, Schroll, & Bero, 2017; Nkansah, Nguyen,

Iraninezhad, & Bero, 2009). To answer that question, we compared the results of industry-funded (medical and nutritional) research with those of studies funded by non-industry, ostensibly “neutral” organisations such as health organisations, in terms of the associations they found (or lack thereof) between dairy intake and the risk of developing type-2 diabetes (T2D) and cardiovascular diseases (CVD) broadly conceived (including stroke and coronary heart disease). We chose to focus our meta-analysis in the foregoing associations because these are the most prevalent chronic diseases that have become an epidemic in this day and age, weighing heavily on governments, health organisations, and individuals.

### 1.2. The controversy surrounding dairy consumption

Over the last few years, consumption of milk and dairy products has become a controversial health issue among professionals and lay persons alike. While some claim that dairy consumption is a source of negative health influences (including increased risk of chronic diseases; Melnik, 2009), others emphasise the protective effects of dairy consumption on sundry diseases and conditions (De Oliveira Otto, 2012; Liu et al., 2006; Malik et al., 2011). Since many

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studies have presented contradicting results, the public is left baffled and overwhelmed, even more so when it comes to industry-funded research that is taken with a grain of salt, not to say outright suspicion. As the dairy industry is a rich funding source that spawns research and data quite often, it might be a waste of scarce resources if pertinent stakeholders dismiss its results and recommendations, thinking they are bound to be prejudiced.

In the sub-section that follows we broach succinctly the association between dairy intake and T2D, as well as the link between dairy consumption and the risk of developing CVD.

### 1.3. The association between dairy consumption and the risk of T2D and CVD

The association between dairy intake and T2D and CVD per se is not the focus of this paper. This association was thoroughly investigated by several groups (Sonestedt et al., 2011; Zong et al., 2014), including, inter alios, Mishali, Prizant-Passal, Avrech, and Shoenfeld (2019). There are some possible explanations for the mechanisms through which these associations play out. Of note is that research varies tremendously in terms of the measures used, the variables adjusted for and the way the consumption of “dairy” and “milk” is taken into account. Some studies use food diaries, whereas others use approximations for dairy intake such as the family income and its socioeconomic status (e.g., Van Der Pols et al., 2007). Numerous studies make a distinction between different dairy products (e.g., Drouin-Chartier et al., 2016) and their fat content (whole versus low-fat milk, fermented versus non-fermented products, cheese, butter, etc.), while others draw no such distinction (Qin et al., 2015). It is thus a rather tall order to draw a conclusion across all those disparate studies. Some explanations have nevertheless been propounded.

A growing body of evidence associates dairy intake with a reduced risk of T2D, probably owing to the protective, beneficial effects of dairy products on obesity and the metabolic syndrome (MetS), which are important, not to say predictive factors for T2D (Lovegrove & Givens, 2016). Moreover, a few dairy components such as protein, Ca, vitamin D, dairy fat and specifically trans-palmitoleic acid have been found to have a separate favourable effect on reducing the risk for T2D (Mozaffarian et al., 2010, 2013).

The connection between dairy consumption and CVD is more convoluted, but scientists tend to divide the factors that bear on that association into lipid and non-lipid risk factors. In terms of the elements that have to do with lipids, one of the established properties of milk fat relative to polyunsaturated oils is the increase in concentration of high density lipids (HDL) in plasma. High HDL-C (colloquially known as “good cholesterol”) is associated with protection from heart disease, even in the face of elevated low density lipid-C (“bad cholesterol”), and low HDL-C is associated with increased risk, with or without elevated triglycerides. HDL are thought to exert beneficial effects on overall health by reversing cholesterol transport, binding and eliminating toxins, delivering bioactive compounds, protecting various cells and lipoproteins from damage and participating in their repair (Drouin-Chartier et al., 2016; German et al., 2009; Qin et al., 2015).

Dairy foods are thought to wield influence on non-lipid risk factors for CVD as well. High dairy consumption has been associated with reducing blood pressure: since hypertension was linked to increased risk of developing CVD, preventing it was linked to reduced risk of CVD. Calcium is thought to be one of the main nutrients responsible for the impact of dairy products on blood pressure (Alonso et al., 2010), and so are potassium and magnesium present in dairy products (Alonso et al., 2010; Alonso, Beunza, Delgado-Rodríguez, Martínez & Martínez González, 2005; Umesawa et al., 2006). Both casein and whey proteins are a rich

source of specific bioactive peptides that have been shown to have an angiotensin-I-converting enzyme inhibitory effect, a key process in blood pressure control. Dietary components including calcium and or its unique proteins, the peptides they release, the phospholipids associated with milk fat or the stimulation of HDL by lipids themselves, may suppress adipose tissue oxidative and inflammatory stress (Lovegrove & Givens, 2016). Dairy foods may beneficially alter circulating C reactive protein and adiponectin levels independently of changes in body weight.

Differently stated, some studies suggest that dairy may reduce inflammation – the high levels of which have been linked to (increased risk of) cardiovascular diseases (Lovegrove & Givens, 2016). Of note, burgeoning research has been calling into question the association between saturated fat (SF) and CVD in general, and especially so when it comes to SF in dairy products. Siri-Tarino, Sun, Hu, and Krauss (2010), for instance, concluded based on their meta-analysis that there was no significant evidence for concluding that dietary saturated fat was associated with an increased risk of CHD or CVD. De Oliveira Otto et al. (2012) went even further, maintaining that there was an inverse correlation between the risk of CVD and high consumption of SF coming from dairy products: a higher intake of dairy SF was associated with lower CVD risk.

## 2. Materials and methods

### 2.1. Literature search and selection of articles: dairy intake and the risk of T2D/CVD

Type-2 diabetes (T2D) and cardiovascular diseases (CVD), two of the most common non-communicable diseases, are increasing rapidly around the world, affecting millions of lives, and are among the leading causes of death (Grantham et al., 2013; Mathers & Loncar, 2006; WHO, 2017). Recent reviews and meta-analyses that examined the association between dairy consumption and the risk of developing T2D or CVD indicated that the consumption of various types of dairy products showed either favourable or neutral associations with respect to these diseases (Alexander et al., 2016; Drouin-Chartier et al., 2016; Ericson et al., 2013; Gao et al., 2013; Lordan, Tsoupras, Mitra, & Zabetakis, 2018; Lovegrove & Givens, 2016).

To determine whether these findings were biased by sponsors, the current meta-analysis examined the assumption that the funding source (i.e., the dairy industry versus non-industry institutions) affected the results regarding the association between dairy consumption and the risk of developing T2D/CVD. A literature review was conducted using the PubMed database for cohort studies published between 2006 and November 2016. The following terms were entered in the keywords and title sections: “dairy”/“milk” and “diabetes”/“CVD”/“stroke” and “cohort”. References from review articles and meta-analyses focussing on dairy and T2D or CVD were also examined to identify additional studies. In keeping with the PICOS search strategy (Table 1), studies were included if they met all the following criteria: (i) the participants in the study were over 18 years old; (ii) the intake of total dairy products/total milk was reported (studies reporting only specific dairy products or only low/high-fat milk data were excluded); (iii) RRs with corresponding 95% CIs adjusted for multivariable factors were reported or could be estimated; (iv) only cohort studies were included.

This study was done in line with PRISMA recommendations.

### 2.2. Data extraction

For each eligible study, information was extracted for the following items: author's name, publication year, country in which the study was conducted, follow-up period, sample size, number of cases, sex, age, dairy product type (total dairy products/total milk),

quantity of intake, and risk estimates with 95% CI for the highest compared with the lowest intake and variables adjusted for in the analysis. Funding source information was extracted by reviewing footnotes “potential conflict of interests” and “acknowledgments” sections reporting the grants or other sponsorships of the article. “Food industry funding source” was defined as including food or nutritional supplement industries; “Neutral funding source” was defined as including health and non-profit research organisations.

### 2.3. Inclusion criteria

A total of 105 articles from PubMed (see Fig. 1) were identified. After screening titles and excluding all articles with the terms “children” (16 articles) and “breastfeeding”/“formula” (16 articles) or reviews (22 reviews), 51 articles remained. Next, only full-text articles reporting data on dairy products (or milk) and their association with T2D in prospective cohort studies were included, which left us with 18 articles. Additional 12 articles (Bonthuis, Hughes, Ibiebele, Green, & Van Der Pols, 2010; Elwood, Pickering, & Fehily, 2007; Goldbohm, Chorus, Galindo Garre, Schouten, & van den Brandt, 2011; Kirii et al., 2009; Kondo et al., 2013; Liu et al., 2006; Lin et al., 2013; Pittas et al., 2006; Praagman et al., 2015b; Struijk et al., 2013; Vang, Singh, Lee, Haddad, & Brinegar, 2008) from bibliographies of meta-analyses and reviews focusing on dairy consumption and T2D were also included. In the full text stage, one article (German et al., 2009) was excluded because RRs could not be extracted. A total of 29 studies were therefore included in the meta-analysis.

The study characteristics are presented in Supplementary material Table S1 (Bonthuis et al., 2010; Dalmeijer et al., 2013; Egger, Davey Smith, Schneider, & Minder, 1997; Liu et al., 2006; Elwood et al., 2007; Kaiser et al., 2012; Kirii et al., 2009; Kondo

et al., 2013; Larsson et al., 2009; Lin et al., 2013; Malik et al., 2011; Margolis et al., 2011; Misirli et al., 2012; Pittas et al., 2006; Sluijs et al., 2012; Sonestedt et al., 2011; Van Dam, Hu, Rosenberg, Krishnan, & Palmer, 2006; Vang et al., 2008; Villegas et al., 2009; Wang, Yatsuya, Tamakoshi, Iso, & Tamakoshi, 2015; Zong et al., 2014) and Supplementary material Table S2 (Gijbers et al., 2016; Goldbohm et al., 2011; Louie et al., 2013a,b; Praagman et al., 2015a,b; Soedamah-Muthu, Masset, Verberne, Geleijnse, & Brunner, 2013; Struijk et al., 2013).

A total of 21 studies with 799,445 total participants and an average of 12.5 years of follow-up were categorised as “neutral organisation-funded” (Supplementary material Table S1). A total of 8 studies with 180,043 total participants and an average of 10 years of follow-up were categorised as “industry-funded” (Supplementary material Table S2). Table 1 lists the criteria for the inclusion and exclusion of studies; Fig. 1 depicts the whole process whereby articles were selected for the meta-analysis.

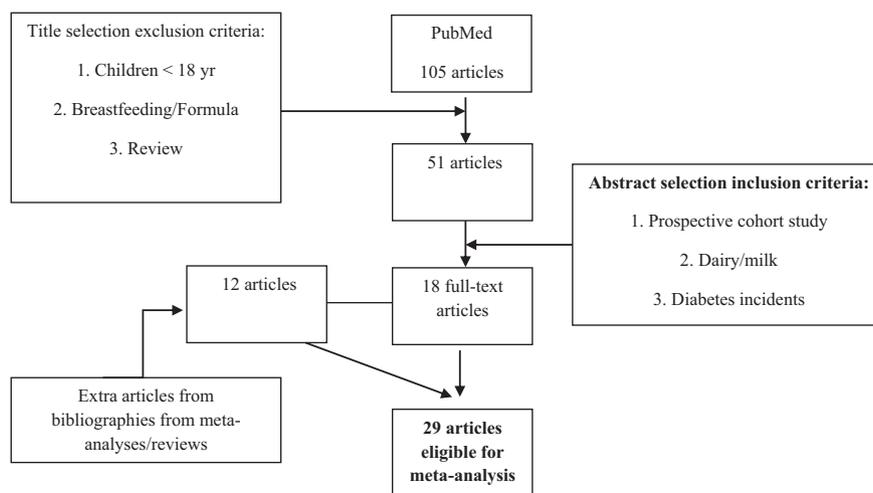
### 2.4. Statistical methods

A random-effects model was used to calculate summary RRs and 95% CIs for the highest amount of dairy product intake compared with the lowest. From each study, the results from the main multivariable model that included most confounders have been used. A 2-tailed  $p$ -value < 0.05 was considered significant. When data from different subgroups were presented separately (e.g., data for men and women were presented independently), the combined result was used. Preliminary tests showed no differences between the pooled RRs of exposure to total dairy products and exposure to milk. Thus, for studies that reported the outcomes of dairy product intake and milk intake separately, we used the combined result.

**Table 1**  
PICOS criteria for the inclusion and exclusion of studies.<sup>a</sup>

Parameter	Inclusion criteria	Exclusion criteria
Population	Men and women >18 years	Population under 18 years of age
Interventions/exposure	Intake of total dairy products/total milk	Studies reporting only specific dairy products (i.e., cheese, yoghurt) or if only low/high-fat milk data were reported
Comparator	Highest vs. lowest categories of exposure	
Outcomes	Type-2 diabetes and cardiovascular disease (including stroke) incidents and mortality	
Study design	Prospective cohort studies	

<sup>a</sup> PICOS: patients, intervention, comparator, outcomes, study design.



**Fig. 1.** Flow chart of literature search for dairy consumption and type 2 diabetes (T2D)/cardiovascular diseases (CVD).

For subgroup analysis, the  $Q$  and  $I^2$  statistics were used to assess heterogeneity and categorical moderators (Guariguata, Whiting, Weil, & Unwin, 2011). The heterogeneity within each group ( $Q_{within}$ ) and the heterogeneity between the groups ( $Q_{between}$ ) were assessed. Significant heterogeneities between groups indicated that the grouping variable (i.e., the moderator) was significant. Egger's linear regression test has been used to test asymmetry. This test has low power to detect possible bias when the number of studies is small; therefore, we set  $p < 0.1$  as our statistical penalty in this test (Lesser, Ebbeling, Gozner, Wypij, & Ludwig, 2007; Sterne, Gavaghan, & Egger, 2000). To address the file-drawer problem, a fail-safe  $N$  was calculated (Rosenthal & Rubin, 1988). In this procedure, an effect was considered robust if the number of studies needed to reduce the effect size to a nonsignificant level exceeds  $5K + 10$  where  $K$  is the number of studies in the meta-analysis. All analyses were conducted using the program Comprehensive Meta-Analysis 3.0 (Borenstein, Rothstein, & Cohen, 2005).

### 2.5. Limitations

This meta-analysis consisted of prospective cohort studies with different sample characteristics and different measures. Although we used a statistical model that takes the diverse nature of these studies into account, these characteristics might have influenced the results. Finally, we only used the PubMed database and the reference lists of reviews for the literature search.

## 3. Results

### 3.1. Dairy consumption and the risk of type-2 diabetes and cardiovascular disease

To estimate the correlation between dairy product consumption and the risk of T2D and CVD, data from 29 prospective cohort studies were analysed. Pooled results indicated an inverse association between the two (RR = 0.923; 95% CI: 0.884–0.964;  $p < 0.001$ ). A significant moderate heterogeneity across studies was observed ( $I^2 = 49.22\%$ ;  $p < 0.01$ ). Egger's test suggested that no publication bias existed ( $p = 0.206$ ). The fail-safe  $N$  was 221 indicating it would require 221 studies with null findings to reduce the effect size to zero. This fail-safe  $N$  is greater than Rosenthal's critical value of 155 studies.

### 3.2. Research funded by neutral organizations

For the association between dairy product consumption and the risk of T2D and CVD among studies funded by neutral organisations, data from 21 studies were analysed. The pooled RR for the studies funded by neutral organisations was 0.920 (95% CI: 0.875–0.967;  $p < 0.01$ ), indicating an 8% decrease in the prevalence of T2D and CVD among the group of people who consumed the largest amount dairy products compared to people who did not consume dairy products at all. A significant, moderate heterogeneity across studies was observed ( $I^2 = 59.30\%$ ;  $p < 0.001$ ). Egger's test suggested that no publication bias existed ( $p = 0.198$ ). The fail-safe  $N$  was 158, indicating it would require 158 studies with null findings to reduce the effect size to zero. This fail-safe  $N$  was greater than Rosenthal's critical value of 115 studies.

### 3.3. Research funded by food industries

To estimate the correlation between dairy product consumption and the risk of T2D and CVD in studies funded by food industries, data from 8 prospective cohort studies were analysed. Pooled

results indicated a nonsignificant association (RR = 0.932; 95% CI: 0.854–1.017;  $p = 0.115$ ). A nonsignificant heterogeneity across studies was observed ( $I^2 = 0.00\%$ ;  $p = 0.543$ ). Egger's linear regression test was conducted to evaluate publication bias, and the results suggested that no such bias existed ( $p = 0.574$ ).

### 3.4. Subgroup analysis according to funding source

To evaluate whether the funding source had any effect on the results of the studies when it came to the association between dairy consumption and T2D/CVD, a subgroup analysis has been conducted. No significant differences between the two funding sources were found.

Specifically, the heterogeneity within the groups was significant ( $Q_{within} = 55.12$ ;  $df = 27$ ;  $p = 0.001$ ;  $I^2 = 51\%$ ) whereas the degree of heterogeneity between the groups was not significant ( $Q_{between} = 0.065$ ;  $df = 1$ ;  $p = 0.799$ ;  $I^2 = 14\%$ ); see [Supplementary material Fig. S1](#). Thus, even though the correlation between dairy consumption and the two diseases was found to be significant in studies funded by neutral organizations but insignificant in studies funded by the industry, the subgroup analysis revealed that there is no significant difference between these two funding groups.

## 4. Discussion

In light of the growing attention to the role of industry funding for medical and nutritional research and its possible implications on public health (Mozaffarian, 2017; Nestle, 2015), the goal of this meta-analysis was to find out if industry-funded research was immanently biased. We wanted to find out if there was any significant difference between industry-funded research versus that funded by "neutral" (non industry) institutions in terms of the correlation they found (and implicitly the concomitant dietary recommendations) or failed to find between dairy consumption and two prevalent chronic diseases.

We found that when it comes to the dairy industry, the suspicion is unfounded. Not only was there no significant difference between the results of the two groups of studies in that regard (i.e., industry vis-à-vis non-industry funded), but it also seemed that being obliged to the principles of transparency and disclosure, the dairy industry published research that did not always fall in line with the healthfulness of its products. When looking separately at each group of studies according to its funding, our sub group analysis demonstrated how the industry-funded studies showed no significant, protective advantage of dairy consumption when it came to type-2 diabetes and cardiovascular diseases, whereas the "neutral", non-industry funded studies did find such a favourable protective effect of dairy products in guarding against these potentially lethal conditions (T2D/CVD). Due to the relatively small number of studies sponsored by the food industry (8 studies), the insignificant differences between these two groups should be considered carefully. Generally speaking, sponsorship might raise suspicions, and it obliges us to be more meticulous and thorough when examining the study, but it by no means disqualifies the study altogether.

## 5. Conclusions

In an age of radical "nutritionism", it is imperative that stakeholders have as many reliable sources as possible of research, information and evidence-based advice. This meta-analysis found that the funding source (i.e., food industry sponsorship versus neutral organisations sponsorship) did not affect the findings of studies in terms of the association between dairy consumption and the risk of developing type-2 diabetes and cardiovascular diseases.

In an ideal world, as long as the methods and science behind the study are rigorous and well-established, and as long as peer-reviewed journals entail elaborate description, disclosure and proper referral to all methods, procedures, databases and statistical tools utilised so that the study can be replicated, industry-funded research should be regarded as a research like any other academic undertaking (Myers, Parrott, Cummins, & Splett, 2011).

In the real world, a research like the current one is of the essence. This meta-analysis suggests that research funded by the dairy industry might not deserve the same dismissive treatment that other industry-funded studies might merit. The examination of publication bias by the “Egger’s linear regression test” indicated that such bias did not exist. Examination of the “file-drawer problem” also revealed that the reported results were robust.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.idairyj.2019.02.019>.

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