

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

The association of food industry ties with findings of studies examining the effect of dairy foods intake on cardiovascular disease and mortality: Systematic review and Meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-039036
Article Type:	Original research
Date Submitted by the Author:	01-Apr-2020
Complete List of Authors:	Chartres, Nicholas; The University of Sydney, Charles Perkins Centre Fabbri, Alice; University of Insubria, Centre for Research in Medical Pharmacology McDonald, Sally ; The University of Sydney, ; the University of Sydney Diong, Joanna; The University of Sydney Faculty of Medicine and Health McKenzie, Joanne; Monash University Bero, Lisa; University of Sydney Faculty of Health Sciences, Pharmacy
Keywords:	STATISTICS & RESEARCH METHODS, NUTRITION & DIETETICS, PUBLIC HEALTH

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 1 **The association of food industry ties with findings of studies examining the effect of**
4 2 **dairy foods intake on cardiovascular disease and mortality: Systematic review and**
5 3 **Meta-analysis**
6
7
8
9 4

10
11 5 **Authors:** Nicholas Chartres¹, Alice Fabbri¹, Sally McDonald¹, Joanna Diong², Joanne
12 6 Mckenzie³, Lisa Bero¹
13
14 7

- 15
16
17 8 1. The University of Sydney, D17, The Hub, 6th floor, Charles Perkins Centre, The
18 9 University of Sydney, New South Wales, 2006, Australia
19
20 10 2. The University of Sydney, School of Medical Sciences, Faculty of Medicine and
21 11 Health, The University of Sydney, New South Wales, 2006, Australia
22
23 12 3. Monash University, 553 St Kilda Road, Melbourne, Victoria, 3004, Australia
24
25
26 13

27
28 14 **Corresponding author:** Lisa Bero, The University of Sydney, D17, The Hub, 6th floor,
29 15 Charles Perkins Centre, The University of Sydney, New South Wales, 2006, Australia, email
30 16 lisa.bero@sydney.edu.au; Telephone +612 8627
31
32
33

34 17
35
36 18 **Word Count: 4530**
37
38 19
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

20 Abstract

21 **Objective:** To determine if the effects of dairy foods on cardiovascular disease outcomes
22 differ between studies with food industry ties versus those without industry ties. To determine
23 whether studies with or without industry ties differ in their risk of bias.

24 **Design:** Systematic review and meta-analysis of observational studies.

25 **Setting:** We searched 8 databases from 2000-2019 and hand searched the reference lists of
26 included studies.

27 **Participants:** We included cohort and case control studies that estimated the effects of dairy
28 foods on cardiovascular disease (CVD) outcomes in healthy adults.

29 **Primary and secondary outcome measures:** Primary, 1) statistical significance of results
30 favourable to dairy, 2) effect size of results, and 3) conclusions; and Secondary, 1) the risk of
31 bias of the included studies, and 2) concordance between study results and conclusions.

32 **Results:** There was no clear evidence of an association between studies with industry ties
33 (1/14) vs. no industry ties (8/29) and the reporting of favourable results, RR= 0.26 (95% CI
34 0.04, 1.87; n=43 studies) and studies with industry ties (4/14) vs. no industry ties (11/29) and
35 favourable conclusions, RR= 0.75 (95% CI 0.29, 1.95; n=43). For most outcomes, we did not
36 find a difference in effect sizes between studies with or without industry ties. Studies with
37 industry sponsorship, (HR =0.78; n= 3 studies) showed a decreased magnitude of risk of
38 CVD outcomes compared to studies with no industry sponsorship (HR=0.97; n=18) (ratio of
39 HRs 0.80 (95% CI 0.66, 0.97)) P=0.03.

40 **Conclusions:** There was no clear evidence of an association between studies with food
41 industry ties and the reporting of favourable results and conclusions compared with studies
42 without industry ties. The statistically significant difference in the magnitude of effects
43 identified in industry sponsored studies compared to non-industry sponsored studies,
44 however, is important in quantifying industry influence on studies included in dietary
45 guidelines.

46
47 **Keywords:** Industry Sponsorship, Conflicts of Interest, Bias, Dietary Guidelines

49 Strengths and limitations of this study

- 50 • This is the first systematic review and meta-analysis to evaluate the association of
51 food industry ties (industry sponsorship and / or author conflicts of interest (COI))

- 1
2
3 52 with the results, conclusions and risk of bias of primary nutrition studies examining
4 53 the effect of dairy foods on cardiovascular disease outcomes and mortality.
5
6
7 54 • We conducted a comprehensive search and followed explicit and well-defined
8 55 inclusion and exclusion criteria for the included studies.
9
10 56 • For studies missing a funding or author COI disclosure, we did not contact the
11 57 authors; thus we may be underestimating the number of studies with industry ties.
12
13 58 • The tool that we used to assess the risk of bias is still under modification, however it
14 59 is unlikely any future changes to the tool will affect the risk of bias ratings.
15
16 60 • We did not analyse studies of low and full fat dairy separately. Industry ties may have
17 61 different effects on studies of low or full fat dairy foods.
18
19
20
21 62

63 INTRODUCTION

64 The effect of dairy foods on cardiovascular disease (CVD) is unclear. Recent systematic
65 reviews and meta-analyses of observational studies have reported conflicting results between
66 the association of total dairy consumption and risk of CVD, with some showing decreased
67 risk and some showing no clear evidence.¹⁻⁴ The beneficial effects of decreasing blood
68 pressure, however, appear more consistent.^{4,5} Further, dairy intake recommendations made in
69 dietary guidelines around the world vary. Although the Australian Dietary Guidelines
70 concluded that there is a probable association between dairy food consumption and a reduced
71 risk of cardiovascular events,⁶ recent amendments to the Eatwell guidelines by Public Health
72 England recommend a significant reduction in the daily intake of dairy foods.⁷

73

74 Food industry sponsors and authors with a conflict of interest (COI) with the food industry
75 may gain financially from finding that dairy foods have health benefits, since such a finding
76 can be used to market dairy products. Such a driver may lead industry sponsors to magnify
77 (or bias) the health benefits of dairy foods by influencing the research agenda, design and
78 conduct of the study, or reporting of the results.⁸⁻¹¹ Prior examinations of pharmaceutical and
79 tobacco research have identified that even when controlling for methodological biases,
80 studies sponsored by industry were more likely to have results that favoured the sponsor than
81 studies with other sources of sponsorship.¹²⁻¹⁴

82

83 The effects of food industry sponsorship or author COI with the food industry on study
84 results needs further examination.¹⁵ A systematic review assessing the effects of wholegrain
85 foods on CVD and mortality found that studies with food industry ties more often have
86 favourable results and conclusions compared to those with no industry ties, but the
87 association was uncertain.¹⁶ One study has demonstrated an association of food industry
88 sponsorship with the magnitude of effect estimates.¹⁷ In this examination, studies of soft
89 drink consumption sponsored by the food industry reported significantly smaller harm effect
90 estimates than those with no food industry sponsorship. A recent dairy industry funded meta-
91 analysis of observational studies found that studies without food industry sponsorship showed
92 that dairy consumption was associated with a statistically significant decreased risk of
93 developing CVD and Type 2 diabetes, while studies with food industry sponsorship did not.¹⁸

1
2
3 94 The primary objective of this systematic review and meta-analysis is to determine whether:
4
5 95 • Studies of observational design examining the effects of dairy foods on CVD with
6
7 96 food industry ties (industry sponsorship and / or authors with a COI) with the food
8
9 97 industry are more likely to have results and / or conclusions that are favourable to
10
11 98 industry than those with no industry ties.
12
13

14
15 100 The secondary objectives of this review are to determine whether observational studies with
16
17 101 food industry ties compared with no industry ties:

- 18
19 102 I. differ in their risk of bias;
20
21 103 II. have a higher level of discordance between study results and conclusions, with the
22
23 104 conclusions more likely to be favourable compared to the results.
24
25

26
27 105

27 106 **METHODS**

28
29 107 We conducted a systematic review of observational studies examining the effect of dairy
30
31 108 consumption on CVD. Our study is registered with Prospero ID CRD42019129659 (see
32
33 109 Supplementary file 1).¹⁹
34
35

36 111 **Search Strategy**

37
38 112 The search included terms to locate observational studies and randomised control trials, the
39
40 113 latter of which are for a separate systematic review. The search used was based on the
41
42 114 Process Manual used to develop the 2013 Australian Dietary Guidelines and the guidance of
43
44 115 an information specialist.²⁰ The search dates used were to ensure that we identified the
45
46 116 studies used to inform the recommendations in these guidelines. We therefore searched the
47
48 117 following databases from January 2000-February 2019: MEDLINE; CINAHL; PubMed;
49
50 118 PreMEDLINE; Cochrane Library; PsycINFO; Science Direct; and ERIC. The search strategy
51
52 119 used for Ovid MEDLINE on February 1, 2019 is shown in Supplementary file 2. We adapted
53
54 120 this strategy for the other databases. We hand searched references lists of the identified
55
56 121 studies and reviews.
57
58
59 122
60

125 **Eligibility Criteria**

126 We included studies of cohort or case control designs that estimated the effects of dairy
127 consumption on CVD outcomes in healthy adults. We focused on these study designs as they
128 are often used to assess the association of diet with long term health outcomes.

129
130 We included studies with no restriction on the authors' definition of dairy. For example, some
131 authors' defined dairy as milk, yogurt and cheese, while others defined dairy as 'whole fat'
132 milk, yogurt and cheese. We included studies that compared dairy foods to other foods or
133 compared various levels of dairy consumption.

134
135 We included studies that measured any clinical outcome of CVD, defined as either mortality
136 related to specific CVD events, and / or CVD events, (e.g., first myocardial infarction, total
137 stroke etc.) or incidence of elevated blood pressure / hypertension.

138
139 We excluded conferences presentations, opinion pieces and letters to the editor. We had no
140 language restrictions.

141 142 **Types of Outcome Measures**

143 **Primary Outcomes**

144 We hypothesized that studies with food industry sponsorship and / or authors with a COI with
145 the food industry would be more likely to have favourable findings than those with no
146 industry ties. We assessed three primary outcomes:

147 1. Statistical significance of results favourable to dairy

148 Favourable results were defined as those that were in the direction of showing a health
149 benefit of dairy product(s), and were statistically significant at the 0.05 level (two tailed),
150 such as a statistically significant decreased risk of CVD compared to the comparator (i.e.
151 another food or lower dairy consumption). Otherwise, results were classified as unfavourable.
152 In the circumstance where a study reported multiple results (e.g. first myocardial infarction
153 and total stroke), only one result needed to be 'favourable' for the study as a whole to be
154 classified as 'favourable'.

155 156 2. Effect size of results

157 Effect size was defined as the risk ratio (RR), hazard ratio (HR) or odds ratio (OR) between
158 dairy foods tested versus comparator on the CVD outcome.

159

3. Conclusions

Conclusions that suggested that the dairy consumption was beneficial to health by decreasing CVD were considered favourable. Otherwise, the conclusions were considered unfavourable. In the circumstance where a study reported multiple results (e.g. first myocardial infarction and total stroke), only one conclusion needed to be 'favourable' for the study as a whole to be classified as 'favourable'.

166

Secondary Outcomes

We assessed two secondary outcomes:

1. The risk of bias of the included studies

To evaluate the risk of bias of included observational studies, we used an adapted version of the Cochrane Collaboration's 'Risk of Bias in Non-Randomized Studies-of Interventions' (ROBINS-I) tool,²¹ the ROBINS-E²². Bias is assessed across seven domains ('Bias due to confounding', 'Bias in selection of participants', 'Bias in classification of exposures', 'Bias due to deviations from exposures', 'Bias due to missing data', 'Bias in measurement of outcomes', 'Bias in selection of reported results'), with each domain classified low, moderate, serious, critical risk of bias, or no information. An overall risk of bias rating for the study is given based on the domain with the highest risk of bias rating. For example, if a study is rated as being at a 'critical' risk of bias in one domain, the overall risk of bias rating is 'critical.' In the circumstance where a study reported multiple results (e.g. stroke and myocardial infarction), the risk of bias was only assessed for one randomly selected outcome.

181

2. Concordance between study results and conclusions

Results unfavourable to the sponsor with conclusions favourable to the sponsor, were considered discordant. Otherwise, the results and conclusions were considered concordant.

185

Selection of studies

Three investigators (NC, SMc & AF), working independently in pairs, screened the titles and abstracts of all records for obvious exclusions. If both investigators agreed on excluding the study, the full text was not retrieved. Three investigators (NC, SMc & AF) working independently in pairs, assessed the full text of potentially eligible studies against the

191 inclusion criteria. If agreement could not be reached, a fourth investigator (LB) resolved the
192 conflict.

193

194 **Selection of results for meta-analysis**

195 If total dairy consumption had been assessed in the study, we included this as our only
196 exposure. If total dairy consumption had not been assessed, we included any type of dairy
197 consumption (e.g. milk, yogurt, and cheese; or low fat, high fat) other than fermented milk as
198 our exposure. We included the results comparing the highest level of dairy consumption to
199 the lowest level of dairy consumption (e.g., 'yes' to dairy consumption vs. 'no' to dairy
200 consumption, tertile 3 vs. tertile 1, quartile 4 vs. quartile 1, quintile 5 vs. quintile 1). For the
201 meta-analyses if our pre-specified rules for selecting results did not allow us to uniquely
202 identify one exposure for inclusion, we randomly selected one result.

203

204 If 'cardiovascular disease mortality/death/s' (verbatim) had been assessed, we included this
205 as our only outcome. If not, we included any type of CVD mortality (e.g., coronary heart
206 disease mortality, stroke mortality etc.) as our outcome. If there were no mortality outcomes
207 assessed in the study, we included any CVD event or incidence of elevated blood pressure /
208 hypertension as our outcome. If a study used a composite outcome, which was a combination
209 of multiple outcomes, the result pertaining to the composite outcome was selected. For the
210 meta-analyses if our pre-specified rules for selecting results did not allow us to uniquely
211 identify one outcome for inclusion, we randomly selected one result.

212

213 **Data Collection**

214 From each study we extracted:

- 215 • Year of publication
- 216 • Study design (cohort or case control)
- 217 • Sample size of study
- 218 • Age of participants (combined or if reported, separately)
- 219 • Exposure duration or observation period
- 220 • How the study defined dairy (verbatim)
- 221 • Disclosure of funding source (no disclosure, yes and there is a sponsor, the authors
222 state they received no funding for their work)
- 223 • Name of the funders of the study (verbatim)

- 1
2
3 224 • Role of the funders (role of the sponsor not mentioned, sponsor not involved in study
4 design and analyses, sponsor involved, N/A)
5 225
6
7 226 • Disclosure of author COI (no disclosure, yes (if at least 1 author had a COI), the authors
8 state they had no conflicts of interest to declare)
9 227
10 228 • Authors COI statement (verbatim)
11
12 229 • Outcomes assessed in the study (any CVD death and/or event or blood
13 pressure/hypertension)
14 230
15 231 • The numerical results of the study (e.g., OR, HR, RR)
16
17 232

19 233 All extracted data from the included studies was stored in REDcap, a secure web-based
20 application for the collection and management of data.²³ Five investigators (NC, SMc, AF,
21 234 AL & JD) working independently in pairs extracted data from the included studies.
22
23 235
24 236 Discrepancies in data extraction were resolved by consensus. If agreement could not be
25 reached, a sixth investigator (LB) resolved the discrepancy.
26 237
27
28 238

29 239 **Classification of industry sponsorship and author conflicts of interest**

31 240 Sponsorship was categorized as 1) industry or 2) non-industry. Industry sponsored studies
32 were defined as those that declared any sponsorship from the food industry, including ‘Big
33 241 Food’ (i.e. Danone, Kraft, Unilever etc), trade associations (i.e. dairy associations and
34 242 organisations) and dairy industry (i.e. primary producers). Studies with food industry
35 243 sponsorship plus any other sponsorship were classified as industry. Any study that did not
36 244 contain a funding disclosure statement was classified as ‘non-industry’.
37
38 245
39
40 246

43 247 Studies with at least one author with any disclosed financial tie with the food industry were
44 classified as having a conflict of interest (COI). Author COI were categorised as 1) COI or 2)
45 248 no COI. Studies with no authors with disclosed financial ties with the food industry were
46 249 classified as ‘no conflict of interest’.
47
48 250
49

51 251
52 252 Since the number of studies with industry sponsorship or author COI was small, we also
53 categorized studies as having “industry ties” for analysis. Studies classified as having an
54 253 industry tie were industry sponsored and / or had an author COI. Otherwise, they were
55 254 classified as having no industry ties.
56
57 255
58
59 256
60

257 **Analysis**

258 We report the frequencies and percentages of the study characteristics across all studies, and
259 separately, by sponsorship, COI and industry ties. We visually present the risk of bias rating
260 for each domain and overall across each study.

261
262 To quantify the association between industry ties, food industry sponsorship, or authors with
263 a conflict of interest with the food industry and (i) favourable results, (ii) favourable
264 conclusions, (iii) overall risk of bias across each study, and (iv) level of concordance, we
265 calculated RR (and 95% confidence intervals). To analyse the risk of bias rating for each
266 study, we dichotomised the overall risk of bias ratings as low (low or moderate) or high
267 (serious or critical).

268
269 To examine whether studies with food industry ties, food industry sponsorship, or authors
270 with a conflict of interest with the food industry modified the magnitude of effect of dairy on
271 CVD outcomes we used meta-analysis. For each outcome, we combined effect estimates
272 using a random effects meta-analysis model using the inverse variance method. DerSimonian
273 and Laird's method of moments estimator was used to estimate between study heterogeneity.
274 We fitted separate meta-analyses for studies that had measured the association using HRs and
275 those that had used either RRs or ORs. It is not recommended to combine HRs with RRs and
276 ORs in a meta-analysis, as HRs represent instantaneous risk over the study time period,
277 whereas RRs and ORs estimate risk/odds at a fixed time point.²⁴ We considered that the ORs
278 approximated RRs given CVD events were rare.

279
280 We undertook a fixed-effects test for subgroup differences (defined by industry sponsorship /
281 authors conflict of interest) using the Chi2 test and calculated the ratio of RRs (ORs) or HRs
282 along with 95% confidence intervals. Analyses were undertaken in Review Manager 5.3.²⁵

283
284 We planned to use sensitivity analysis to assess the influence of risk of bias by restricting the
285 analysis to studies at 'low risk of bias' overall (i.e. an overall risk of bias rating of low or
286 moderate). However, as the overall risk of bias was high across all studies, this was not
287 undertaken.

288

289

290 **RESULTS**

291 As shown in Figure 1, there were 1, 858 studies screened for inclusion and 43 studies were
292 included (3 case controls, 40 cohorts). See Supplementary file 3 for ‘List of excluded studies
293 and reasons for exclusion’.

295 **Characteristics of included Studies**

296 All studies were published between 2001 and 2019. All but one contained a funding
297 disclosure. Eight studies disclosed food industry sponsorship, but only two of these studies
298 described the role of the sponsor. Six studies did not contain an author COI disclosure
299 statement. Ten studies contained an author with a COI with the food industry. Fourteen
300 studies were classified as having industry ties, disclosing food industry sponsorship and / or
301 an author with a COI.

302
303 As shown in Table 1, most characteristics were similarly distributed across studies with
304 industry ties or no industry ties. Studies with industry ties (64%) were more likely to have
305 sample sizes <5000 than non-industry sponsored studies (34%). A greater proportion of
306 industry sponsored studies (100%) than non-industry sponsored studies (83%) focused on
307 total dairy intake rather than a specific food. Details of the individual studies are in
308 Supplementary file 4.

309

310

311

312

313

314

315

316

317

318

319 **Table 1. Characteristics of the included studies by sponsorship, author conflict of**
 320 **interest and industry ties**

321 Funding Source, n (%^a)

Characteristic	Category	Total N = 43	Sponsorship		COI		Industry Ties	
			Industr y N= 8	Non- Industry N=35	COI N =10	No COI N=33	Industry /COI N = 14	Non- Industry/ No COI N = 29
Sex	Male	5 (12)	0 (0)	5 (14)	0 (0)	5 (15)	0 (0)	5 (17)
	Female	2 (5)	0 (0)	2 (6)	0 (0)	2 (6)	0 (0)	2 (7)
	Both	36 (84)	8 (100)	28 (80)	10 (100)	26 (79)	14 (100)	22 (76)
Sample Size	<5000	19 (44)	6 (75)	13 (37)	7 (70)	12 (36)	9 (64)	10 (34)
	5000-50,000	18 (42)	0 (0)	18 (51)	2 (20)	16 (48)	2 (14)	16 (55)
	>50,000	6 (14)	2 (25)	4 (11)	1 (10)	5 (15)	3 (21)	3 (10)
Length of Follow up	N/A*	3 (7)	2 (25)	1 (3)	1 (10)	2 (6)	2 (14)	1 (3)
	<10 years	11 (26)	3 (38)	8 (23)	2 (20)	9 (27)	3 (21)	8 (28)
	10-15 years	21 (49)	2 (25)	19 (54)**	6 (60)	15 (45)**	7 (50)	14 (48)
	>15 years	8 (19)	1 (13)	7 (20)	1 (10)	7 (21)	2 (14)	6 (21)
Type of Dairy	Total Dairy Intake***	37 (86)	8 (100)	29 (83)	9 (90)	28 (85)	13 (93)	24 (83)
	Individual Dairy Foods****	6 (14)	0 (0)	6 (17)	1 (10)	5 (15)	1 (7)	5 (17)

322 ^a Percentages may not add to 100 due to rounding

323 * Follow up is not applicable for case control studies

324 ** Follow up for Johansson, I 2018 described the follow up as '8-12 years', we took the median of 10 years

325 *** This includes studies that looked at nutrients e.g calcium, fat & protein by measuring total dairy intake

326 ****Individual foods included milk, cheese & yogurt

327 **Risk of bias in included studies**

328 Every study was classified as having an overall high risk of bias, with 10 assessed as having a
329 serious risk of bias and 33 as having a critical risk of bias (Figure 2). Most studies were
330 assessed as having a critical risk of bias rating for the domain 'Bias due to confounding'. For
331 example, a confounder was fruit and vegetable intake. If these confounders were not
332 controlled for appropriately when measuring the effect of dairy intake on a CVD outcome,
333 the study was classified as having a risk of bias for the confounding domain.

334
335 Studies without industry ties or without an author with a COI were more likely to have a
336 serious or critical risk of bias rating for 'Bias in classification of exposures'. For example, if a
337 study did not use a validated food frequency questionnaire to measure the dietary intake of
338 dairy, the study was classified as having a risk of bias for the domain of classification of
339 exposures. For all other domains, the risk of bias classifications were similarly distributed
340 across studies with industry ties, industry sponsorship or COI vs no industry ties, industry
341 sponsorship or COI, respectively (see Supplementary file 5).

343 **Favourable results - Statistical significance: Industry ties vs no industry ties; industry 344 sponsorship vs no sponsorship; COI v no COI**

345 There was no clear evidence of an association between the reporting of favourable results and
346 studies with industry ties (1/14) compared to those with no industry ties (8/29), RR= 0.26
347 (95% CI 0.04, 1.87; n=43 studies) (Supplementary file 6). When comparing studies with
348 industry sponsorship (1/8) with those with no industry sponsorship (8/35), there was no clear
349 evidence of an association, RR = 0.55 (95% CI 0.08, 3.77; n=43 studies). There was again no
350 clear evidence of an association between the reporting of favourable results and studies with
351 an author with a COI (0/10) than those with no COI (9/33), RR= 0.16 (95% CI 0.01, 2.57;
352 n=43 studies).

354 **Effect Size, Cardiovascular Disease: Industry ties v no industry ties; industry 355 sponsorship vs no industry sponsorship; COI v no COI**

356 For studies that quantified the association between dairy consumption and CVD outcomes
357 using a RR, we found no important difference in the magnitude of the effect in studies with
358 industry ties (RR = 0.89; n=3 studies) compared with those studies with no industry ties, (RR
359 = 0.99; n=7 studies) (ratio of RRs 0.90 (95% CI 0.74, 1.09)); P=0.27 (Supplementary file 7).

1
2
3 360 For studies that had quantified the association using HRs, we similarly did not find an
4
5 361 important difference in the magnitude of HRs between studies with industry ties, (HR=0.96;
6
7 362 n=7 studies) and those studies with no industry ties, (HR=0.95; n=14 studies) (ratio of HRs
8
9 363 1.01 (95% CI 0.90, 1.13)); P=0.86.

10 364
11
12 365 In our analysis comparing studies with industry sponsorship, (RR 0.83; n=2 studies) and
13
14 366 those with no industry sponsorship, (RR 0.97; n=8 studies) we again did not find an
15
16 367 important difference in the magnitude of RRs (ratio of RRs 0.86 (95% CI 0.44, 1.66));
17
18 368 P=0.65 (Supplementary file 7). However, when we compared industry sponsored studies,
19
20 369 (HR =0.78; n=3 studies) and non-industry sponsored studies, (HR=0.97; n=18 studies) that
21
22 370 measured the association using HRs, we found a statistically significant difference in the
23
24 371 magnitude of the HRs (ratio of HRs 0.80 (95%CI 0.66, 0.97)); P=0.03 (Figure 3).

25 372
26 373 In our analysis comparing studies with an author with a COI (RR 0.89; n=2 studies) and those
27
28 374 with no COI, (RR 0.99; n= 8 studies) we found no important difference in the magnitude of
29
30 375 RRs (ratio of RRs 0.90 (95% CI 0.76-1.07)); P=0.22 (Supplementary file 7). When we
31
32 376 compared studies with a COI, (HR =1.00; n= 5 studies) and studies with no COI, (HR=0.93;
33
34 377 n=16 studies) that measured the association using HRs, we again found no difference in the
35
36 378 magnitude of the HRs (ratio of HRs 1.08 (95% CI 0.99, 1.17)); P=0.12.

37 379
38 380 **Effect Size, Elevated Blood Pressure / Hypertension: Industry ties v no industry ties,**
39
40 381 **and industry sponsorship vs no sponsorship**

41 382 We found no important difference in the magnitude of the HRs for elevated blood pressure /
42
43 383 hypertension in studies with industry ties, (HR = 0.89; n =2) and those studies with no
44
45 384 industry ties, (HR = 0.78; n= 5) (ratio of HRs 1.14 (95% CI 0.88, 1.49); P=0.32
46
47 385 (Supplementary file 7).

48 386
49
50 387 All of these studies with industry ties also had industry sponsorship, so the ratio of HRs was
51
52 388 the same.

53 389
54
55 390 **Favourable conclusions: Industry ties vs no industry ties; industry sponsorship vs no**
56
57 391 **sponsorship; COI v no COI**

58 392 There was no clear evidence of an association between the reporting of favourable
59
60 393 conclusions and studies with industry ties (4/14) compared to those with no industry ties

1
2
3 394 (11/29), RR= 0.75 (95% CI 0.29, 1.95; n=43) (Supplementary file 6). When we compared
4
5 395 studies only by industry sponsorship, there was no clear evidence of an association between
6
7 396 industry sponsored studies (3/8), compared to studies with no sponsorship (12/35), RR = 1.09
8
9 397 (95% CI 0.40, 2.99; n=43). There was again no clear evidence of an association between the
10
11 398 reporting of favourable conclusions and studies with an author with a COI (2/10) than those
12
13 399 without a COI (13/33), RR= 0.51 (95% CI 0.14, 1.88; n=43 studies).

400

401 **Risk of Bias Assessment by Industry Ties**

402 As every study had an overall high (serious or critical) risk of bias rating, there was no
403
404 difference in the proportion of studies at a high risk of bias between those with industry ties,
405
406 industry sponsorship or COI and those without industry ties, sponsorship or COI.

405

406 **Concordance between study results and conclusions**

407 Six (of 43) studies, all with unfavorable results, overemphasized the benefits of the dairy
408
409 exposure in their conclusions and thus were coded as 'favourable' conclusions.

409 There was no clear evidence of an association between discordant results and conclusions and
410
411 studies with industry ties (3/14) than those with no industry ties (3/29), RR = 2.07 (95% CI
412
413 0.48, 8.99; n=43) (Supplementary file 6). There was no clear evidence of an association when
414
415 comparing studies with industry sponsorship (2/8) to those with no industry sponsorship
416
417 (4/35), RR = 2.19 (95% CI 0.48-9.94). There was again no clear evidence of an association
418
419 between studies with an author with a COI (2/10) than those with no COI (4/33), RR = 1.65
420
421 (95% CI 0.35, 7.72; n=43).

416

417 **DISCUSSION**

418 There was no clear evidence of an association between studies with food industry ties and the
419
420 reporting of favourable results and conclusions of observational studies measuring the effects
421
422 of dairy foods on cardiovascular disease outcomes. The 'mixed' group of funders we
423
424 identified in the industry sponsored studies may influence these results, as the funding effect
425
426 may be diluted by this heterogeneous group of sponsors. Unlike in drug studies,¹² the funders
427
428 in the studies included in this review were extremely diverse, with Big Food and trade
429
430 association jointly sponsoring several studies. Thus, dairy foods are not their sole interest.

1
2
3 425 The meta-analysis of hazard ratios of CVD outcomes found that studies with industry
4 sponsorship showed a greater benefit from dairy than studies without industry sponsorship,
5 426 and this difference was statistically significant. The meta-analysis of risk ratios of CVD
6
7 427 outcomes found a similar estimate; however, this was not statistically significant. The likely
8
9 428 reason for this was that the meta-analysis of RRs had fewer studies, and so the ratio of RRs
10
11 429 could not be as precisely estimated. We found no evidence of a clinically important
12
13 430 difference in the magnitude of effect between studies with industry ties or authors with a COI
14
15 431 compared to those with no industry ties or no COI for other outcomes.
16
17 432
18 433

19 434 For every study, the overall risk of bias was classified as high (meaning either serious or
20
21 435 critical). Therefore, differences in the risk of bias across studies with and without industry
22
23 436 ties would not seem to provide an explanation for our findings. However, the version of the
24
25 437 ROBINS-E tool that we used may not have been able to adequately discriminate across the
26
27 438 studies, as perhaps is indicated by the uniformity in risk of bias classification.²⁶ Therefore, we
28
29 439 cannot rule out the possibility that differences in bias across studies with and without industry
30
31 440 ties may partly explain our findings.
32
33 441

34 442 **Strengths and limitations of this review**

35
36 443 Our review was prospectively registered in Prospero.¹⁹ We followed explicit inclusion and
37
38 444 exclusion criteria, conducted a comprehensive search across multiple databases and hand
39
40 445 searched reference lists for the included studies.
41
42 446

43 447 For those studies missing a funding or author COI disclosure, we did not contact the authors
44
45 448 and we therefore may be underestimating the number of studies with industry ties. The tool
46
47 449 that we used to assess the risk of bias is still under development, however it is unlikely any
48
49 450 future changes to the tool will affect the risk of bias ratings.²² We did not analyse studies of
50
51 451 low and full fat dairy separately. Industry ties may have different effects on studies of low or
52
53 452 full fat dairy foods.
54
55 453
56 454
57
58 455
59
60

456 **Agreements and disagreements with other studies or reviews**

457 The observed greater benefit of dairy on CVD outcomes in industry sponsored studies
458 compared to non-industry sponsored studies corroborates previous research that has
459 demonstrated studies sponsored by the food industry reported smaller harmful effect sizes for
460 soft drink consumption, compared with non-industry sponsored studies.¹⁷ It is not consistent,
461 however, with a recent meta-analysis funded by the Israel Dairy Board that found non
462 statistically significant differences in the estimated associations between industry and non-
463 industry funded studies.¹⁸ The differences in the results of our current review and this
464 previous study can be attributed to a number of important factors in how the studies were
465 conducted, including how the exposures were classified, the outcomes selected for the meta-
466 analyses and the analysis method used. For the exposures, our review included yogurt and
467 cheese, as well as ‘total dairy’ and milk, whereas the Dairy Board study included only ‘total
468 dairy’ and milk as exposures. We included all outcomes related to CVD, and the Dairy Board
469 study included only CVD and stroke, as well as Type 2 diabetes. For the analysis method, we
470 fitted separate meta-analyses for studies that had measured the association using HRs and
471 those that had used either RRs or ORs, while the Dairy Board study only measured the
472 associations using RRs.

473
474 The lack of difference in the risks of bias between studies with industry ties and those with no
475 industry ties, is consistent with a previous review that examined the association of industry
476 ties with outcomes of studies examining the effect of wholegrain foods on CVD and mortality
477 that used the same tool to assess risk of bias.¹⁶ These findings have also been shown in
478 pharmaceutical and tobacco research that have demonstrated industry sponsored studies are
479 of equal or better internal validity than studies with no sponsorship.^{12, 13, 15, 27, 28}

481 **Implications for clinicians, policy makers and future research**

482 As dietary guidelines depend on an evidence base that should be as free as possible of bias,
483 the difference in the magnitude of effects between industry sponsored studies compared to
484 non-industry sponsored studies is concerning. Therefore, the dairy intake recommendations
485 made in dietary guidelines should account for the potential influence of industry sponsorship
486 on evidence of health effects.

1
2
3 488 Industry sponsors may bias research via different mechanisms, including the design and
4
5 489 conduct of a study, the selective reporting of results and by spinning conclusions,¹¹ as well as
6
7 490 how the questions are asked.²⁹ It has been suggested that the dairy industry may preferentially
8
9 491 fund research on topics which will provide them with more favourable outcomes.³⁰ The
10
11 492 influence of the food industry on the research agenda has been demonstrated in an
12
13 493 examination of research topics covered by samples of randomised controlled trials included
14
15 494 in systematic reviews of nutrition studies and obesity.³¹ It was shown that most food industry
16
17 495 studies focused on the manipulations of specific nutrients, and not on dietary behaviours,
18
19 496 therefore limiting the public health relevance of rigorous evidence available for use in both
20
21 497 systematic reviews and dietary guidelines.³¹ The topics examined in cohort studies on the
22
23 498 relationship of nutrition and obesity, which tend to focus on more complex exposures than
24
25 499 trials, did not demonstrate a similar influence of funding source. However, the disclosure of
26
27 500 food industry sponsorship was low, making a comparison difficult.³²

501

502

503 **Conclusion**

504 There was no clear evidence of an association between studies with food industry ties and the
505 reporting of favourable results and conclusions compared with studies without industry ties.
506 However, the statistically significant difference in the magnitude of effects identified in
507 industry sponsored studies compared to non-industry sponsored studies is important in
508 quantifying industry influence on studies included in dietary guidelines.

1
2
3 509 **Acknowledgements:** We thank Agnes Lau, University of California, San Francisco, for her
4
5 510 assistance with data collection.
6
7 511

8
9 512 **Contributors:** NC, AF and LB designed and wrote the review protocol. NC wrote the search
10
11 513 strategy and undertook the literature search. NC, AF and SMc, conducted the title and
12
13 514 abstract screening and full article screening for final study inclusion. NC, AF, JD, AL and
14
15 515 SMc conducted data collection and cleaning, LB supervised. NC and JMc undertook all data
16
17 516 analysis. LB advised on methods, statistical analyses, and interpretation of findings. All
18
19 517 authors contributed to the final manuscript. NC and LB are guarantors.
20
21 518

22
23 519 **Funding:** This work was supported by Australian Health and Medical Research Council
24
25 520 Project Grant APP 1139997. Nicholas Chartres is a recipient of the James Millner PhD
26
27 521 Scholarship in Pharmacy from the University of Sydney.
28
29 522

30
31 523 **Competing interests:** None declared.
32
33 524

34
35 525 **Data sharing statement:** Available from The University of Sydney data repository. DOI to
36
37 526 be determined.
38
39 527

40
41
42 528 **Patient consent for publication:** Not required.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Qin LQ, Xu JY, Han SF, et al. Dairy consumption and risk of cardiovascular disease: an updated meta-analysis of prospective cohort studies. *Asia Pac J Clin Nutr*. 2015;24(1):90-100.
2. Alexander DD, Bylsma LC, Vargas AJ, et al. Dairy consumption and CVD: a systematic review and meta-analysis. *Br J Nutr*. 2016;115(4):737-50.
3. Gholami F, Khoramdad M, Esmailnasab N, et al. The effect of dairy consumption on the prevention of cardiovascular diseases: A meta-analysis of prospective studies. *J Cardiovasc Thorac Res*. 2017;9(1):1-11.
4. Drouin-Chartier JP, Brassard D, Tessier-Grenier M, et al. Systematic Review of the Association between Dairy Product Consumption and Risk of Cardiovascular-Related Clinical Outcomes. *Adv Nutr*. 2016;7(6):1026-40.
5. Lee M, Lee H, Kim J. Dairy food consumption is associated with a lower risk of the metabolic syndrome and its components: a systematic review and meta-analysis. *Br J Nutr*. 2018;120(4):373-84.
6. National Health and Medical Research Council: Department of Health and Ageing. Australian Dietary Guidelines. Canberra, Commonwealth of Australia: NHMRC; 2013.
7. Public Health England. The Eatwell Guide. [Internet]. 2016. Available from: <https://www.gov.uk/government/publications/the-eatwell-guide>. Accessed 18 March, 2016.
8. Lexchin J. Those who have the gold make the evidence: how the pharmaceutical industry biases the outcomes of clinical trials of medications. *Sci Eng Ethics*. 18(2):247-61.
9. Sismondo S. How pharmaceutical industry funding affects trial outcomes: causal structures and responses. *Social science & medicine* (1982). 2008;66(9):1909-14.
10. Boutron I, Dutton S, Ravaud P, et al. Reporting and interpretation of randomized controlled trials with statistically nonsignificant results for primary outcomes. *JAMA*. 2010;303(20):2058-64.
11. Odierna DH, Forsyth SR, White J, et al. The cycle of bias in health research: a framework and toolbox for critical appraisal training. *Account Res*. 2013;20(2):127-41.
12. Lundh A, Lexchin J, Mintzes B, et al. Industry sponsorship and research outcome. *Cochrane Database Syst Rev*. 2017;2:Mr000033.
13. Barnes DE, Bero LA. Industry-funded research and conflict of interest: an analysis of research sponsored by the tobacco industry through the Center for Indoor Air Research. *J Health Polit Policy Law*. 1996;21(3):515-42.
14. Yank V, Rennie D, Bero LA. Financial ties and concordance between results and conclusions in meta-analyses: retrospective cohort study. *BMJ*. 335(7631):1202-5.
15. Chartres N, Fabbri A, Bero LA. Association of industry sponsorship with outcomes of nutrition studies: A systematic review and meta-analysis. *JAMA Intern Med*. 2016;176(12):1769-77.
16. Chartres N, Fabbri A, McDonald S, et al. Association of industry ties with outcomes of studies examining the effect of wholegrain foods on cardiovascular disease and mortality: systematic review and meta-analysis. *BMJ Open*. 2019;9(5):e022912.
17. Vartanian LR, Schwartz MB, Brownell KD. Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis. *Am J Public Health*. 2007;97(4):667-75.
18. Mishali M, Kisner M, Avrech T. Funding sources and outcomes of dairy consumption research – a meta-analysis of cohort studies: The case of type-2 diabetes and cardiovascular diseases. *Int Dairy J*. 2019.
19. National Institute for Health Research. International Prospective Register for Systematic Reviews [Internet]. 2015 [Available from: <http://www.crd.york.ac.uk/PROSPERO/>. Accessed 11 March, 2016.
20. Dietitians Association of Australia. A review of the evidence to address targeted questions to inform the revision of the Australian dietary guidelines 2009: Process Manual. 2011.
21. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355.

- 1
2
3 580 22. University of Bristol. The ROBINS-E tool (Risk Of Bias In Non-randomized Studies - of
4 581 Exposures) 2019 [Available from: [https://www.bristol.ac.uk/population-health-
6 583 sciences/centres/cresyda/barr/riskofbias/robins-e/](https://www.bristol.ac.uk/population-health-
5 582 sciences/centres/cresyda/barr/riskofbias/robins-e/).
7 584 23. Harris PA, Taylor R, Thielke R, et al. Research Electronic Data Capture (REDCap) - A
8 584 metadata-driven methodology and workflow process for providing translational research informatics
9 585 support. *J Biomed Inform X*. 2009;42(2):377-81.
10 586 24. Tierney JF, Stewart LA, Ghersi D, et al. Practical methods for incorporating summary time-to-
11 587 event data into meta-analysis. *Trials*. 2007;8:16.
12 588 25. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic
13 589 Cochrane Centre, The Cochrane Collaboration, 2014.
14 590 26. Bero L, Chartres N, Diong J, et al. The risk of bias in observational studies of exposures
15 591 (ROBINS-E) tool: concerns arising from application to observational studies of exposures. *Syst Rev*.
16 592 2018;7(1):242.
17 593 27. Mandrioli D, Kearns CE, Bero LA. Relationship between Research Outcomes and Risk of Bias,
18 594 Study Sponsorship, and Author Financial Conflicts of Interest in Reviews of the Effects of Artificially
19 595 Sweetened Beverages on Weight Outcomes: A Systematic Review of Reviews. *PloS one*.
20 596 2016;11(9):e0162198.
21 597 28. Cho MK, Bero LA. The quality of drug studies published in symposium proceedings. *Ann*
22 598 *Intern Med*. 1996;124(5):485-9.
23 599 29. Fabbri A, Lai A, Grundy Q, et al. The Influence of Industry Sponsorship on the Research
24 600 Agenda: A Scoping Review. *Am J Public Health*. 2018;108(11):e9-e16.
25 601 30. Wilde P, Morgan E, Roberts J, et al. Relationship between funding sources and outcomes of
26 602 obesity-related research. *Physiol & Behav*. 2012;107(1):172-5.
27 603 31. Fabbri A, Chartres N, Bero LA. Study sponsorship and the nutrition research agenda: analysis
28 604 of cohort studies examining the association between nutrition and obesity. *Public Health Nutr*.
29 605 2017;20(17):3193-9.
30 606 32. Fabbri A, Chartres N, Bero LA. Study sponsorship and the nutrition research agenda: analysis
31 607 of cohort studies examining the association between nutrition and obesity. *Public Health Nutr*.
32 608 2017;20(17):3193-9.

609

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

610 **Figures**

611 **Figure 1. Study Flow Diagram**

612 **Figure 2. Risk of Bias in Included Studies**

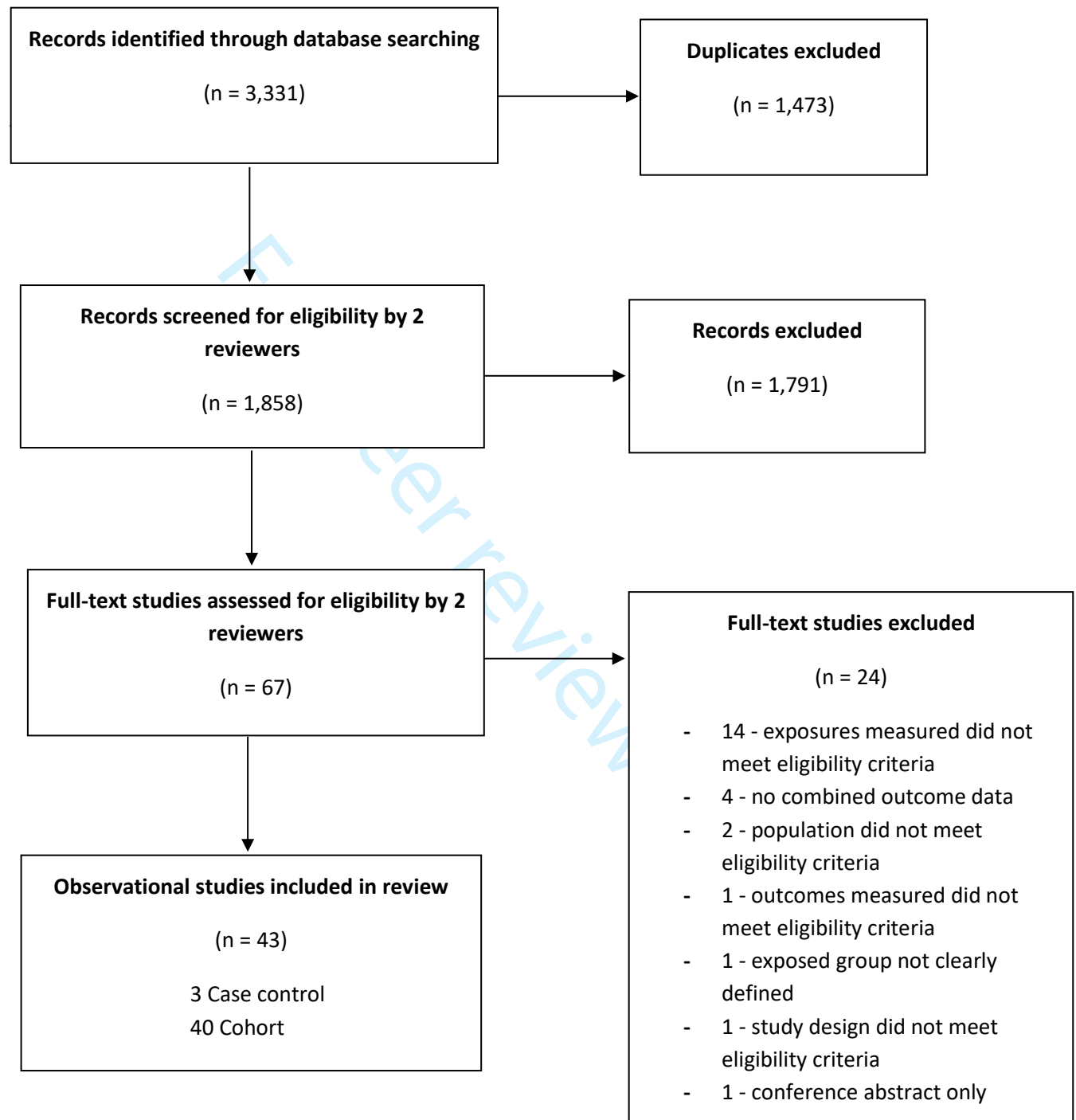
613 **Figure 3. Effect Size, Cardiovascular Disease: Industry sponsorship vs no industry**
614 **sponsorship, Hazard Ratio**

615

616

For peer review only

Figure 1. Study Flow Diagram



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Measurement of outcomes	Selection of the reported result	Overall bias
Aerde, M 2013	●	○	○	○	○	○	○	●
Al-Delaimy, WK 2003	○	○	○	●	●	●	○	○
Alonso A, 2005	●	○	○	○	○	○	○	●
Altorf-van der Kuil, W 2012	●	○	○	○	○	○	○	●
Avalos, EE 2013	●	○	●	●	○	○	○	●
Bernstein, AM 2012	○	○	○	●	●	○	○	○
Biong, A 2008	○	●	○	●	○	○	○	○
Bonthuis, M 2010	●	○	●	○	○	●	○	●
Buendia, JR 2018	○	○	○	●	○	○	○	○
Chen, M 2016	●	○	○	●	●	●	○	●
Dalmeijer, G 2013	●	○	○	○	○	○	○	●
Dauchet, L 2007	●	○	○	○	●	○	○	●
Dehghan, M 2018	●	○	○	○	○	○	○	●
Elwood, PC 2004	●	○	○	○	○	●	○	●
Engberink, MF 2009	●	○	○	○	○	○	○	●
Farvid, MS 2017	●	○	○	○	○	●	○	●
Haring, B 2014	●	○	○	○	●	○	○	●
He, K 2003	○	○	○	○	●	○	○	○
Heraclides, A 2012	●	○	○	○	○	○	○	●
Johansson, I 2018	●	○	○	○	●	●	○	●
Johansson, I 2019	●	○	○	○	●	●	○	●
Kim, D 2017	●	○	○	○	○	●	○	●

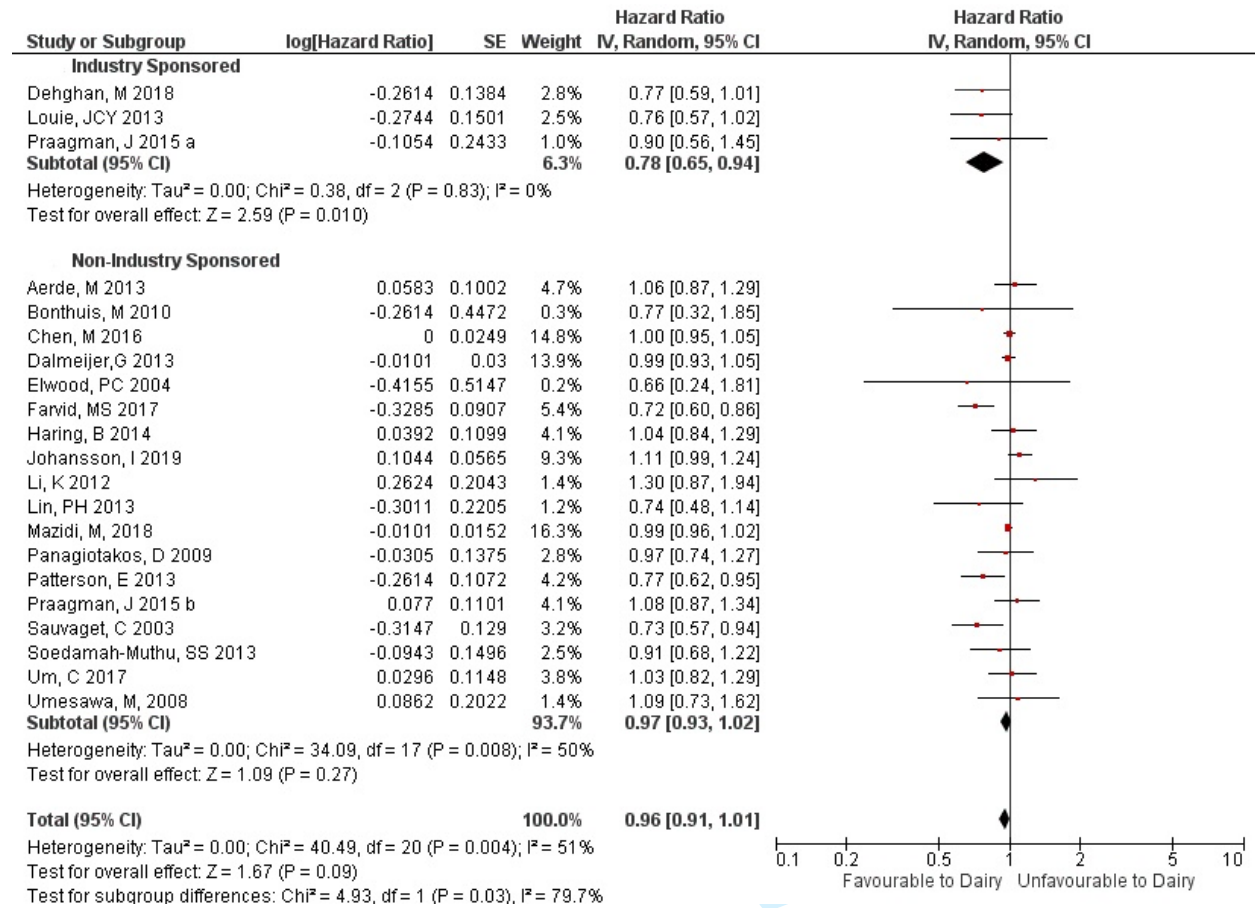
-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Larsson, S 2009	○	○	○	○	○	○	○	○
Larsson, SC 2012	●	○	○	○	○	○	○	●
Li, K 2012	●	○	○	○	○	○	○	●
Lin, PH 2013	●	○	○	○	○	○	○	●
Lockheart, MSK 2007	●	○	○	○	○	○	○	●
Louie, JCY 2013	●	○	○	○	○	○	○	●
Mazidi, M, 2018	●	○	○	○	○	○	○	●
Nettleton, J 2008	○	○	○	○	○	○	○	○
Panagiotakos, D 2009	●	○	○	○	○	○	○	●
Patterson, E 2013	○	○	○	○	○	○	○	○
Praagman, J 2015	●	○	○	○	○	○	○	●
Praagman, J 2015	●	○	○	○	○	○	○	●
Sauvaget, C 2003	●	○	○	○	○	○	○	●
Snijder, MB 2008	●	○	○	○	○	○	○	●
Soedamah-Muthu, SS 2013	●	○	○	○	○	○	○	●
Steffen, LM 2005	○	○	○	○	○	○	○	○
Tavani, A 2002	○	○	○	○	○	○	○	○
Um, C 2017	●	○	○	○	○	○	○	●
Umesawa, M, 2008	●	○	○	○	○	○	○	●
Wang, L 2008	●	○	○	○	○	○	○	●

Low	Moderate	Serious	Critical	No Information
-----	----------	---------	----------	----------------

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41

Figure 3. Effect Size, Cardiovascular Disease, Industry sponsorship vs no Industry sponsorship, Hazard Ratio



PROSPERO**International prospective register of systematic reviews**

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

Please complete all mandatory fields below (marked with an asterisk *) and as many of the non-mandatory fields as you can then click *Submit* to submit your registration. You don't need to complete everything in one go, this record will appear in your *My PROSPERO* section of the web site and you can continue to edit it until you are ready to submit. Click *Show help* below or click on the icon to see guidance on completing each section.

This record cannot be edited because it has been rejected

1. * Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

The association of food industry ties with findings of studies examining the effect of dairy foods intake with cardiovascular disease and mortality: Systematic review and Meta-analysis: protocol registration:

2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. * Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

01/09/2016

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

01/06/2019

5. * Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.

Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.

This field should be updated when any amendments are made to a published record and on completion and publication of the review. If this field was pre-populated from the initial screening questions then you are not able to edit it until the record is published.

The review has not yet started: No

PROSPERO

International prospective register of systematic reviews

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	Yes	No
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

6. * Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Nicholas Chartres

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Mr Chartres

7. * Named contact email.

Give the electronic mail address of the named contact.

ngar0960@uni.sydney.edu.au

8. Named contact address

Give the full postal address for the named contact.

The University of Sydney, D17, the Hub, 6th Floor, Charles Perkins Centre | the University of Sydney | Nsw |
2006

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

02 8627 4328

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

University of Sydney

Organisation web address:

11. * Review team members and their organisational affiliations.

PROSPERO

International prospective register of systematic reviews

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country are now mandatory fields for each person.**

Mr Nicholas Chartres. University of Sydney

Dr Alice Fabbri. The University of Sydney

Agnes Lau. University of California

Dr Joanna Diong. The University of Sydney

Assistant/Associate Professor Joanne Mckenzie. Monash University

Professor Lisa Bero. The University of Sydney

12. * Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

Nicholas Chartres is a scholarship recipient (James Milner PhD scholarship in Pharmacy) from the University of Sydney.

Grant number(s)

13. * Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country are now mandatory fields for each person.**

15. * Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

The objective of this study is to determine if the presence of food industry sponsorship in primary nutrition studies examining the association of dairy foods with cardiovascular outcomes is associated with effect sizes, statistical significance of results and/ or conclusions that are favorable to the sponsor. We will also determine whether primary nutrition studies assessing the association of dairy foods with cardiovascular outcomes with industry sponsorship differ in their risk of bias compared with studies with no or other sources of sponsorship.

16. * Searches.

State the sources that will be searched. Give the search dates, and any restrictions (e.g. language or publication period). Do NOT enter the full search strategy (it may be provided as a link or attachment.)

We will search the following databases from 2000-March 2019: Ovid MEDLINE; CINAHL; PubMed;

Cochrane Library; and ScienceDirect. No language restrictions will be applied

PROSPERO

International prospective register of systematic reviews

17. URL to search strategy.

Give a link to a published pdf/word document detailing either the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies), or upload your search strategy. Do NOT provide links to your search results.

https://www.crd.york.ac.uk/PROSPEROFILES/129659_STRATEGY_20190322.pdf

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

To determine whether industry sponsorship and/or study methods are associated with the results and/or conclusions of primary nutrition studies assessing the association of dairy foods and cardiovascular outcomes.

19. * Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

We will include primary research studies of any design that quantitatively examine the association of dairy foods with cardiovascular outcomes in healthy adults.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed.

- The study quantitatively measures the effects of dairy consumption in humans.
- The study evaluates the effectiveness, efficacy or harms of dairy consumption.
- The study compares dairy food to control OR dairy food to other foods OR different levels of dairy consumption
- The study evaluates cow, goat or sheep milk, yogurt, cheese or custard. We will include and use the studies definition of dairy it is broader than milk, yogurt, cheese or custard.
- The study evaluates skim, low or full fat dairy products
- The study evaluates the effect of nutrients, e.g calcium and vitamin D when consumed within a dairy product

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Dairy vs Dairy (different doses) Dairy vs Dairy (different fat content) Dairy vs No dairy Dairy vs Other food

PROSPERO

International prospective register of systematic reviews

Other (mixed intervention)

22. * Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

RCTs, Controlled Trials, Cohort, Case-control, Pre/Post, Other/Various

23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

- The study has a test of interest (e.g. risk ratio/hazard ratio) of cardiovascular mortality, nonfatal heart attack, stroke, etc.) and/or the surrogate outcomes of Blood Pressure (mmHg)

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

a. Primary Outcome 1 and 2

- o Statistical significance of results
- o Effect size of outcomes

For each study, the result reported for each primary outcome will be categorized as:

(1) Favourable if the result are statistically significant ($p < 0.05$ or 95% confidence interval [CI] excluding no difference) and in the direction of dairy being more efficacious, less harmful or no more harmful than the comparator;

(2) Unfavourable if the result was statistically significant (e.g. $P < 0.05$ or 95% confidence interval including the possibility of no difference) in the direction of the comparator being more efficacious or less harmful.

We will also extract the effect estimates for primary outcomes.

We will classify the results of the study as favourable if the stated primary outcome is reported as favourable.

If the study has multiple primary outcomes we will report the study as favourable if at least one of the outcomes is reported as favourable.

b. Primary Outcome 3 (Conclusions)

The conclusions reported in the published papers will be categorized as:

(1) Favourable if the dairy intervention was preferred to comparator

(2) Unfavourable if the comparator intervention was preferred to the test one OR if the test intervention

PROSPERO

International prospective register of systematic reviews

showed a risk increase.

* Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

As this is not relevant to our study, we have nothing to include.

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

~~We used the Cochrane Risk of Bias tool for randomised studies (15) to measure the methodological quality of randomized controlled trials. The tool assesses bias across 7 domains and each of these will be reported separately. To measure methodological quality in observational studies we will use the ROBINS-I tool for non-randomized studies (ROBINS-I)(16), which also measures bias across 7 domains.~~

d. Secondary Outcome 2 (Concordance between results and conclusions)

We will classify concordance between study results and conclusions as 'yes' if the authors' conclusions are supported by all outcomes. This will include the reporting of all significant and non-significant results.

Otherwise, concordance will be classified as 'no'

* Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

As this is not relevant to our study, we have nothing to include.

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Selection Process

Two investigators (NC & AF) will independently screen the titles and abstracts of all retrieved records for obvious exclusions. Two investigators (NC & AF) will then assess the remaining papers based on full text, applying the aforementioned inclusion criteria for included studies. Agreement will be reached on any discrepancies by consensus between the two assessors. If agreement cannot be reached, a third assessor (LB) will make a decision. The reasons for the eligible papers being excluded will be described in

PROSPERO

International prospective register of systematic reviews

'Characteristics of excluded papers' table.

Data collection process

- a) Title of the paper
- b) Year of publication
- c) Study design
- d) Comparisons:
- e) Sample size of study
- f) Mean age of participants
- g) Intervention or observation period
- h) Definition of intervention and exposure
- i) Risk of Bias
- j) Primary Hypothesis of the study (Verbatim)
- k) Primary outcomes measures
- l) Conclusion
- m) Concordance between conclusions and results
- n) Industry Sponsorship
- o) Role of the Funder: Information about the role of the sponsor as stated in the study
- p) The institutional affiliation of the corresponding author will be obtained from the article and classified into the following categories
- q) Country of origin (verbatim)
- r) Author COI

27. * Risk of bias (quality) assessment.

Describe the method of assessing risk of bias or quality assessment. State which characteristics of the studies will be assessed and any formal risk of bias tools that will be used.

We will use the Cochrane Risk of Bias tool for randomised studies (15) to measure the methodological quality of randomized controlled trials. The tool assesses bias across 7 domains and each of these will be reported separately. To measure methodological quality in observational studies we will use the ROBINS-I tool for non-randomized studies (ROBINS-I)(16), which also measures bias across 7 domains.

28. * Strategy for data synthesis.

Provide details of the planned synthesis including a rationale for the methods selected. This **must not be generic text** but should be **specific to your review** and describe how the proposed analysis will be applied to your data.

To test our hypothesis that studies with dairy industry sponsorship will be more likely to have favourable

PROSPERO

International prospective register of systematic reviews

1
2
3
4 results, we will compare the risk of dairy industry sponsored studies having a favourable result with the risk
5 of non-dairy industry funded studies having a favorable result. Using Rev Manager we will calculate the
6 pooled risk ratio (RR) and its 95% confidence interval using the Mantel-Haenszel fixed-effect model.

7
8 However, when substantial heterogeneity is observed, we will use an inverse variance DerSimonian-Laird
9 random-effects model. We will assess heterogeneity using I^2 and use a random-effects model when
10 statistical heterogeneity is substantial, defined as an I^2 50%.

11
12 To test our hypothesis that effect estimates will differ between studies with dairy industry sponsorship and
13 those without sponsorship, we will compare the pooled effect estimates from dairy vs. non-dairy sponsored
14 studies. We will pool the effect estimates of homogenous studies measuring dichotomous outcomes, (e.g.
15 RR, HR, OR for all-cause mortality, CVD mortality, cardiovascular events, etc) calculating pooled risk ratios
16 as described above. Blood pressure is a continuous outcome, so we will attempt to pool homogeneous
17 studies and measure the mean difference from baseline measures.

18
19 To test our hypothesis that studies with dairy industry sponsorship would be more likely to have favourable
20 conclusions we will compare the risk of dairy industry sponsored studies having favourable conclusions with
21 the risk of non-dairy industry funded studies having a favorable conclusion. We will calculate the pooled risk
22 ratio (RR) and its 95% confidence interval using the Mantel-Haenszel fixed-effect model. However, when
23 substantial heterogeneity is observed, we will use an inverse variance DerSimonian-Laird random-effects
24 model. We will assess heterogeneity using I^2 and use a random-effects model when statistical heterogeneity
25 is substantial, defined as an I^2 50%.

26 27 28 29 30 31 32 33 34 35 36 37 38 **29. * Analysis of subgroups or subsets.**

39 State any planned investigation of 'subgroups'. Be clear and specific about which type of study or
40 participant will be included in each group or covariate investigated. State the planned analytic approach.

41 We will conduct an a priori subgroup analysis on low fat and full fat dairy products to determine if studies
42 measuring the effects of low fat products have different results from studies that measure full fat dairy
43 products.

44 We will conduct an a priori subgroup analysis by the risks of bias of the included studies to determine if
45 studies that have a high risk of bias have different results from studies that have a low risk of bias. We
46 hypothesize that industry sponsored studies will have the same level of risk of bias as non-industry
47 sponsored studies.

48 49 50 51 52 53 54 **30. * Type and method of review.**

55 Select the type of review and the review method from the lists below. Select the health area(s) of interest for
56 your review.

57 58 **Type of review**

59 Cost effectiveness
60

PROSPERO

International prospective register of systematic reviews

1 No
 2
 3
 4 Diagnostic
 5 No
 6 Epidemiologic
 7 No
 8 Individual patient data (IPD) meta-analysis
 9 No
 10 Intervention
 11 No
 12 Meta-analysis
 13 Yes
 14 Methodology
 15 No
 16 Narrative synthesis
 17 No
 18 Network meta-analysis
 19 No
 20 Pre-clinical
 21 No
 22 Prevention
 23 No
 24 Prognostic
 25 No
 26 Prospective meta-analysis (PMA)
 27 No
 28 Review of reviews
 29 No
 30 Service delivery
 31 No
 32 Synthesis of qualitative studies
 33 No
 34 Systematic review
 35 Yes
 36 Other
 37 No
 38
 39
 40
 41
 42
 43
 44
 45 **Health area of the review**
 46 Alcohol/substance misuse/abuse
 47 No
 48 Blood and immune system
 49 No
 50 Cancer
 51 No
 52 Cardiovascular
 53 Yes
 54 Care of the elderly
 55 No
 56 Child health
 57 No
 58 Complementary therapies
 59
 60

For peer review only

PROSPERO**International prospective register of systematic reviews**

1
2
3
4 No
5 Crime and justice
6 No
7 Dental
8 No
9 Digestive system
10 No
11 Ear, nose and throat
12 No
13 Education
14 No
15 Endocrine and metabolic disorders
16 No
17 Eye disorders
18 No
19 General interest
20 No
21 Genetics
22 No
23 Health inequalities/health equity
24 No
25 Infections and infestations
26 No
27 International development
28 No
29 Mental health and behavioural conditions
30 No
31 Musculoskeletal
32 No
33 Neurological
34 No
35 Nursing
36 No
37 Obstetrics and gynaecology
38 No
39 Oral health
40 No
41 Palliative care
42 No
43 Perioperative care
44 No
45 Physiotherapy
46 No
47 Pregnancy and childbirth
48 No
49 Public health (including social determinants of health)
50 Yes
51 Rehabilitation
52 No
53 Respiratory disorders
54 No
55
56
57
58
59
60

PROSPERO

International prospective register of systematic reviews

Service delivery

No

Skin disorders

No

Social care

No

Surgery

No

Tropical Medicine

No

Urological

No

Wounds, injuries and accidents

No

Violence and abuse

No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.

English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

Australia

33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one

Give the link to the published protocol.

Alternatively, upload your published protocol to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

1 **PROSPERO**
2 **International prospective register of systematic reviews**
3
4

5 **Do you intend to publish the review on completion?**

6 Yes
7

8 **36. Keywords.**
9

10 Give words or phrases that best describe the review. Separate keywords with a semicolon or new line.
11 Keywords will help users find the review in the Register (the words do not appear in the public record but are
12 included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless
13 these are in wide use.
14

15 Nutrition, Industry Sponsorship, Conflict of Interest, Bias, Food Industry
16

17 **37. Details of any existing review of the same topic by the same authors.**
18

19 Give details of earlier versions of the systematic review if an update of an existing review is being registered,
20 including full bibliographic reference if possible.

21 CRD42017055841 The association of industry sponsorship with outcomes of studies examining the effect of
22 intake of wholegrain foods with cardiovascular disease and mortality: protocol
23
24

25 **38. * Current review status.**
26

27 Review status should be updated when the review is completed and when it is published. For
28 newregistrations the review must be Ongoing.

29 Please provide anticipated publication date

30 Review_Ongoing
31
32

33 **39. Any additional information.**
34

35 Provide any other information the review team feel is relevant to the registration of the review.
36

37 **40. Details of final report/publication(s).**
38

39 This field should be left empty until details of the completed review are available.

40 Give the link to the published review.
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary file 2. Search Strategy OVID Medline: Dairy, CVD, Adults

1. Randomized controlled trial*.tw.
2. experimental design.tw.
3. intervention*.tw.
4. (RCT* or rct*).tw.
5. random* control* trial*.tw.
6. clinical trial*.tw.
7. field trial*.tw.
8. community trial*.tw.
9. controlled clinical trial*.tw.
10. pragmatic trial*.tw.
11. observational stud*.tw.
12. cohort stud*.tw.
13. prospective cohort*.tw.
14. retrospective cohort*.tw.
15. case control*.tw.
16. ecological stud*.tw.
17. time series analys?s*.tw.
18. before-after stud*.tw.
19. pre-post stud*.tw.
20. follow up stud*.tw.
21. comparative stud*.tw.
22. evaluation stud*.tw.
23. dairy.mp.
24. dairy intake*.mp.

- 1
- 2
- 3 25. dairy consumption.mp.
- 4
- 5 26. dairy food*.mp.
- 6
- 7 27. Dairy Products/ or dairy product*.mp.
- 8
- 9 28. dairy serv*.mp.
- 10
- 11 29. dairy type*.mp.
- 12
- 13 30. dairy source*.mp.
- 14
- 15
- 16 31. (calcium adj15 food sourc*).mp. [mp=title, abstract, original title, name of substance word,
- 17 subject heading word, keyword heading word, protocol supplementary concept word, rare
- 18 disease supplementary concept word, unique identifier]
- 19
- 20
- 21 32. (vitamin D adj15 food sourc*).mp. [mp=title, abstract, original title, name of substance word,
- 22 subject heading word, keyword heading word, protocol supplementary concept word, rare
- 23 disease supplementary concept word, unique identifier]
- 24
- 25
- 26 33. (milk and (cow or goat or sheep)).mp. [mp=title, abstract, original title, name of substance
- 27 word, subject heading word, keyword heading word, protocol supplementary concept word, rare
- 28 disease supplementary concept word, unique identifier]
- 29
- 30
- 31 34. yogurt.mp. or Yogurt/
- 32
- 33 35. cheese.mp. or Cheese/
- 34
- 35 36. custard.mp.
- 36
- 37 37. (milk and (skim or full fat or low fat)).mp. [mp=title, abstract, original title, name of
- 38 substance word, subject heading word, keyword heading word, protocol supplementary concept
- 39 word, rare disease supplementary concept word, unique identifier]
- 40
- 41
- 42 38. (yogurt and (skim or full fat or low fat)).mp. [mp=title, abstract, original title, name of
- 43 substance word, subject heading word, keyword heading word, protocol supplementary concept
- 44 word, rare disease supplementary concept word, unique identifier]
- 45
- 46
- 47 39. Milk/
- 48
- 49 40. 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or
- 50 39
- 51
- 52 41. cardiovascular disease.mp. or exp Cardiovascular Diseases/
- 53
- 54 42. coronary*.tw.
- 55
- 56
- 57
- 58
- 59
- 60

- 1
- 2
- 3 43. heart*.tw.
- 4
- 5 44. cardia*.tw.
- 6
- 7 45. cardio*.tw.
- 8
- 9 46. myocard*.tw.
- 10
- 11 47. isch?em*.tw.
- 12
- 13 48. angina*.tw.
- 14
- 15 49. ventric*.tw.
- 16
- 17 50. tachycardi*.tw.
- 18
- 19 51. pericard*.tw.
- 20
- 21 52. endocardi*.tw.
- 22
- 23 53. atrial fibrillat*.tw.
- 24
- 25 54. arrhythmi*.tw.
- 26
- 27 55. athero*.tw.
- 28
- 29 56. arterio*.tw.
- 30
- 31 57. exp Atherosclerosis/
- 32
- 33 58. exp Arteriosclerosis/
- 34
- 35 59. HDL.tw.
- 36
- 37 60. LDL.tw.
- 38
- 39 61. VLDL.tw.
- 40
- 41 62. lipid*.tw.
- 42
- 43 63. lipoprotein*.tw.
- 44
- 45 64. triacylglycerol*.tw.
- 46
- 47 65. exp Hyperlipidemias/
- 48
- 49 66. hyperlipid*.tw.
- 50
- 51 67. hypercholesterol*.tw.
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

- 1
- 2
- 3 68. hypercholester?emia*.tw.
- 4
- 5 69. hypertriglycerid?emia*.tw.
- 6
- 7 70. exp Cholesterol/
- 8
- 9 71. cholesterol*.tw.
- 10
- 11 72. exp Stroke/
- 12
- 13 73. stroke*.tw.
- 14
- 15 74. CVA.tw.
- 16
- 17 75. cerebrovasc*.tw.
- 18
- 19 76. "vascular accident".tw.
- 20
- 21 77. TIA.tw.
- 22
- 23 78. cerebral vascular.tw.
- 24
- 25 79. thrombo*.tw.
- 26
- 27 80. emboli*.tw.
- 28
- 29 81. apoplexy.tw.
- 30
- 31 82. (brain adj2 accident*).tw.
- 32
- 33 83. ((brain* or cerebral or lacunar) adj2 infarct*).tw.
- 34
- 35 84. Hypertension/
- 36
- 37 85. exp Blood Pressure/
- 38
- 39 86. hypertensi*.tw.
- 40
- 41 87. blood pressure*.tw.
- 42
- 43 88. systolic blood pressure.tw.
- 44
- 45 89. diastolic blood pressure.tw.
- 46
- 47 90. peripheral arter* disease*.tw.
- 48
- 49 91. (coronar\$ adj5 (bypas\$ or graft\$ or disease\$ or event\$)).tw.
- 50
- 51 92. (cerebrovasc\$ or cardiovasc\$ or mortal\$ or angina\$ or stroke or strokes).tw.
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

1
2
3 93. (myocardi\$ adj5 (infarct\$ or revascular\$ or ischaemi\$ or ischemi\$)).tw.
4

5 94. (morbid\$ adj5 (heart\$ or coronar\$ or ischaem\$ or ischem\$ or myocard\$)).tw.
6

7 95. (vascular\$ adj5 (peripheral\$ or disease\$ or complication\$)).tw.
8

9 96. (heart\$ adj5 (disease\$ or attack\$ or bypass\$)).tw.
10

11 97. 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or
12 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73
13 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or
14 90 or 91 or 92 or 93 or 94 or 95 or 96
15
16

17 98. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or
18 19 or 20 or 21 or 22
19
20

21 99. 40 and 97 and 98
22

23 100. limit 99 to yr="2000 - 2019"
24

25 101. limit 100 to humans
26

27 102. limit 101 to "all adult (19 plus years)"
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary file 3: List of excluded studies and reasons for exclusion

Author	Title	Reason for Exclusion
Akbaraly, T 2013 ¹	Does overall diet in midlife predict future aging phenotypes? A cohort study	Dietary patterns only were assessed, not dairy foods
Anderson, LA 2011 ²	Dietary Patterns and Survival of Older Adults	No relevant outcomes were measured
Baylin, A 2003 ³	High 18:2 trans-fatty acids in adipose tissue are associated with increased risk of nonfatal acute myocardial infarction in Costa Rican adults	Effects of dairy foods not measured
Beydoun, MA 2018 ⁴	Dairy product consumption and its association with metabolic disturbance in a prospective study of urban adults	Groups exposed to dairy not clearly defined
Biong, AS 2006 ⁵	Intake of milk fat, reflected in adipose tissue fatty acids and risk of myocardial infarction: a case-control study	Effects of dairy foods not measured
Chen, y 2013 ⁶	Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh	Dietary patterns only were assessed, not dairy foods
Ding, M 2017 ⁷	Dairy consumption, systolic blood pressure, and risk of hypertension: Mendelian randomization study	Not an observational design study
Eguchi, E 2012 ⁸	Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study	Dietary patterns only were assessed, not dairy foods
Geleijnse, JM 2017 ⁹	Dietary Patterns in Relation to Cardiovascular Disease Incidence and Risk Markers in a Middle-Aged British Male Population: Data from the Caerphilly Prospective Study	Dietary patterns only were assessed, not dairy foods
Goldbohm, RA 2011 ¹⁰	Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in the Netherlands	No combined outcome data
Julián-Almárcegui, C 2016 ¹¹	Association of heart rate and blood pressure among European adolescents with usual food consumption: The HELENA study	Participants were adolescents, not adults
Larsson, SC 2018 ¹²	Dietary patterns, food groups, and incidence of aortic valve stenosis: A prospective cohort study	Dietary patterns only were assessed, not dairy foods
Lupton, BS 2003 ¹³	The Finnmark Intervention Study: is it possible to change CVD risk factors by community-based intervention in an Arctic village in crisis?	No combined outcome data
Meyer, J 2011 ¹⁴	Dietary patterns, subclinical inflammation, incident coronary heart disease and mortality	Dietary patterns only were assessed, not dairy foods

	in middle-aged men from the MONICA/KORA Augsburg cohort study	
Michaelsson, K 2013 ¹⁵	Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study	Dietary calcium only was assessed, not dairy foods
Oomen, CM 2000 ¹⁶	Arginine intake and risk of coronary heart disease mortality in elderly men	Effects of dairy foods not measured
Paillard, F 2015 ¹⁷	Cardiovascular risk and lifestyle habits of consumers of a phytosterol-enriched yogurt in a real-life setting	Yogurt was enriched with phytosterols
Praagman, J 2016 ¹⁸	The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort	Effects of dairy foods not measured
Streppel, MT 2014 ¹⁹	Nutrient-rich foods, cardiovascular diseases and all-cause mortality: the Rotterdam study	Dietary patterns only were assessed, not dairy foods
Umesawa, M 2006 ²⁰	Dietary intake of calcium in relation to mortality from cardiovascular disease: the JACC Study	No combined outcome data
van der Pols, J C 2009 ²¹	Childhood dairy and calcium intake and cardiovascular mortality in adulthood: 65-year follow-up of the Boyd Orr cohort	Participants were children, not adults
Warensjo, E 2009 ²²	Stroke and plasma markers of milk fat intake – a prospective nested case-control study	Effects of dairy foods not measured
Warensjo, E 2009 ²³	Milk Fat Biomarkers and the Risk of a First Ever Acute Myocardial Infarction - A Prospective Nested Case-Control Study. <i>Journal of the American Dietetic Association.</i> 2009;1	Poster presentation only, full study not available
Warensjo, E 2010 ²⁴	Biomarkers of milk fat and the risk of myocardial infarction in men and women: a prospective, matched case-control study	No combined outcome data

1. Akbaraly T, Sabia S, Hagger-Johnson G, et al. Does overall diet in midlife predict future aging phenotypes? A cohort study. *The American journal of medicine.* 2013;126(5):411-419.e413.
2. Anderson AL, Harris TB, Tylavsky FA, et al. Dietary Patterns and Survival of Older Adults. *Journal of the American Dietetic Association.* 2011;111(1):84-91.
3. Baylin A, Kabagambe EK, Ascherio A, et al. 18:2 trans-fatty acids in adipose tissue are associated with increased risk of nonfatal acute myocardial infarction in costa rican adults. *Journal of Nutrition.* 2003;133(4):1186-1191.
4. Beydoun MA, Fanelli-Kuczmarski MT, Beydoun HA, et al. Dairy product consumption and its association with metabolic disturbance in a prospective study of urban adults. *British Journal of Nutrition.* 2018;119(6):706-719.

5. Biong AS, Veierod MB, Ringstad J, et al. Intake of milk fat, reflected in adipose tissue fatty acids and risk of myocardial infarction: a case-control study. *European Journal of Clinical Nutrition*. 2006;60(2):236-244.
6. Chen Y, McClintock TR, Segers S, et al. Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh. *International Journal of Cardiology*. 2013;167(4):1495-1501.
7. Ding M, Huang T, Bergholdt HK, et al. Dairy consumption, systolic blood pressure, and risk of hypertension: Mendelian randomization study. *Bmj*. 2017;356:j1000.
8. Eguchi E, Iso H, Tanabe N, et al. Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study. *European heart journal*. 2012;33(4):467-477.
9. Geleijnse JM, Mertens E, Markey O, et al. Dietary Patterns in Relation to Cardiovascular Disease Incidence and Risk Markers in a Middle-Aged British Male Population: Data from the Caerphilly Prospective Study. *Nutrients*. 2017;9(1):75.
10. Goldbohm RA, Chorus AMJ, Galindo Garre F, et al. Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in the Netherlands. *American Journal of Clinical Nutrition*. 2011;93(3):615-627 613p.
11. Julián-Almárcegui C, Vandevijvere S, Gottrand F, et al. Association of heart rate and blood pressure among European adolescents with usual food consumption: The HELENA study. *Nutrition, Metabolism & Cardiovascular Diseases*. 2016;26(6):541-548.
12. Larsson SC, Wolk A, Bäck M. Dietary patterns, food groups, and incidence of aortic valve stenosis: A prospective cohort study. *International Journal of Cardiology*. 2018.
13. Lupton BS, Fonnebo V, Sogaard AJ, et al. The Finnmark Intervention Study: is it possible to change CVD risk factors by community-based intervention in an Arctic village in crisis? *Scandinavian Journal of Public Health*. 2003;31(3):178-186.
14. Meyer J, Doring A, Herder C, et al. Dietary patterns, subclinical inflammation, incident coronary heart disease and mortality in middle-aged men from the MONICA/KORA Augsburg cohort study. *European journal of clinical nutrition*. 2011;65(7):800-807.
15. Michaëlsson K, Melhus H, Warensjö E, et al. Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study. *Bmj*. 2013;346:f228.
16. Oomen CM, van Erk MJ, Feskens EJ, et al. Arginine intake and risk of coronary heart disease mortality in elderly men. *Arteriosclerosis, thrombosis, and vascular biology*. 2000;20(9):2134-2139.
17. Paillard F, Bruckert E, Naelten G, et al. Cardiovascular risk and lifestyle habits of consumers of a phytosterol-enriched yogurt in a real-life setting. *Journal of Human Nutrition & Dietetics*. 2015;28(3):226-235 210p.
18. Praagman J, Beulens JW, Alsema M, et al. The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort. *American Journal of Clinical Nutrition*. 2016;103(2):356-365.
19. Streppel MT, Sluik D, van Yperen JF, et al. Nutrient-rich foods, cardiovascular diseases and all-cause mortality: the Rotterdam study. *European journal of clinical nutrition*. 2014;68(6):741-747.
20. Umesawa M, Iso H, Date C, et al. Dietary intake of calcium in relation to mortality from cardiovascular disease: the JACC Study. *Stroke*. 2006;37(1):20-26.
21. van der Pols JC, Gunnell D, Williams GM, et al. Childhood dairy and calcium intake and cardiovascular mortality in adulthood: 65-year follow-up of the Boyd Orr cohort. *Heart*. 2009;95(19):1600-1606.
22. Warensjö E, Smedman A, Stegmayr B, et al. Stroke and plasma markers of milk fat intake--a prospective nested case-control study. *Nutrition Journal*. 2009;8:21.

- 1
2
3 23. Warensjo E, Sjogren P, Cederholm T, et al. Milk Fat Biomarkers and the Risk of a First Ever
4 Acute Myocardial Infarction - A Prospective Nested Case-Control Study. *Journal of the*
5 *American Dietetic Association*. 2009;109(9, Supplement):A51.
6 24. Warensjö E, Jansson JH, Cederholm T, et al. Biomarkers of milk fat and the risk of myocardial
7 infarction in men and women: a prospective, matched case-control study. *American Journal of*
8 *Clinical Nutrition*. 2010;92(1):194-202 199p.
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary file 4: Characteristics of included studies

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Verbatim)	Funding Source	Disclosed author conflicts of interest
Aerde, M 2013 ⁽¹⁾	Cohort	12.4 years	1,956 men & women	61.6 years	Total Dairy, 271 g/day per SD of the mean intake for Total dairy (all dairy products except butter)		Fatal CVD	Non-Industry ¹	Yes ^a
Al-Delaimy, WK 2003 ⁽²⁾	Cohort	12 years	39,800 men	40-75 years	Dairy Calcium Q5, 819 mg/day (median) (dairy calcium intake summed the calcium intake from whole milk, skim or low-fat milk, yogurt, ice cream, cottage cheese, and other cheese was summed)	Q1, 106 mg/day	Fatal Ischemic Heart Disease	Non Industry ²	No ^b
Alonso A, 2005 ⁽³⁾	Cohort	27 months	5,880 men & women	37 years	Dairy Q 5, 798.8 g/day (whole-fat milk, partially skim milk, skim milk, condensed milk, whipped cream, yogurt, skim yogurt, milk-shake, cottage cheese or junket, petit Suisse cheese, spreadable cheese wedges, soft unripened cheese, other cheese, custard, and ice cream)	Q 1, 155.6 g/day	Hypertension	Non-industry ³	No ^c

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Altorf-van der Kuil, W2012 ⁽⁴⁾	Cohort	Mean follow up 7.5 years	3,588 men & women	44 years	Dairy Protein T3, ≥ 27 g/day (dairy protein was calculated as protein from milk, yogurt, coffee creamer, curd, pudding, porridge, custard, whipped cream and cheese)	T1, ≤ 19 g/day	Hypertension	Industry ⁴	Yes ^d
Avalos, EE 2013 ⁽⁵⁾	Cohort	Mean follow up 16.2 years	1,759 men & women	70.6 years men, 70.1 women	Whole Milk, Non-Fat Milk, Yogurt & Cheese, Sometimes/often (included daily, 4–6 times/week, 1–3 times/week and 1–3 times/months)	Rarely/never (included never & 1–11 times/year)	Incident CHD	Non-industry ⁵	No ^e
Bernstein, AM 2012 ⁽⁶⁾	2 Cohorts	26 and 22 years of follow-up in women and men, respectively	127,160 (43 150 men 84 010 women)	Men 40 to 75 years, Woman 30 to 55 years	Whole Fat Q 5, Men 2.55 servings/day, Woman 2.81 servings/day (whole milk, ice cream, hard cheese, full fat cheese, cream, sour cream, cream cheese, butter) Low Fat Q5, Men 2.64 servings/day, Women 2.20 servings/day (skim/low-fat milk, 1% and 2% milk, yogurt, cottage and ricotta cheeses, low-fat cheese, sherbet)	Q 1, Men 0.21 servings/day, Woman 0.34 servings/day. Low Fat Q1, Men 0.11 servings/day, Women 0.07 servings/day	Total Stroke	Non-industry ⁶	Yes ^f
Biong, A 2008 ⁽⁷⁾	Case Control		218 men & women	62.4 years	Dairy Fat, > 34.1 g/day	<14.6 g/day	First Myocardial Infarction	Industry ⁷	Yes ^g

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Bonthuis, M 2010 ⁽⁸⁾	Cohort	Mean 14.4 years	1,529 men & women	25–78 years	Total Dairy T3, 599 g/day (median) ('low-fat dairy products was computed by adding daily servings (in grams) of skim milk, low-fat milk, low-fat yoghurt, cottage or ricotta cheese, whereas the food group 'high-fat/unmodified dairy' included whole milk, cream, ice cream, yoghurt, full-fat cheese and custard. Total dairy intake was the sum of intake of all these dairy foods)	T1, 174 g/day	Cardiovascular Disease Mortality	Non-Industry ⁸	No ^h
Buendia, JR 2018 ⁽⁹⁾	3 Cohorts	30 years of follow-up in NHS, 20 years in NHS II, 24 years in the HPFS	NHS (N=69298), NHS II (N=84368), HPFS (N=30512)	Mean baseline ages in the 3 cohorts were 44.6, 35.8, and 50.7 years, respectively	Total Dairy Q4, 3 - <6 servings/day (total dairy intake included: milk (skim, low-fat, whole), ice cream, sherbet/ frozen yogurt, cheese (cottage, ricotta, hard, sliced), and yogurt (all types)	Q1, <0.5 servings/day	High Blood Pressure	Industry ⁹	No ⁱ
Chen, M 2016 ⁽¹⁰⁾	3 Cohorts	24 years in the HPFS, 32 years NHS, 20 years in NHS II	222,234 - 43,652 men HPFS, 87,907 women NHS, 90,675 women NHS II	40–75 years HPFS, 30–55 years NHS, 25–42 y NHS II	Dairy Fat, Q5	Q1	VD	Non-Industry ¹⁰	No ⁱ

36/bmjopen-2020-039132 on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Dalmeijer, G 2013 ⁽¹¹⁾	Cohort	13 years	33,625 men & women	49.0 years	Total dairy and its subtypes were evaluated as continuous variables per standard deviation of the mean intake which is 265 g/d for total dairy (total dairy included all dairy food products except for butter and ice cream. Milk and milk products included all kinds of milk, yogurt, coffee creamers, curd, pudding, porridge, custard, and whipping cream)		Incident of Coronary Heart Disease & Incident Stroke	Non-Industry ¹¹	Yes ^k
Dauchet, L 2007 ⁽¹²⁾	Cohort	5.4 years	2,341 men & women	Men 52.7 years, Women 46.9 years	Dairy Q4, 456 g/day (dairy products including milk, cheese, yogurt, and other dairy products)	Q1, 84 g/day	Systolic & Diastolic Blood Pressure	Non-Industry ¹²	No ^l

36/bmjopen-2020-039138 on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Deign	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Dehghan, M 2018 ⁽¹³⁾	Cohort	9.1 yrs	136,384 men & women	50·1 years	Dairy Q4, >2 servings/day (median) (dairy comprised milk, yoghurt, various types of cheese, yoghurt drink, and mixed dishes prepared with dairy. Mixed dishes prepared with dairy were dis- aggregated into their constituents and a proportional weight was assigned to each component. Then each component was included in the related dairy group.	Q1, 0 servings/day	Cardiovascular Mortality or Major Events	Industry ¹³	No ^m
Elwood, PC 2004 ⁽¹⁴⁾	Cohort	20-24 years	2,403 men	45-59 years	Milk Q4, >1 pint per day	Q1, None	ascular Event	Non-Industry ¹⁴	No disclosure

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Engberink, MF 2009 ⁽¹⁵⁾	Cohort	6 years	2,245 men & women	>55 years	Dairy Q4, 691 g/day (i.e. 4.5 servings/day) (median intake) (calculated total dairy intake by summing the intake of individual dairy items, except butter and ice cream. The category "milk and milk products" included all kinds of milk, yogurt, coffee creamer, curd, pudding, porridge, custard, and whipped cream. The category "cheese" included all kinds of cheese products, ie, soft cheese, hard cheese, and cheese spreads)	Q1, 164 g/day (i.e. 1 serving/day) (median intake)	Hypertension	No disclosure	No ⁿ
Farvid, MS 2017 ⁽¹⁶⁾	Cohort	8 years	42,403 men & women	51.6 years	Total Dairy Q5, 2.4 servings/day (median) (total dairy product items listed in the food frequency questionnaire included milk, cheese, yogurt, liquid yogurt (doogh), dried yogurt paste (kashk), and cream)	Q1, 0.4 servings/day (median)	Cardiovascular Disease Mortality	Non-Industry ¹⁵	No ^o
Haring, B 2014 ⁽¹⁷⁾	Cohort	22 years (median)	12,066 men & women	45-64 years	Dairy Protein Q5, 2.9 servings/day	Q1, 0.1 median servings/day	Coronary Heart Disease	Non-Industry ¹⁶	No ^p
He, K 2003 ⁽¹⁸⁾	Cohort	14 years	43,732 men	40-75 years	High Fat Dairy Q5, ≥1/day	Q1, <1/week	Thrombotic & Haemorrhagic Stroke	Non-Industry ¹⁷	No ^q

36/bmjopen-2020-039136 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> by guest. Protected by copyright.

Study ID	Study Deign	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Heraclides, A 2012 ⁽¹⁹⁾	Cohort	10 years	1,750 men & women	Men 43 years, Women 53 years	Total Dairy T3, 309.0 g/day (median) (full-fat milk; semi-skimmed milk; skimmed milk; milk-containing beverages (full fat, semi-skimmed and skimmed); full-fat cheese; low-fat cheese; full-fat yoghurt; low-fat yoghurt; fruit-flavoured yoghurt (full fat and low fat); and milk-based puddings)	T1, 224.1 g/day	Incident Hypertension	Non-Industry ¹⁸	Yes ^r
Johansson, I 2018 ⁽²⁰⁾	Cohort	8-12 years	27,682 men & women	29-65 years	Dairy Q 5, 7.1 servings/day (median)	Q1, 1.6 servings/day (median)	Blood Pressure	Non-Industry ¹⁹	No ^s
Johansson, I 2019 ⁽²¹⁾	Cohort	14.2 years	108,065 men & women	calculated mean = 52.5 years *	High Fat & Low Fat Non-Fermented Milk & Cheese Q 4, high dose	Q1, low dose	Myocardial Infarction & Stroke	Non-Industry ²⁰	No ^t
Kim, D 2017 ⁽²²⁾	Cohort	67·4 months	4,335 men & women	40-69 years	Total Dairy Q 5, >7 servings/week	Q 1, <1 servings/week	Blood Pressure	Non-Industry ²¹	No ^u
Larsson,S 2009 ⁽²³⁾	Cohort	13.6 years	26,556 men	50-69 years	Dairy Q5, 1295.6 g/day (median) (including low-fat milk, whole milk, sour milk, yogurt, cheese, cream, ice cream, and butter)	Q1 286.5 g/day	Cerebral Infarction, Intracerebral Haemorrhage, Subarachnoid Hemorrhage	Non-Industry ²²	No disclosure

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Larsson, SC 2012 ⁽²⁴⁾	Cohort	10.2 years	74,961 men & women	45-83 years	Dairy Q5, 9.3 servings/day (median) (dairy foods included low-fat milk (0.5% fat), medium-fat milk (1.5% fat), full-fat milk (3% fat), milk in pancakes, low-fat sour milk/yogurt (0.5% fat), full-fat sour milk/yogurt (3% fat), cottage cheese (4% fat), low-fat cheese (10%-17% fat), full-fat cheese (approximately 28% fat), ice cream, cream, and creme fraiche)	Q1, 2.3 servings/day	Total Stroke	Non-Industry ²³	No ^v
Li, K 2012 ⁽²⁵⁾	Cohort	11 years	23,980 men & women	35-64 years	Dairy Calcium Q4, 780 mg/day	Q1, 188 mg/day	CVD Mortality	Non-Industry ²⁴	No ^w
Lin, PH 2013 ⁽²⁶⁾	Cohort	12 years	2,061 men & women	45.8 years (no information for stroke group)	Dairy T3, (dairy milk of any kind, cheese, yogurt).	T1	Total Stroke	Non-Industry ²⁵	No ^x
Lockheart, MSK 2007 ⁽²⁷⁾	Case Control		211 men & women	62.5 years cases and 62.2 years controls	Low Fat Dairy T3, 618 g/day (Low-fat milk, skimmed milk, light sour cream)	T 1, 48 g/day	First Myocardial Infarction	Industry ²⁶	No disclosure
Louie, JCY 2013 ⁽²⁸⁾	Cohort	15 years	2,625 men & women	49-97 years	Total Dairy T3, 2.9 servings/day (median) (included all dairy foods)	T1, 0.6 servings/day	Total CVD	Industry ²⁷	No disclosure
Mazidi, M, 2018 ⁽²⁹⁾	Cohort	76.4 months	24,474 men & women	47.6 years	Total Dairy Q4, 3.08 cup equivalent servings/day (total dairy, milk, cheese, and yogurt)	Q1, 0.25 cup equivalent servings/day	CHD Mortality Cerebrovascular Disease mortality	Non-Industry ²⁸	No ^y

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Ness, AR 2001 ⁽³⁰⁾	Cohort	25 years	5,765 men	35-64 years	Milk T3, > 1 pint (= 0.568 liters)	T1, None	Cardiovascular Disease Deaths	Non-Industry ²⁹	No ^z
Nettleton, J 2008 ⁽³¹⁾	Cohort	13.3 years	14,153 men & women	45 to 64 years	High Fat Dairy, per 1 daily serving difference in food group intake		Incident Heart Failure	Non Industry ³⁰	No ^{aa}
Panagiotakos, D 2009 ⁽³²⁾	Cohort	5 years	3,042 men & women	18-89 years	Low Fat Dairy, 1-unit increase in components' scores (0%, 2% or total fat), like cheese, yogurt, milk)		CVD Events	Non-Industry ³¹	No disclosure
Patterson, E 2013 ⁽³³⁾	Cohort	11.6 years	33,636 women	48-83 years	Total Dairy, Q5 8.4 servings/day (median) (total dairy intake was the sum of milk [full-fat ($\geq 3.0\%$ fat), semi-skimmed ($\leq 1.5\%$ fat), skimmed (0.5% fat), and pancakes], cultured milk/yogurt [full-fat ($\geq 3.0\%$ fat) and low-fat ($\leq 1.5\%$ fat)], cheese [full-fat ($>17\%$ fat), low-fat ($\leq 17\%$ fat), and cottage cheese/ quark], cream and creme fariche (full fat and low fat) intakes)	Q1, 2.2 servings/day	Myocardial Infarction	Non Industry ³²	No ^{bb}
Praagman, J 2015 (a) ⁽³⁴⁾	Cohort	13.3 years (median)	4,235 men & women	66.9 years	Total Dairy, T3 >400g/day (total dairy included milk, buttermilk, yogurt, coffee creamer, curd, pudding, porridge, custard, whipped cream, ice cream, and cheese, but not butter)	Total Dairy, T 1 <200 g/day	Fatal Stroke & Fatal CHD	Industry ³³	Yes ^{cc}

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Praagman, J 2015 (b) ⁽³⁵⁾	Cohort	15 years	34,409 men & women	Men 51 years & women 43 years	Total Yogurt & Cheese Q4, (fermented dairy foods)	Q1	CVD Mortality	Non-Industry ³⁴	Yes ^{dd}
Sauvaget, C 2003 ⁽³⁶⁾	Cohort	16 years	37,130 men & women	56 years	Dairy Q4, Almost Daily (dairy products (butter and cheese, excluding margarine))	Q1, Never	Total Stroke	Non-Industry ³⁵	No disclosure
Snijder, MB 2008 ⁽³⁷⁾	Cohort	6.4 years	1,124 men & women	50–75 years	Dairy Q4, 5.75-17.24 servings/day (range) (total dairy consumption was categorized as low-fat dairy ($\leq 2\%$ fat) or high-fat dairy ($> 2\%$ fat). The variable dairy desserts included yoghurt, curds, and custard. The variable milk included low-fat, skim, and, whole milk. The variable yoghurt included all low-fat, skim, and whole yoghurts)	Q1 0-2.97 servings/day (range)	Systolic & Diastolic Blood Pressure	Industry ³⁶	Yes ^{ee}
Soedamah-Muthu, SS 2013 ⁽³⁸⁾	Cohort	10.8 years	4,255 men & women	56 years	Dairy, T3 575 g/day (median) (all dairy products, except butter and ice cream)	T1, 246 g/day (median)	Fatal & Non-Fatal CHD	Non-Industry ³⁷	Yes ^{ff}
Steffen, LM 2005 ⁽³⁹⁾	Cohort	15 years	4,304 men & women	18-30 years	Dairy Foods Q5, > 3.4 times/day (dairy foods, including milk, cheese, yogurt, and dairy desserts)	Q1, < 1.1 times/day	Blood Pressure	Non-Industry ³⁸	No ^{gg}

36/bmjopen-2020-039139 on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Tavani, A 2002 ⁽⁴⁰⁾	Case Control		985 men & women	61 years (median)	Total milk >7 cups/week, Yogurt >= 7 portions/week, Cheese >=350g/week	Total milk 0 cups/week, Yogurt 0 portions/week, Cheese <200g/week	Acute Myocardial Infarction	Non-Industry ³⁹	No ^{hh}
Um, C 2017 ⁽⁴¹⁾	Cohort	5.7 years of follow-up	21,427 men & women	calculated mean = 64.8 years**	Total Dairy Q5, 17.8 servings/day (dairy products (milk, cream, fermented dairy products, ice cream, butter, cheeses))	Q1, 0.9 servings/day	CVD Mortality	Non-Industry ⁴⁰	No ⁱⁱ
Umesawa, M, 2008 ⁽⁴²⁾	Cohort	12.9-year follow-up	41,526 men & women	40-59 years	Dairy Calcium, Q5, 116 mg/day (median) (to calculate dairy calcium intake, we specified 2 kinds of dairy products, ie, cheese and dairy products except cheese, for the baseline questionnaire, and 4 kinds, ie, whole milk, low fat milk, cheese, and yogurt, for the 5-year follow-up questionnaire)	Q1, 0 mg/day	Total Stroke & CHD	Non-Industry ⁴¹	No ^{jj}

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

36/bmjopen-2020-039138 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Deign	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Wang,L 2008 ⁽⁴³⁾	Cohort	10 years	28,886 women	53.8 years	Total Dairy Q5, 3.69 servings/day (median) (total dairy product intake was calculated by summing the intake of individual dairy items: low-fat dairy items include skim or low-fat milk, sherbet, yogurt, and cottage/ricotta cheese, high-fat dairy items include whole milk, cream, sour cream, ice cream, cream cheese, and other cheese)	Q1, 0.56 servings/day (median)	Hypertension	Non-Industry ⁴²	No ^{kk}

* We calculated the mean age score of participants by summing Non-cases, T2D, MI and stroke cases at baseline and dividing them by 4

**We calculated the mean age score of participants by summing all quintiles 1, 3, & 5 (they were the only ones available) at baseline and dividing them by 5

Description of Funding Source (Verbatim)

1. The Hoorn Study has been made possible by the Vrije Universiteit Amsterdam and the VU University Medical Center, and by grants from the Dutch Diabetes Research Foundation, the Dutch Organization for Scientific Research, the Netherlands Heart Foundation, and the Health Research and Development Council of the Netherlands.
2. Supported by research grants HL24074, HL34594, DK36798, and CA87969 from the National Institutes of Health.
3. Supported by the Spanish Ministry of Health (grants PI040233 and G03-140), the Navarra Regional Government (141-2005), and the University of Navarra (línea especial Nutricio LE-97). AA was supported partially by a Fulbright fellowship and an MMA Foundation grant.
4. The Doetinchem Cohort Study was financially supported by the Ministry of Health, Welfare and Sport of the Netherlands and the National Institute for Public Health and the Environment. For the present analysis, Wageningen University was supported by the Top Institute Food and Nutrition, which is a public/private partnership that generates vision on scientific breakthroughs in food and nutrition, resulting in the development of innovative products and technologies. Partners are major Dutch Food companies and research organisations.
5. The study was supported by grants AG007181 and AG028507 from the National Institutes of Health/National Institute on Aging, and by grant DK31801 from the National Institute of Diabetes and Digestive and Kidney Diseases.
6. This study was supported by grant P01CA087969 from the National Institutes of Health, Department of Health and Human Services. A.M.B. was supported through the Harvard Human Nutrition Program.
7. The study was supported financially by the Research Council of Norway, Throne Holst's Foundation for Nutrition Research, The Norwegian Association of Margarine Producers, DeNoFa Fabrikker A/S and Tine BA. Tine BA is a dairy company.
8. This study was supported by the National Health and Medical Research Council of Australia.
9. Funding sources: The Nurses' Health Study and Health Professionals Follow-up Study cohorts are supported by grants UM1 CA186107, UM1 CA176726, and UM1 CA167552 from the National Institutes of Health. The current analyses were supported by small grants from the National Dairy Council, the General Mills Bell Institute for Health and Nutrition, and the Boston Nutrition and Obesity Research Center.
10. Supported by the NIH (grants R01 HL034594, UM1 CA176726, UM1 CA186107, R01 HL35464, R01 HL088521, R01 CA67262, HL60712, and UM1 CA167552).
11. This research was supported by a personal Dr. Dekker postdoctoral grant (2008T062) from The Netherlands Heart Foundation (JWJ Beulens).
12. The SU.VI.MAX study is supported by the Direction Générale de la Santé, the Ministère de la Santé, and the Institut Virtuel de Recherche en Santé Publique (groupe cohorte) INSERM.
13. The PURE Study is an investigator-initiated study that is funded by the Population Health Research Institute, the Canadian Institutes of Health Research (CIHR), Heart and Stroke Foundation of Ontario, support from CIHR's Strategy for Patient Oriented Research (SPOR) through the Ontario SPOR Support Unit, as well as the Ontario Ministry of Health and Long-Term Care and through unrestricted grants from several pharmaceutical companies, with major contributions from AstraZeneca (Canada), Sanofi-Aventis (France and Canada), Boehringer Ingelheim (Germany and Canada), Servier, and GlaxoSmithKline, and additional contributions from Novartis and King Pharma and from various

- national or local organisations in participating countries. These include Brazil: Unilever Health Institute, Brazil; South Africa: The SA Sugar Association (SASA).
14. The Medical Research Council, the University of Wales College of Medicine and Bristol University, Food Standards Agency.
 15. This work was supported by Tehran University of Medical Sciences (grant 82-603); Cancer Research UK (grant C20/A5860); the Intramural Research Program of the National Cancer Institute, US National Institutes of Health (grant Z01 CP000185-03); and various collaborative research agreements with the International Agency for Research on Cancer. M.F. was supported by a Takemi Fellowship from the Japan Pharmaceutical Manufacturers Association.
 16. The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C).
 17. This work was supported by the research grant HL35464 and CA55075 from the National Institutes of Health.
 18. The study was funded by the Medical Research Council, and some aspects of the analysis were funded by The European Commission, Quality of Life and Management of Living Resources Programme, contract number QLGI-CT-2000-01643.
 19. The present study was supported by the Swedish Research Council for Health, Working Life and Welfare (FORTE).
 20. This research was funded by The Swedish Research Council for Health, Working Life and Welfare (FORTE), grant number 2016-00960. The Northern Sweden Diet Database has been supported by the Swedish Research Council for Health, Working Life and Welfare (FORTES) and The Swedish Research Council.
 21. This research was supported by the Basic Science Research Program of the National Research Foundation of Korea (NRF), funded by the Ministry of Education, Science, and Technology (NRF2016R1D1A1B03931307).
 22. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study was supported by Public Health Service contracts N01-CN-45165, N01-RC-45035 and N01-RC-37004 from the US National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Md. Dr. Larsson's research at the National Public Health Institute in Helsinki, Finland, was supported by a grant from the Swedish Council for Working Life and Social Research.
 23. This study was supported by a research grant from the Swedish Council for Working Life and Social Research (FA), the Swedish Research Council, and by a Research Fellow grant from Karolinska Institutet (to Dr Larsson).
 24. This work was supported by supported by the Deutsche Krebshilfe (grant-No70-488-Ha I) and the Graduiertenkolleg 793: Epidemiology of communicable and chronic non-communicable disease and their inter-relationships.
 25. Data collection was supported by the Department of Health in Taiwan.
 26. The present study was supported by NIH NRSA T32HL007779, CVD Epidemiology and Prevention, American Heart Association – Greater Midwest Affiliate, Throne Holst's Foundation for Nutrition Research, The Norwegian Association of Margarine Producers, DeNoFa Fabriker A/S and Tine Norwegian Dairies.
 27. This study was funded by Dairy Australia.

- 1
2
3 28. This manuscript was written independently; no company or institution supported it financially.
4 29. Funding: this study was provided with funding by a grant from the NHS Management Executive Cardiovascular Disease and Stroke Research
5 and Development Initiative.
6
7 30. This research was supported by the National Institutes of Health grant HL73366, training grant T32 HL07779, and contracts N01-HC-55015,
8 N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, and N01-HC-55022 from the National Heart, Lung, and
9 Blood Institute.
10
11 31. The ATTICA study was supported by research grants from the Hellenic Cardiological Society (HCS2002).
12 32. Supported by research grants from the Swedish Council for Working Life and Social Research and from the Swedish Research
13 Council/Infrastructure Medicine.
14 33. This study was supported by an unrestricted grant from the Dutch Dairy Organization (NZO) for epidemiological analyses on dairy intake and
15 cardiovascular diseases.
16 34. The present study was supported by a personal Dr Dekker postdoctoral grant (2008T062) from the Netherlands Heart Foundation (J. W. J. B.).
17 35. This publication is based on research performed at the Radiation Effects Research Foundation (RERF), Hiroshima and Nagasaki, Japan. RERF
18 is a private nonprofit foundation funded equally by the Japanese Ministry of Health, Labor and Welfare and the US Department of Energy
19 through the National Academy of Sciences.
20
21 36. This particular study has been supported by a grant from the Dutch Dairy Association (NZO).
22 37. The Whitehall II study was supported by grants from the Medical Research Council (G0902037), the British Heart Foundation (RG/07/
23 008/23674), the Stroke Association, the National Heart Lung and Blood Institute (5RO1 HL036310), the National Institute on Aging
24 (5RO1AG13196) and the Agency for Health Care Policy Research (5RO1AG034454).
25
26 38. The CARDIA Study is supported by National Heart, Lung, and Blood Institute contracts N01-HC-48047, N01-HC-48048, N01-HC-48049,
27 N01- HC-48050, and N01-HC-95095.
28
29 39. Funding: partly supported by the Italian Ministry of Health (Programmi Speciali).
30 40. The REGARDS research project is supported by a cooperative agreement U01 NS041588 from the National Institute of Neurological
31 Disorders and Stroke, National Institutes of Health, Department of Health and Human Service. Additional support provided by the Franklin
32 Foundation.
33
34 41. This study was supported by grants-in-aid for cancer research and by the Third Term Comprehensive Ten-Year Strategy for Cancer Control
35 from the Ministry of Health, Labor and Welfare of Japan.
36 42. This work was supported by research grants CA-047988 and HL-080467 from the National Institutes of Health, Bethesda, Md.

Description of Author Disclosure Statement (Verbatim)

- 1
- 2
- 3 a) Sabita S. Soedamah-Muthu and Johanna M. Geleijnse obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out
- 4 meta-analyses on the association between dairy products and CVD.
- 5
- 6 b) None of the authors had any conflict of interest from a financial, personal, or professional aspect in relation to the findings of this study.
- 7
- 8 c) None of the authors had any conflicts of interest.
- 9
- 10 d) Altorf-van der Kuil W, Engberink MF, Geleijnse JM - Top Institute Food and Nutrition, PO Box 557, 6700 AN, Wageningen, The
- 11 Netherlands.
- 12 e) The authors have no conflicts of interest.
- 13 f) D.M. received research grants for studying the effects of diet on cardiometabolic diseases from the National Institutes of Health; the Searle
- 14 Scholar Award from the Searle Funds at The Chicago Community Trust; the Genes and Environment Initiative at the Harvard School of
- 15 Public Health; and the Gates Foundation/World Health Organization Global Burden of Diseases, Injuries, and Risk Factors Study; and from
- 16 GlaxoSmithKline, Sigma Tau, Pronova, and the National Institutes of Health for an investigator-initiated, not-for-profit clinical trial of fish oil
- 17 and postsurgical complications. He also received ad hoc travel reimbursement and/or honoraria for research presentations from the Chicago
- 18 Council, International Life Sciences Institute, Aramark, Unilever, SPRIM, Nutrition Impact, Norwegian Seafood Export Council, United
- 19 Nations Food and Agricultural Organization, World Health Organization, US Food and Drug Administration, and several universities. He
- 20 received ad hoc consulting fees from Foodminds and royalties from UpToDate for an online chapter on fish oil.
- 21 g) A. S. Biong is employed as a Ph.D. student in a research project funded jointly by TINE BA, a Norwegian dairy company, and the Norwegian
- 22 Research Council.
- 23
- 24 h) The authors declare no conflict of interest.
- 25
- 26 i) There are no conflicts of interest.
- 27
- 28 j) None of the authors reported a conflict of interest related to the study.
- 29
- 30 k) SS-Mand MG obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out meta-analyses on the association between
- 31 dairy products and cardiovascular diseases.
- 32
- 33 l) None of the authors had any personal or financial conflicts of interest.
- 34
- 35 m) We declare no competing interests.
- 36
- 37 n) There were no conflicts of interest.
- 38
- 39 o) Conflict of interest: none declared
- 40
- 41 p) The authors have declared that no competing interests exist.
- 42
- 43 q) Competing interests: None declared.
- 44
- 45 r) SSM, JMG and AH and were supported by an unrestricted grant from the Dutch dairy industry (NZO).
- 46
- 47 s) The authors declare that they have no competing interests.
- t) The authors declare no conflict of interest
- u) The authors have no conflicts of interest to declare.

- 1
2
3 v) Disclosures: None.
4 w) Competing interests None.
5 x) AUTHOR DISCLOSURES None.
6 y) All authors have nothing to declare in relation to the subject of this paper.
7 z) Conflicts of interest: none.
8
9 aa) The authors have no conflicts of interest to report.
10 bb) Author disclosures: E. Patterson, S. C. Larsson, A. Wolk, and A. A kesson, no conflicts of interest.
11 cc) J.M.G and S.S.S.M received an unrestricted grant from the Dutch Dairy Organization (NZO) for epidemiological analyses on dairy intake and
12 cardiovascular diseases.
13 dd) S. S. S. M. received an unrestricted research grant from the Global Dairy Platform, Dairy Research Institute and Dairy Australia for a meta-
14 analysis project on the effect of cheese on lipids.
15 ee) Gerrit J. Hiddink - Dutch Dairy Association (NZO), Zoetermeer, The Netherlands.
16 ff) S. S. S.-M., L. V. and J. M. G. obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out meta-analyses on the
17 association between dairy products.
18 gg) None of the authors had any conflicts of interest.
19 hh) Conflicts of interest: none.
20 ii) Conflict of Interests: None.
21 jj) Disclosures: None.
22 kk) Disclosures: None.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

References

1. Aerde M, Soedamah-Muthu S, Geleijnse J, et al. Dairy intake in relation to cardiovascular disease mortality and all-cause mortality: the Hoorn Study. *European Journal of Nutrition*. 2013;52(2):609-16 8p.
2. Al-Delaimy WK, Rimm E, Willett WC, et al. A prospective study of calcium intake from diet and supplements and risk of ischemic heart disease among men. *American Journal of Clinical Nutrition*. 2003;77(4):814-8 5p.
3. Alonso A, Beunza JJ, Delgado-Rodriguez M, et al. Low-fat dairy consumption and reduced risk of hypertension in the Seguimiento Universidad de Navarra (SUN) cohort. *American Journal of Clinical Nutrition*. 2005;82(5):972-9.
4. Altorf-van der Kuil W, Engberink MF, Geleijnse JM, et al. Sources of dietary protein and risk of hypertension in a general Dutch population. *British Journal of Nutrition*. 2012;108(10):1897-903 7p.
5. Avalos EE, Barrett-Connor E, Kritiz-Silverstein D, et al. Is dairy product consumption associated with the incidence of CHD? *Public health nutrition*. 2013;16(11):2055-63.
6. Bernstein AM, Pan A, Rexrode KM, et al. Dietary protein sources and the risk of stroke in men and women. *Stroke*. 2012;43(3):637-44.
7. Biong AS, Rebnord HM, Fimreite RL, et al. Intake of dairy fat and dairy products, and risk of myocardial infarction: A case-control study. *International Journal of Food Sciences and Nutrition*. 2008;59(2):155-65.
8. Bonthuis M, Hughes MCB, Ibiebele TI, et al. Dairy consumption and patterns of mortality of Australian adults. *European journal of clinical nutrition*. 2010;64(6):569-77.
9. Buendia JR, Yanping L, Hu FB, et al. Long-term yogurt consumption and risk of incident hypertension in adults. *Journal of Hypertension*. 2018;36(8):1671-9.
10. Chen M, Li Y, Sun Q, et al. Dairy fat and risk of cardiovascular disease in 3 cohorts of US adults. *American Journal of Clinical Nutrition*. 2016;104(5):1209-17.
11. Dalmeijer GW, Struijk EA, van der Schouw YT, et al. Dairy intake and coronary heart disease or stroke—A population-based cohort study. *International Journal of Cardiology*. 2013;167(3):925-9.
12. Dauchet L, Kesse-Guyot E, Czernichow S, et al. Dietary patterns and blood pressure change over 5-y follow-up in the SU.VI.MAX cohort. *The American journal of clinical nutrition*. 2007;85(6):1650-6.
13. Dehghan M, Mente A, Rangarajan S, et al. Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. *Lancet*. 2018;392 North American Edition(10161):2288-97.
14. Elwood PC, Pickering JE, Fehily AM, et al. Milk drinking, ischaemic heart disease and ischaemic stroke I. Evidence from the Caerphilly cohort. *European Journal of Clinical Nutrition*. 2004;58(5):711-7.
15. Engberink MF, Hendriksen MA, Schouten EG, et al. Inverse association between dairy intake and hypertension: the Rotterdam Study. *The American journal of clinical nutrition*. 2009;89(6):1877-83.
16. Farvid MS, Malekshah AF, Pourshams A, et al. Dairy Food Intake and All-Cause, Cardiovascular Disease, and Cancer Mortality. *American Journal of Epidemiology*. 2017;185(8):697-711.

17. Haring B, Gronroos N, Nettleton JA, et al. Dietary Protein Intake and Coronary Heart Disease in a Large Community Based Cohort: Results from the Atherosclerosis Risk in Communities (ARIC) Study. *PloS one*. 2014;9(10):e109552.
18. He K, Merchant A, Rimm EB, Rosner BA, et al. Dietary fat intake and risk of stroke in male US healthcare professionals: 14 year prospective cohort study. *BMJ*. 2003;327(7418):777-82.
19. Heraclides A, Mishra GD, Hardy RJ, et al. Dairy intake, blood pressure and incident hypertension in a general British population: the 1946 birth cohort. *European journal of nutrition*. 2012;51(5):583-91.
20. Johansson I, Nilsson LM, Esberg A, et al. Dairy intake revisited - associations between dairy intake and lifestyle related cardio-metabolic risk factors in a high milk consuming population. *Nutrition Journal*. 2018;17(1):N.PAG-N.PAG.
21. Johansson I, Esberg A, Nilsson LM, et al. Dairy Product Intake and Cardiometabolic Diseases in Northern Sweden: A 33-Year Prospective Cohort Study. *Nutrients*. 2019;11(2):284.
22. Kim D, Kim J. Dairy consumption is associated with a lower incidence of the metabolic syndrome in middle-aged and older Korean adults: the Korean Genome and Epidemiology Study (KoGES). *British Journal of Nutrition*. 2017;117(1):148-60.
23. Larsson SC, Männistö S, Virtanen MJ, et al. Dairy foods and risk of stroke. *Epidemiology (Cambridge, Mass)* [Internet]. 2009; 20(3):[355-60 pp.]. Available from: <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/629/CN-00701629/frame.html>.
24. Larsson SC, Virtamo J, Wolk A. Dairy consumption and risk of stroke in Swedish women and men. *Stroke*. 2012;43(7):1775-80.
25. Li K, Kaaks R, Linseisen J, et al. Associations of dietary calcium intake and calcium supplementation with myocardial infarction and stroke risk and overall cardiovascular mortality in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition study (EPIC-Heidelberg). *Heart*. 2012;98(12):920-5.
26. Lin PH, Yeh WT, Svetkey LP, et al. Dietary intakes consistent with the DASH dietary pattern reduce blood pressure increase with age and risk for stroke in a Chinese population. *Asia Pacific journal of clinical nutrition*. 2013;22(3):482-91.
27. Lockheart MSK, Steffen LM, Rebnord HM, et al. Dietary patterns, food groups and myocardial infarction: a case-control study. *British Journal of Nutrition*. 2007;98(2):380-7.
28. Louie JCY, Flood VM, Burlutsky G, et al. Dairy consumption and the risk of 15-year cardiovascular disease mortality in a cohort of older Australians. *Nutrients*. 2013;5(2):441-54.
29. Mazidi M, Mikhailidis DP, Sattar N, et al. Consumption of dairy product and its association with total and cause specific mortality - A population-based cohort study and meta-analysis. *Clin Nutr*. 2018.
30. Ness AR, Smith GD, Hart C. Milk, coronary heart disease and mortality. *Journal of Epidemiology & Community Health*. 2001;55(6):379-82.
31. Nettleton JA, Steffen LM, et al. Incident heart failure is associated with lower whole-grain intake and greater high-fat dairy and egg intake in the Atherosclerosis Risk in Communities (ARIC) study. *Journal of the American Dietetic Association*. 2008;108(11):1881-7.
32. Panagiotakos D, Pitsavos C, Chrysohoou C, et al. Dietary patterns and 5-year incidence of cardiovascular disease: A multivariate analysis of the ATTICA study. *Nutrition, Metabolism and Cardiovascular Diseases*. 2009;19(4):253-63.
33. Patterson E, Larsson SC, Wolk A, et al. Association between dairy food consumption and risk of myocardial infarction in women differs by type of dairy food. *The Journal of nutrition*. 2013;143(1):74-9.

- 1
2
3 34. Praagman J, Franco OH, Ikram MA, et al. Dairy products and the risk of stroke and coronary heart disease: the Rotterdam Study. European journal of nutrition. 2015;54(6):981-90.
- 4
5 35. Praagman J, Dalmeijer GW, van der Schouw YT, et al. The relationship between fermented food intake and mortality risk in the European
6 Prospective Investigation into Cancer and Nutrition-Netherlands cohort. British Journal of Nutrition. 2015;113(3):498-506.
- 7
8 36. Sauvaget C, Nagano J, Allen N, et al. Intake of animal products and stroke mortality in the Hiroshima/Nagasaki Life Span Study.
9 International journal of epidemiology. 2003;32(4):536-43.
- 10 37. Snijder MB, van Dam RM, Stehouwer CD, et al. A prospective study of dairy consumption in relation to changes in metabolic risk factors:
11 the Hoorn Study. Obesity (Silver Spring, Md). 2008;16(3):706-9.
- 12 38. Soedamah-Muthu SS, Masset G, Verberne L, Geleijnse JM, et al. Consumption of dairy products and associations with incident diabetes,
13 CHD and mortality in the Whitehall II study. The British journal of nutrition. 2013;109(4):718-26.
- 14 39. Steffen LM, Kroenke CH, Yu X, et al. Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood
15 pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. American Journal of Clinical
16 Nutrition. 2005;82(6):1169-77; quiz 363-4.
- 17 40. Tavani A, Gallus S, Negri E, et al. Milk, dairy products, and coronary heart disease. Journal of Epidemiology & Community Health.
18 2002;56(6):471-2.
- 19 41. Um CY, Judd SE, Flanders WD, et al. Associations of Calcium and Dairy Products with All-Cause and Cause-Specific Mortality in the
20 REasons for Geographic and Racial Differences in Stroke (REGARDS) Prospective Cohort Study. Nutrition & Cancer. 2007;69(8):1185-95.
- 21 42. Umesawa M, Iso H, Ishihara J, et al. Dietary calcium intake and risks of stroke, its subtypes, and coronary heart disease in Japanese: the
22 JPHC Study Cohort I. Stroke. 2008;39(9):2449-56.
- 23 43. Wang L, Manson JE, Buring JE, et al. Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged
24 and older women. Hypertension. 2008;51(4):1073-9.
- 25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Supplementary File 5. Risk of bias in included studies

Funding Source, n (%^a)

Characteristic	Category	Total N = 43	Sponsorship		COI		Industry Ties	
			Industr y N= 8	Non- Industry N=35	COI N =10	No COI N=33	Industry /COI N = 14	Non- Industry/ No COI N = 29
Risk of Bias Assessment								
	Serious/Critical Bias due to confounding	43 (100)	8 (100)	35 (100)	10 (100)	33 (100)	14 (100)	29 (100)
	Serious/Critical Bias in selection of participants into the study	6 (14)	1 (13)	5 (14)	1 (10)	5 (15)	2 (14)	4 (14)
	Serious/Critical Bias in classification of exposures	16 (37)	3 (38)	13 (37)	2 (20)	14 (42)	3 (21)	13 (44)
	Serious/Critical Bias due to deviations from exposures	21 (49)	3 (38)	18 (51)	6 (60)	15 (45)	7 (50)	14 (48)
	Serious/Critical Bias due to missing data	10 (23)	2 (25)	8 (23)	3 (30)	7 (21)	3 (21)	7 (24)

	Serious/Critical Bias in measurement of outcomes	6 (14)	2 (25)	4 (11)	1 (10)	5 (15)	2 (14)	4 (14)
	Serious/Critical Bias in selection of reported results	4 (9)	1 (13)	3 (9)	2 (20)	2 (6)	2 (14)	2 (7)
	Serious/Critical overall risk of bias	43 (100)	8 (100)	35 (100)	10 (100)	33 (100)	14 (100)	29 (100)

^a Percentages may not add to 100 due to rounding

36/bmjopen-2020-0199036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Supplementary File 6: Favorable Outcomes by Industry Ties v No Industry Ties, Industry Sponsorship v No Industry Sponsorship and Conflicts of Interest v No Conflicts of Interest

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
Aerde, M 2013	Non-Industry	Yes	U	U	Al-Delaimy, WK 2003	Non Industry	No	U	U
Altorf-van der Kuil, W2012	Industry	Yes	U	U	Alonso A, 2005	Non-industry	No	U	U
Bernstein, AM 2012	Non-industry	Yes	U	U	Avalos, EE 2013	Non-industry	No	U	U
Biong, A 2008	Industry	Yes	U	F	Bonthuis, M 2010	Non-Industry	No	U	U
Buendia, JR 2018	Industry	No	F	F	Chen, M 2016	Non-Industry	No	U	F
Dalmeijer, G 2013	Non-Industry	Yes	U	F	Dauchet, L 2007	Non-Industry	No	U	U
Dehghan, M 2018	Industry	No	U	F	Elwood, PC 2004	Non-Industry	No disclosure	U	U
Heraclides, A 2012	Non-Industry	Yes	U	U	Engberink, MF 2009	No disclosure	No	U	F
Lockheart, MSK 2007	Industry	No disclosure	U	U	Farvid, MS 2017	Non-Industry	No	F	F
Louie, JCY 2013	Industry	No disclosure	U	U	Haring, B 2014	Non-Industry	No	U	U
Praagman, J 2015	Industry	Yes	U	U	He, K 2003	Non-Industry	No	U	U

36/bmjopen-2020-019036 on 14 September 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
Praagman J, 2015	Non-Industry	Yes	U	U	Johansson, I 2018	Non-Industry	No	U	U
Snijder, MB 2008	Industry	Yes	U	U	Johansson, I 2019	Non-Industry	No	U	U
Soedamah-Muthu, SS 2013	Non-Industry	Yes	U	U	Kim, D 2017	Non-Industry	No	F	F
					Larsson,S 2009	Non-Industry	No disclosure	U	U
					Larsson, SC 2012	Non-Industry	No	U	U
					Li, K 2012	Non-Industry	No	U	U
					Lin, PH 2013	Non-Industry	No	U	U
					Mazidi, M, 2018	Non-Industry	No	F	F
					Ness, AR 2001	Non-Industry	No	U	U
					Nettleton, J 2008	Non-Industry	No	U	U
					Panagiotakos, D 2009	Non-Industry	No disclosure	U	U
					Patterson, E 2013	Non-Industry	No	F	F
					Sauvaget, C 2003	Non-Industry	No disclosure	F	F
					Steffen, LM 2005	Non-Industry	No	U	U

36/bmjopen-2020-019036 on 14 September 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
					Tavani, A 2002	Non-Industry	No	F	F
					Um, C 2017	Non-Industry	No	U	F
					Umesawa, M, 2008	Non-Industry	No	F	F
					Wang,L 2008	Non-Industry	No	F	F

Favourable results - Statistical significance: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no COI

Industry Ties

	Industry/COI	Non-Industry/No COI
Favourable	1	8
Unfavourable	13	21

RR= 0.26 (95% CI 0.04, 1.87)

Industry Sponsorship

	Industry	Non-Industry
Favourable	1	8
Unfavourable	7	27

RR = 0.55 (95% CI 0.08, 3.77)

Conflicts of Interest

	COI	No/COI
Favourable	0	9
Unfavourable	10	24

RR= 0.16 (95% CI 0.01, 2.57)

Favourable conclusions: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no COI

Industry Ties

	Industry/COI	Non-Industry/NO COI
Favourable	4	11
Unfavourable	10	18

RR = 0.75 (95% CI 0.29, 1.95)

Industry Sponsorship

	Industry	Non-Industry
Favourable	3	12
Unfavourable	5	23

RR= 1.09 (95% CI 0.40, 2.99)

Conflicts of Interest

	COI	No COI
Favourable	2	13
Unfavourable	8	20

RR =0.51 (95% 0.14, 1.88)

Concordance between study results and conclusions: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no

COI Industry Ties

Industry Ties

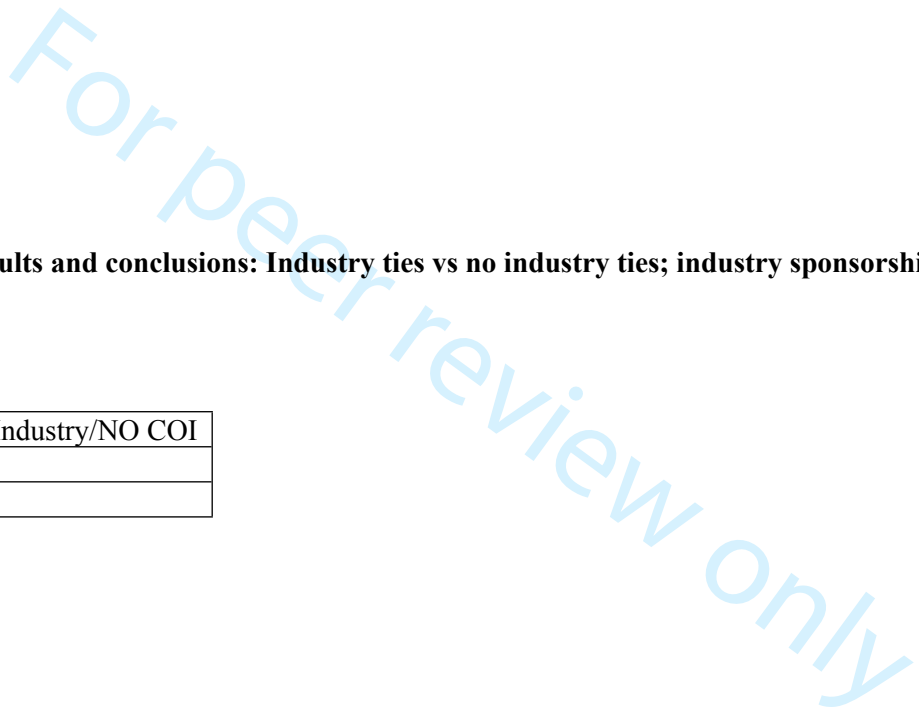
	Industry/COI	Non-Industry/NO COI
Discord	3	3
Concord	11	26

RR = 2.07 (95% CI 0.48, 8.99)

Industry Sponsorship

	Industry	Non-Industry
Discord	2	4
Concord	6	31

RR = 2.19 (95% CI 0.48, 9.94)



Conflicts of Interest

	COI	No/COI
Favourable	2	4
Unfavourable	8	29

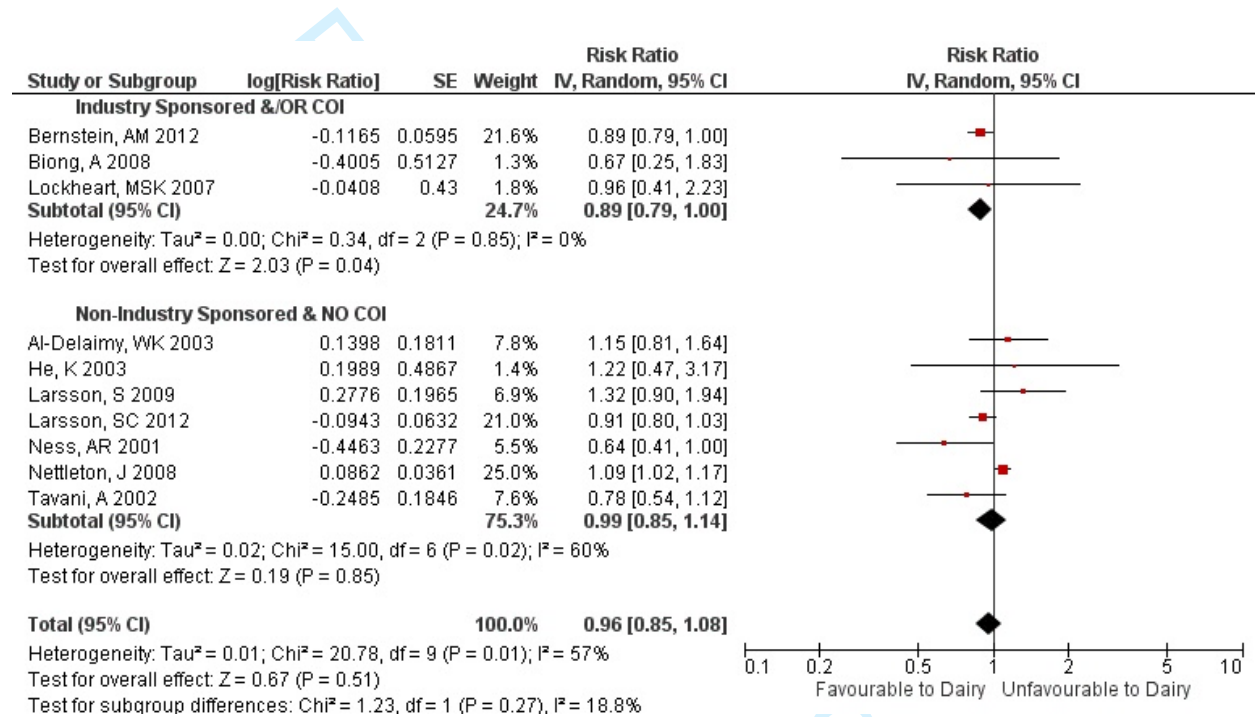
RR = 1.65 (95% CI 0.35, 7.72)

For peer review only

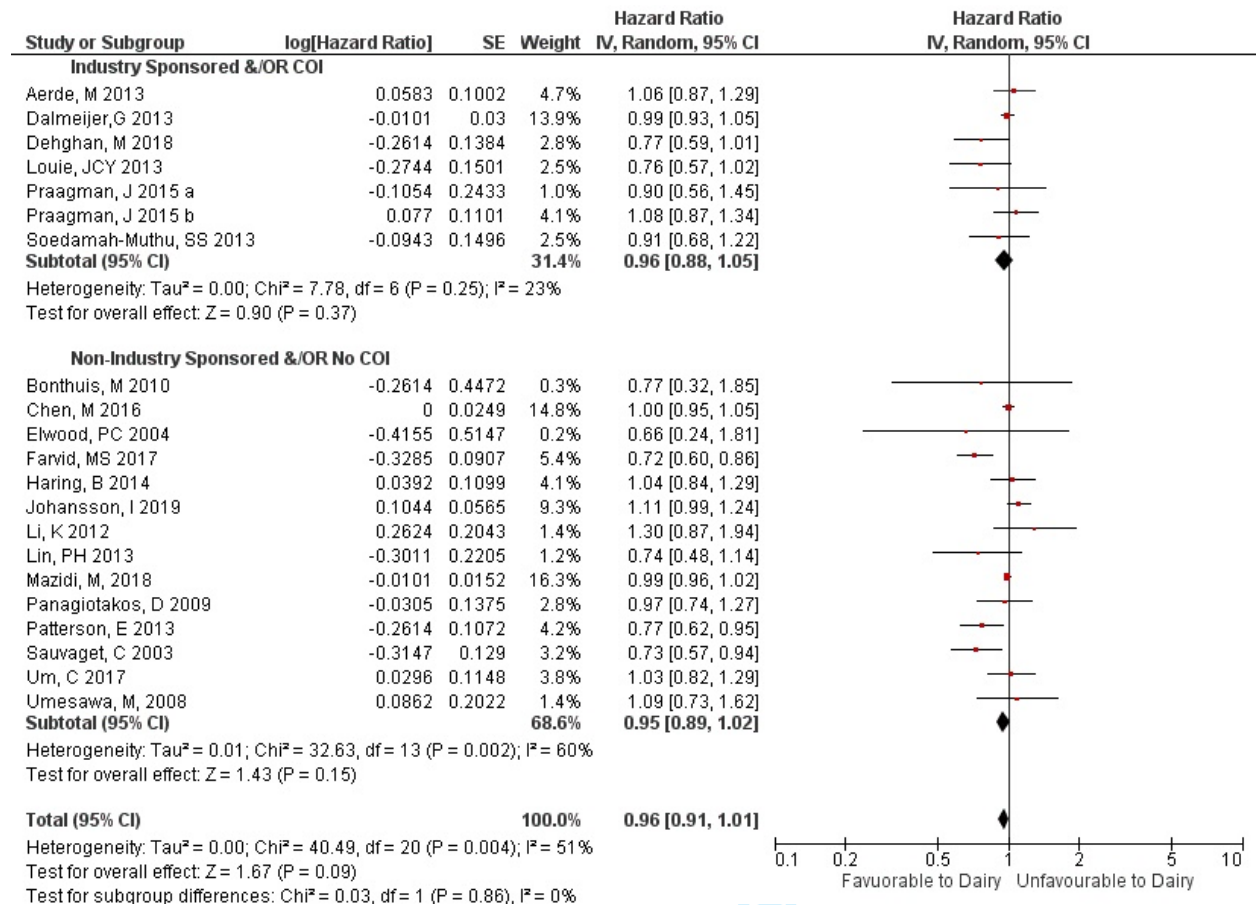
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Supplementary File 7. Results for each of the meta-analyses conducted

Effect Size, Cardiovascular Disease: Industry ties v no industry ties, Risk Ratio

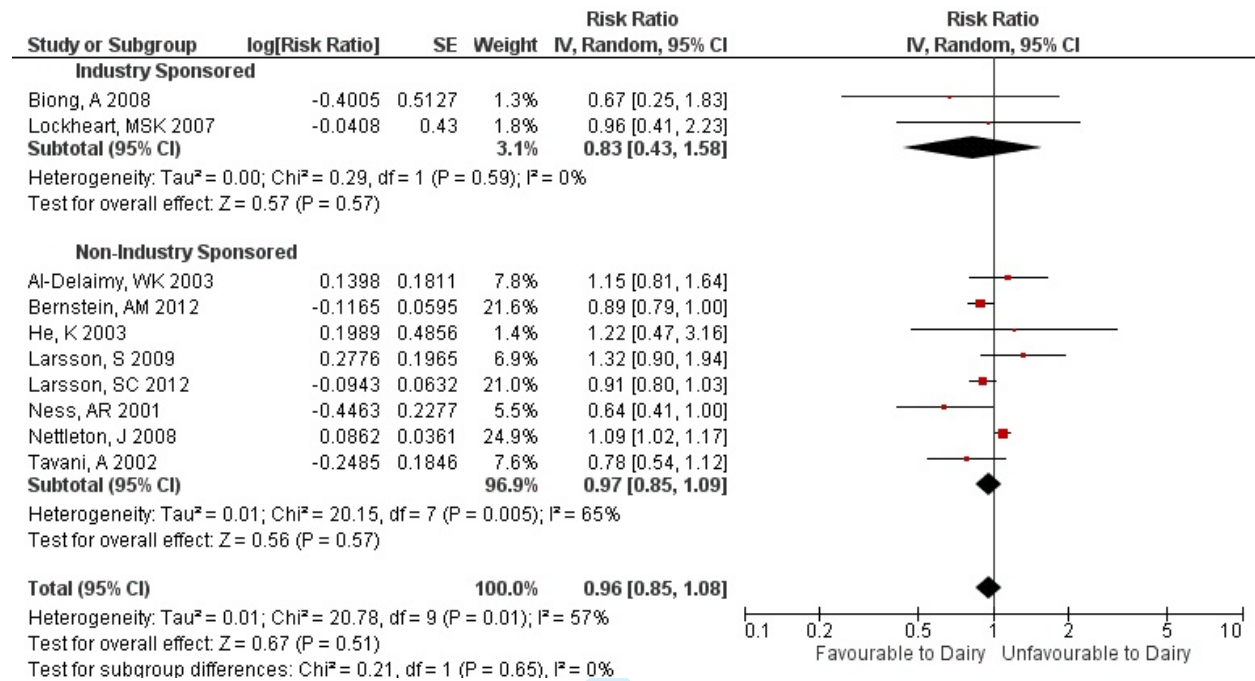


Effect Size, Cardiovascular Disease: Industry ties v no industry ties, Hazard Ratio

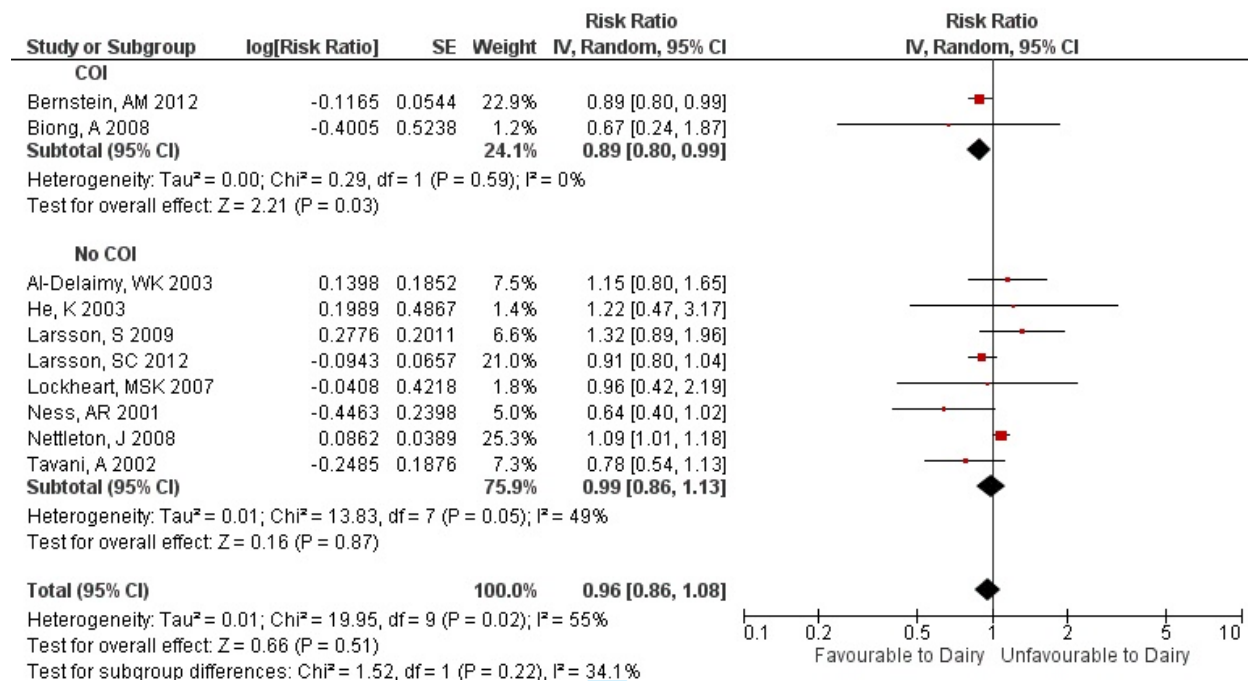


BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Effect Size, Cardiovascular Disease: Industry sponsorship vs no industry sponsorship, Risk Ratio

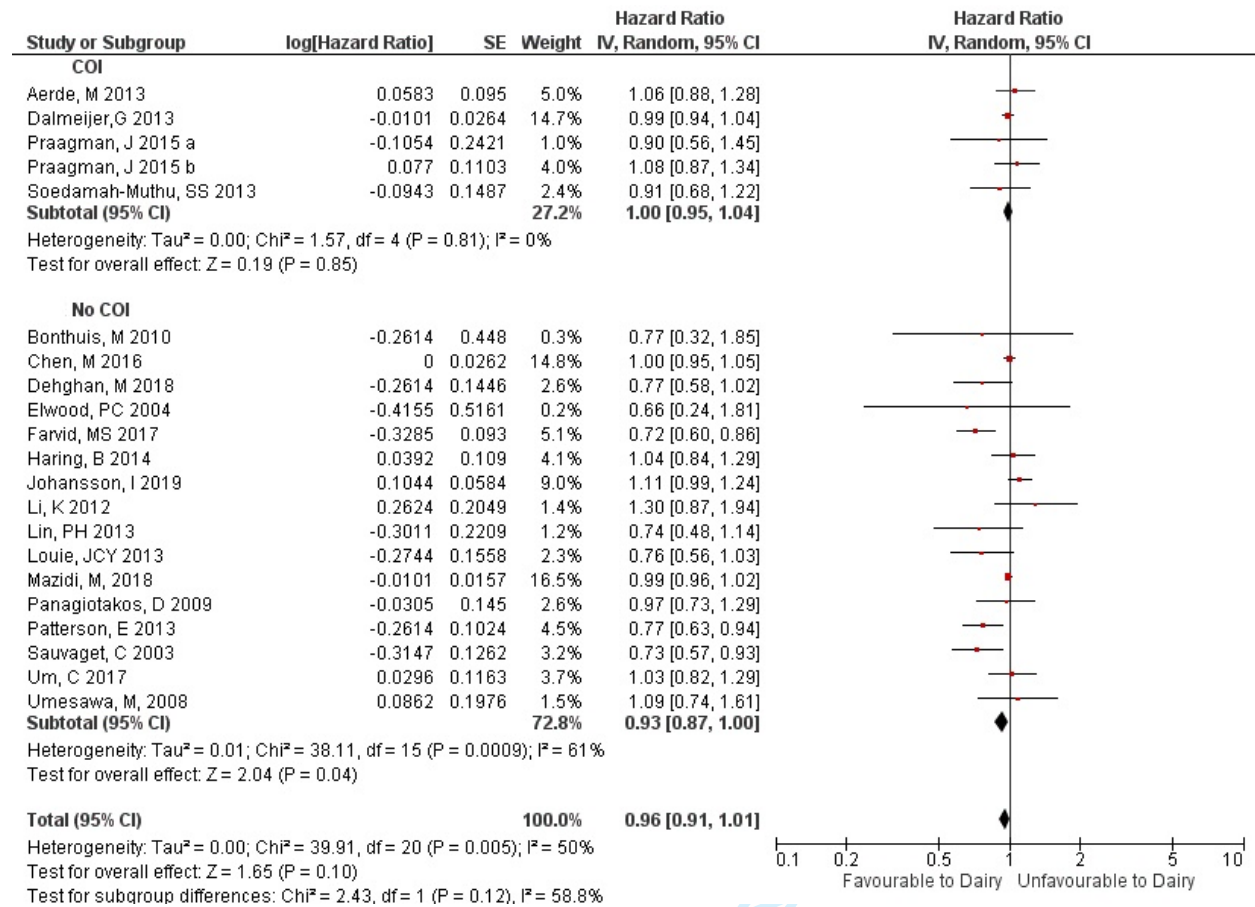


Effect Size, Cardiovascular Disease: COI vs No COI, Risk Ratio

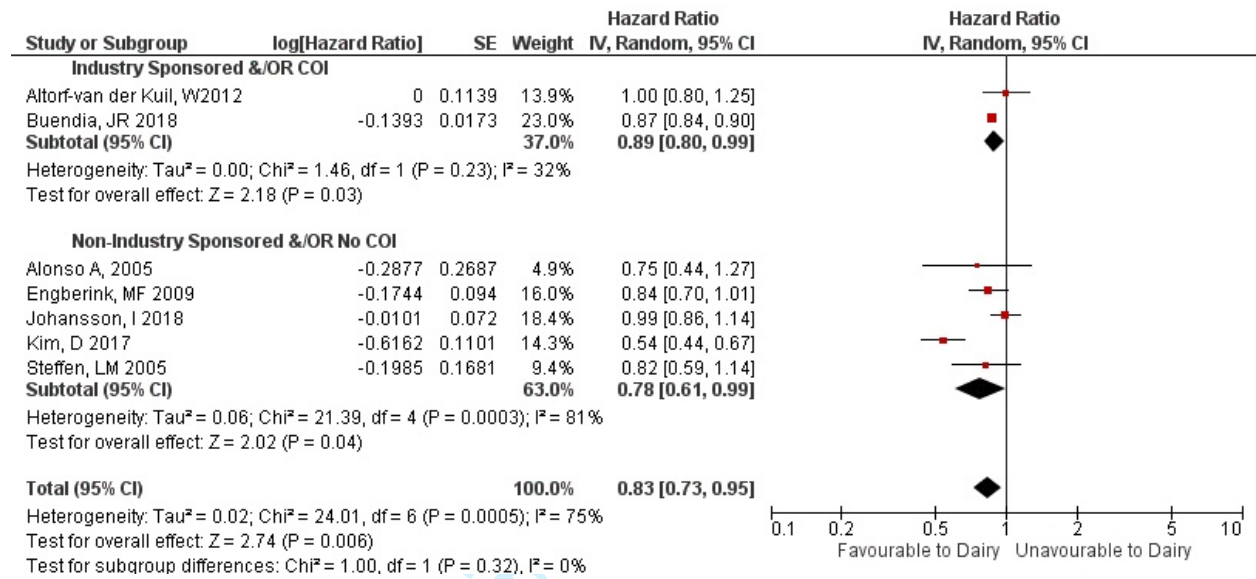


BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Effect Size, Cardiovascular Disease: COI vs no COI, Hazard Ratio



Effect Size, Elevated Blood Pressure / Hypertension: Industry ties v no industry ties



BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5, Supp file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7 & 10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6 & 10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2 for each meta-analysis).	10



PRISMA 2009 Checklist

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11, Figure 1, Supp file 3
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICO(S), follow-up period) and provide the citations.	Supp file 4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	13, Supp File 5, Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13-15
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	13-15, Supp file 6 & 7, Figure 3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	13, Supp file 5, Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16



PRISMA 2009 Checklist

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data), role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Page 2 of 2

For peer review only

36/bmjopen-2020-033036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

BMJ Open

The association of food industry ties with findings of studies examining the effect of dairy foods intake on cardiovascular disease and mortality: Systematic review and Meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-039036.R1
Article Type:	Original research
Date Submitted by the Author:	16-Sep-2020
Complete List of Authors:	Chartres, Nicholas; The University of Sydney, Charles Perkins Centre Fabbri, Alice; University of Insubria, Centre for Research in Medical Pharmacology McDonald, Sally ; The University of Sydney, ; the University of Sydney Diong, Joanna; The University of Sydney Faculty of Medicine and Health McKenzie, Joanne; Monash University Bero, Lisa; University of Sydney Faculty of Health Sciences, Pharmacy
Primary Subject Heading:	Research methods
Secondary Subject Heading:	Public health, Epidemiology, Health policy, Nutrition and metabolism
Keywords:	STATISTICS & RESEARCH METHODS, NUTRITION & DIETETICS, PUBLIC HEALTH

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 1 **The association of food industry ties with findings of studies examining the effect of**
4 **dairy foods intake on cardiovascular disease and mortality: Systematic review and**
5 **Meta-analysis**
6
7
8

9 4

10
11 5 **Authors:** Nicholas Chartres¹, Alice Fabbri¹, Sally McDonald¹, Joanna Diong², Joanne
12 Mckenzie³, Lisa Bero¹
13
14
15 7

16
17 8 1. The University of Sydney, D17, The Hub, 6th floor, Charles Perkins Centre, The
18 University of Sydney, New South Wales, 2006, Australia

19 9
20 10 2. The University of Sydney, School of Medical Sciences, Faculty of Medicine and
21 Health, The University of Sydney, New South Wales, 2006, Australia
22 11

23 12 3. Monash University, 553 St Kilda Road, Melbourne, Victoria, 3004, Australia
24 12
25
26 13

27
28 14 **Corresponding author:** Lisa Bero, The University of Sydney, D17, The Hub, 6th floor,
29 Charles Perkins Centre, The University of Sydney, New South Wales, 2006, Australia, email
30 lisa.bero@sydney.edu.au; Telephone +612 8627
31 16
32
33

34 17

35
36 18 **Word Count: 5006**
37
38 19
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

20 Abstract

21 **Objective:** To determine if the association of dairy foods with cardiovascular disease
22 outcomes differs between studies with food industry ties versus those without industry ties.

23 To determine whether studies with or without industry ties differ in their risk of bias.

24 **Eligibility criteria:** We included cohort and case control studies that estimated the
25 association of dairy foods with cardiovascular disease (CVD) outcomes in healthy adults.

26 **Information sources:** We searched eight databases on February 1, 2019 from 2000-2019 and
27 hand searched reference lists

28 **Risk of bias:** We used the Risk of Bias in Non-Randomized Studies-of Exposure (ROBINS-
29 E) tool.

30 **Included studies:** 43 studies (3 case controls, 40 cohorts).

31 **Synthesis of results:** There was no clear evidence of an association between studies with
32 industry ties (1/14) vs. no industry ties (8/29) and the reporting of favourable results, RR=
33 0.26 (95% CI 0.04, 1.87; n=43 studies) and studies with industry ties (4/14) vs. no industry
34 ties (11/29) and favourable conclusions, RR= 0.75 (95% CI 0.29, 1.95; n=43).. Studies with
35 industry sponsorship, (HR =0.78; n= 3 studies) showed a decreased magnitude of risk of
36 CVD outcomes compared to studies with no industry sponsorship (HR=0.97; n=18) (ratio of
37 HRs 0.80 (95% CI 0.66, 0.97)) P=0.03.

38 **Strengths and Limitations of evidence:** Every study had an overall high risk of bias rating;
39 this was primarily due to confounding.

40 **Interpretation:** There was no clear evidence of an association between studies with food
41 industry ties and the reporting of favourable results and conclusions compared with studies
42 without industry ties. The statistically significant difference in the magnitude of effects
43 identified in industry sponsored studies compared to non-industry sponsored studies,
44 however, is important in quantifying industry influence on studies included in dietary
45 guidelines.

46 **Funding:** This work was supported by Australian Health and Medical Research Council
47 Project Grant APP 1139997.

48 **Registration:** Prospero ID CRD42019129659

51 **Keywords:** Industry Sponsorship, Conflicts of Interest, Bias, Dietary Guidelines

53 **Strengths and limitations of this study**

- 1
2
3
4 54 • This is the first systematic review and meta-analysis to evaluate the association of
5 55 food industry ties (industry sponsorship and / or author conflicts of interest (COI))
6 56 with the results, conclusions and risk of bias of primary nutrition studies examining
7 57 the association of dairy foods with cardiovascular disease outcomes and mortality.
8
9 58 • We conducted a comprehensive search and followed explicit and well-defined
10 59 inclusion and exclusion criteria for the included studies.
11
12 60 • For studies missing a funding or author COI disclosure, we did not contact the
13 61 authors; thus we may be underestimating the number of studies with industry ties.
14
15 62 • The tool that we used to assess the risk of bias is still under modification, however it
16 63 is unlikely any future changes to the tool will affect the risk of bias ratings.
17
18 64 • We did not analyse studies of low and full fat dairy separately. Industry ties may have
19 65 different effects on studies of low or full fat dairy foods.
20
21
22
23
24 66
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

67 INTRODUCTION

68 The effect of dairy foods on cardiovascular disease (CVD) is unclear. Recent systematic
69 reviews and meta-analyses of observational studies have reported conflicting results between
70 the association of total dairy consumption and risk of CVD, with some showing decreased
71 risk and some showing no clear evidence.¹⁻⁴ The beneficial effects of decreasing blood
72 pressure, however, appear more consistent.^{4,5} Further, dairy intake recommendations made in
73 dietary guidelines around the world vary. Although the Australian Dietary Guidelines
74 concluded that there is a probable association between dairy food consumption and a reduced
75 risk of cardiovascular events,⁶ recent amendments to the Eatwell guidelines by Public Health
76 England recommend a significant reduction in the daily intake of dairy foods.⁷

77

78 Food industry sponsors and authors with a conflict of interest (COI) with the food industry
79 may gain financially from finding that dairy foods have health benefits, since such a finding
80 can be used to market dairy products. Such a driver may lead industry sponsors to magnify
81 (or bias) the health benefits of dairy foods by influencing the research agenda, design and
82 conduct of the study, or reporting of the results.⁸⁻¹¹ Prior examinations of pharmaceutical and
83 tobacco research have identified that even when controlling for methodological biases,
84 studies sponsored by industry were more likely to have results that favoured the sponsor than
85 studies with other sources of sponsorship.¹²⁻¹⁴

86

87 The effects of food industry sponsorship or author COI with the food industry on study
88 results needs further examination.¹⁵ A systematic review assessing the association of
89 wholegrain foods with CVD and mortality found that studies with food industry ties more
90 often have favourable results and conclusions compared to those with no industry ties, but the
91 association was uncertain.¹⁶ One study has demonstrated an association of food industry
92 sponsorship with the magnitude of effect estimates.¹⁷ In this examination, studies of soft
93 drink consumption sponsored by the food industry reported significantly smaller harm effect
94 estimates than those with no food industry sponsorship. A recent dairy industry funded meta-
95 analysis of observational studies found that studies without food industry sponsorship showed
96 that dairy consumption was associated with a statistically significant decreased risk of
97 developing CVD and Type 2 diabetes, while studies with food industry sponsorship did not.¹⁸

1
2
3 98 The primary objective of this systematic review and meta-analysis is to determine whether:
4

- 5 99
- 6 • Studies of observational design examining the associations of dairy foods with CVD
7 100 with food industry ties (industry sponsorship and / or authors with a COI) are more
8 101 likely to have results and / or conclusions that are favourable to industry than those
9 102 with no industry ties.
10
11
12 103

13
14 104 The secondary objectives of this review are to determine whether observational studies with
15 105 food industry ties compared with no industry ties:

- 16
17
18 106 I. differ in their risk of bias;
19 107 II. have a higher level of discordance between study results and conclusions, with the
20 108 conclusions more likely to be favourable compared to the results.
21
22
23
24 109

25 26 27 110 **METHODS**

28
29 111 We conducted a systematic review of observational studies examining the effect of dairy
30 112 consumption on CVD. Our study is registered with Prospero ID CRD42019129659 (see
31 113 Supplementary file 1).¹⁹
32
33
34 114

35 36 115 **Search Strategy**

37
38 116 The search included terms to locate observational studies and randomised control trials, the
39 117 latter of which are for a separate systematic review. The search used was based on the
40 118 Process Manual used to develop the 2013 Australian Dietary Guidelines and the guidance of
41 119 an information specialist.²⁰ The search dates used were to ensure that we identified the
42 120 studies used to inform the recommendations in these guidelines. We therefore searched the
43 121 following databases from January 2000-February 2019: MEDLINE; CINAHL; PubMed;
44 122 PreMEDLINE; Cochrane Library; PsycINFO; Science Direct; and ERIC. The search strategy
45 123 used for Ovid MEDLINE on February 1, 2019 is shown in Supplementary file 2. We adapted
46 124 this strategy for the other databases. We hand searched references lists of the identified
47 125 studies and reviews.
48
49
50
51
52
53
54
55
56
57
58
59 128
60

129 **Eligibility Criteria**

130 We included studies of cohort or case control designs that estimated the effects of dairy
131 consumption on CVD outcomes in healthy adults. We focused on these study designs as they
132 are often used to assess the association of diet with long term health outcomes.

133
134 We included studies with no restriction on the authors' definition of dairy. For example, some
135 authors' defined dairy as milk, yogurt and cheese, while others defined dairy as 'whole fat'
136 milk, yogurt and cheese. We included studies that compared dairy foods to other foods or
137 compared various levels of dairy consumption.

138
139 We included studies that measured any clinical outcome of CVD, defined as either mortality
140 related to specific CVD events, and / or CVD events, (e.g., first myocardial infarction, total
141 stroke etc.) or incidence of elevated blood pressure / hypertension.

142
143 We excluded conferences presentations, opinion pieces and letters to the editor. We had no
144 language restrictions.

145

146 **Types of Outcome Measures**

147 **Primary Outcomes**

148 We hypothesized that studies with food industry sponsorship and / or authors with a COI with
149 the food industry would be more likely to have favourable findings than those with no
150 industry ties. We assessed three primary outcomes:

151 1. Statistical significance of results favourable to dairy

152 Favourable results were defined as those that were in the direction of showing a health
153 benefit of dairy product(s), and were statistically significant at the 0.05 level (two tailed),
154 such as a statistically significant decreased risk of CVD compared to the comparator (i.e.
155 another food or lower dairy consumption). Otherwise, results were classified as unfavourable.
156 In the circumstance where a study reported multiple results (e.g. first myocardial infarction
157 and total stroke), only one result needed to be 'favourable' for the study as a whole to be
158 classified as 'favourable'.

159

160 2. Effect size of results

161 Effect size was defined as the risk ratio (RR), hazard ratio (HR) or odds ratio (OR) between
162 dairy foods tested versus comparator on the CVD outcome.

163

3. Conclusions

Conclusions that suggested that the dairy consumption was beneficial to health by decreasing CVD were considered favourable. Otherwise, the conclusions were considered unfavourable. In the circumstance where a study reported multiple results (e.g. first myocardial infarction and total stroke), only one conclusion needed to be 'favourable' for the study as a whole to be classified as 'favourable'.

170

Secondary Outcomes

We assessed two secondary outcomes:

1. The risk of bias of the included studies

To evaluate the risk of bias of included observational studies, we used an adapted version of the Cochrane Collaboration's 'Risk of Bias in Non-Randomized Studies-of Interventions' (ROBINS-I) tool,²¹ the ROBINS-E²². Bias is assessed across seven domains ('Bias due to confounding', 'Bias in selection of participants', 'Bias in classification of exposures', 'Bias due to deviations from exposures', 'Bias due to missing data', 'Bias in measurement of outcomes', 'Bias in selection of reported results'), with each domain classified low, moderate, serious, critical risk of bias, or no information. The first step in using the ROBINS-E tool is to identify all possible confounders that a study should control. We developed this list of confounders by searching the literature for the most recent systematic reviews on possible confounders and having this list reviewed by expert Professors in nutrition at The University of Sydney (see Supplementary file 3 for list of confounder). An overall risk of bias rating for the study is given based on the domain with the highest risk of bias rating. For example, if a study is rated as being at a 'critical' risk of bias in one domain, the overall risk of bias rating is 'critical.' In the circumstance where a study reported multiple results (e.g. stroke and myocardial infarction), the risk of bias was only assessed for one randomly selected outcome.

190

2. Concordance between study results and conclusions

Results unfavourable to the sponsor with conclusions favourable to the sponsor, were considered discordant. Otherwise, the results and conclusions were considered concordant.

194

Selection of studies

195

1
2
3 196 Three investigators (NC, SMC & AF), working independently in pairs, screened the titles and
4
5 197 abstracts of all records for obvious exclusions. If both investigators agreed on excluding the
6
7 198 study, the full text was not retrieved. Three investigators (NC, SMC & AF) working
8
9 199 independently in pairs, assessed the full text of potentially eligible studies against the
10
11 200 inclusion criteria. If agreement could not be reached, a fourth investigator (LB) resolved the
12
13 201 conflict.

15 203 **Selection of results for meta-analysis**

16
17 204 If total dairy consumption had been assessed in the study, we included this as our only
18
19 205 exposure. If total dairy consumption had not been assessed, we included any type of dairy
20
21 206 consumption (e.g. milk, yogurt, and cheese; or low fat, high fat) other than fermented milk as
22
23 207 our exposure. We included the results comparing the highest level of dairy consumption to
24
25 208 the lowest level of dairy consumption (e.g., 'yes' to dairy consumption vs. 'no' to dairy
26
27 209 consumption, tertile 3 vs. tertile 1, quartile 4 vs. quartile 1, quintile 5 vs. quintile 1). For the
28
29 210 meta-analyses if our pre-specified rules for selecting results did not allow us to uniquely
30
31 211 identify one exposure for inclusion, we randomly selected one result.

32
33 213 If 'cardiovascular disease mortality/death/s' (verbatim) had been assessed, we included this
34
35 214 as our only outcome. If not, we included any type of CVD mortality (e.g., coronary heart
36
37 215 disease mortality, stroke mortality etc.) as our outcome. If there were no mortality outcomes
38
39 216 assessed in the study, we included any CVD event or incidence of elevated blood pressure /
40
41 217 hypertension as our outcome. If a study used a composite outcome, which was a combination
42
43 218 of multiple outcomes, the result pertaining to the composite outcome was selected. For the
44
45 219 meta-analyses if our pre-specified rules for selecting results did not allow us to uniquely
46
47 220 identify one outcome for inclusion, we randomly selected one result.

48 222 **Data Collection**

49
50 223 From each study we extracted:

- 51 224 • Year of publication
 - 52
53 225 • Study design (cohort or case control)
 - 54
55 226 • Sample size of study
 - 56
57 227 • Age of participants (combined or if reported, separately)
 - 58
59 228 • Exposure duration or observation period
- 60

- 1
2
3 229 • How the study defined dairy (verbatim)
4
5 230 • Disclosure of funding source (no disclosure, yes and there is a sponsor, the authors
6 state they received no funding for their work)
7 231
8 232 • Name of the funders of the study (verbatim)
9
10 233 • Role of the funders (role of the sponsor not mentioned, sponsor not involved in study
11 design and analyses, sponsor involved, N/A)
12 234
13 235 • Disclosure of author COI (no disclosure, yes (if at least 1 author had a COI), the authors
14 state they had no conflicts of interest to declare)
15 236
16 237 • Authors COI statement (verbatim)
17
18 238 • Outcomes assessed in the study (any CVD death and/or event or blood
19 pressure/hypertension)
20 239
21 240 • The numerical results of the study (e.g., OR, HR, RR)
22
23 241

24
25 242 All extracted data from the included studies was stored in REDcap, a secure web-based
26 application for the collection and management of data.²³ Five investigators (NC, SMc, AF,
27 AL & JD) working independently in pairs extracted data from the included studies.
28 243
29 244 Discrepancies in data extraction were resolved by consensus. If agreement could not be
30 reached, a sixth investigator (LB) resolved the discrepancy.
31 245
32 246
33 247

248 **Classification of industry sponsorship and author conflicts of interest**

249 Sponsorship was categorized as 1) industry or 2) non-industry. Industry sponsored studies
250 were defined as those that declared any sponsorship from the food industry, including 'Big
251 Food' (i.e. Danone, Kraft, Unilever etc), trade associations (i.e. dairy associations and
252 organisations) and dairy industry (i.e. primary producers). Studies with food industry
253 sponsorship plus any other sponsorship were classified as industry. Any study that did not
254 contain a funding disclosure statement was classified as 'non-industry'.
255

256 Studies with at least one author with any disclosed financial tie with the food industry were
257 classified as having a conflict of interest (COI). Author COI were categorised as 1) COI or 2)
258 no COI. Studies with no authors with disclosed financial ties with the food industry were
259 classified as 'no conflict of interest'.
260

1
2
3 261 Since the number of studies with industry sponsorship or author COI was small, we also
4 262 categorized studies as having “industry ties” for analysis. Studies classified as having an
5 263 industry tie were industry sponsored and / or had an author COI. Otherwise, they were
6 264 classified as having no industry ties.
7
8
9

10 265

11 266 **Analysis**

12 267 We report the frequencies and percentages of the study characteristics across all studies, and
13 268 separately, by sponsorship, COI and industry ties. We visually present the risk of bias rating
14 269 for each domain and overall across each study.
15
16
17
18

19 270

20 271 To quantify the association between industry ties, food industry sponsorship, or authors with
21 272 a conflict of interest with the food industry and (i) favourable results, (ii) favourable
22 273 conclusions, (iii) overall risk of bias across each study, and (iv) level of concordance, we
23 274 calculated RR (and 95% confidence intervals). To analyse the risk of bias rating for each
24 275 study, we dichotomised the overall risk of bias ratings as low (low or moderate) or high
25 276 (serious or critical).
26
27
28
29
30

31 277

32 278 We conducted meta-analysis to examine whether studies with food industry ties, food
33 279 industry sponsorship, or authors with a conflict of interest with the food industry modified the
34 280 magnitude of effect of dairy on CVD outcomes.. For each outcome, we combined effect
35 281 estimates using a random effects meta-analysis model using the inverse variance method.
36 282 DerSimonian and Laird’s method of moments estimator was used to estimate between study
37 283 heterogeneity. We fitted separate meta-analyses for studies that had measured the association
38 284 using HRs and those that had used either RRs or ORs. It is not recommended to combine HRs
39 285 with RRs and ORs in a meta-analysis, as HRs represent instantaneous risk over the study time
40 286 period, whereas RRs and ORs estimate risk/odds at a fixed time point.²⁴ We considered that
41 287 the ORs approximated RRs given CVD events were rare.
42
43
44
45
46
47
48
49

50 288

51 289 We undertook a fixed-effects test for subgroup differences (defined by industry sponsorship /
52 290 authors conflict of interest) using the Chi² test and calculated the ratio of RRs (ORs) or HRs
53 291 along with 95% confidence intervals. Analyses were undertaken in Review Manager 5.3.²⁵
54
55
56
57

58 292

1
2
3 293 We planned to use sensitivity analysis to assess the influence of risk of bias by restricting the
4 294 analysis to studies at ‘low risk of bias’ overall (i.e. an overall risk of bias rating of low or
5 295 moderate). However, as the overall risk of bias was high across all studies, this was not
6 296 undertaken.

7
8
9 297

10 298 **Patient and Public Involvement**

11 299 No patient involved

12 300

13 301 **RESULTS**

14 302 As shown in Figure 1, there were 1, 858 studies screened for inclusion and 43 studies were
15 303 included (3 case controls, 40 cohorts). See Supplementary file 4 for ‘List of excluded studies
16 304 and reasons for exclusion’.

17 305

18 306 **Characteristics of included Studies**

19 307 All studies were published between 2001 and 2019. All but one contained a funding
20 308 disclosure. Eight studies disclosed food industry sponsorship, but only two of these studies
21 309 described the role of the sponsor. Six studies did not contain an author COI disclosure
22 310 statement. Ten studies contained an author with a COI with the food industry. Fourteen
23 311 studies were classified as having industry ties, disclosing food industry sponsorship and / or
24 312 an author with a COI.

25 313

26 314 As shown in Table 1, most characteristics were similarly distributed across studies with
27 315 industry ties or no industry ties. Studies with industry ties (64%) were more likely to have
28 316 sample sizes <5000 than non-industry sponsored studies (34%). A greater proportion of
29 317 industry sponsored studies (100%) than non-industry sponsored studies (83%) focused on
30 318 total dairy intake rather than a specific food. Details of the individual studies are in
31 319 Supplementary file 5.

32 320

33 321

34 322

35 323

36 324

325 **Table 1. Characteristics of the included studies by sponsorship, author conflict of**
 326 **interest and industry ties**

327 Funding Source, n (%^a)

Characteristic	Category	Total N = 43	Sponsorship		COI		Industry Ties	
			Industr y N= 8	Non- Industry N=35	COI N =10	No COI N=33	Industry /COI N = 14	Non- Industry/ No COI N = 29
Sex	Male	5 (12)	0 (0)	5 (14)	0 (0)	5 (15)	0 (0)	5 (17)
	Female	2 (5)	0 (0)	2 (6)	0 (0)	2 (6)	0 (0)	2 (7)
	Both	36 (84)	8 (100)	28 (80)	10 (100)	26 (79)	14 (100)	22 (76)
Sample Size	<5000	19 (44)	6 (75)	13 (37)	7 (70)	12 (36)	9 (64)	10 (34)
	5000-50,000	18 (42)	0 (0)	18 (51)	2 (20)	16 (48)	2 (14)	16 (55)
	>50,000	6 (14)	2 (25)	4 (11)	1 (10)	5 (15)	3 (21)	3 (10)
Length of Follow up	N/A*	3 (7)	2 (25)	1 (3)	1 (10)	2 (6)	2 (14)	1 (3)
	<10 years	11 (26)	3 (38)	8 (23)	2 (20)	9 (27)	3 (21)	8 (28)
	10-15 years	21 (49)	2 (25)	19 (54)**	6 (60)	15 (45)**	7 (50)	14 (48)
	>15 years	8 (19)	1 (13)	7 (20)	1 (10)	7 (21)	2 (14)	6 (21)
Type of Dairy	Total Dairy Intake***	37 (86)	8 (100)	29 (83)	9 (90)	28 (85)	13 (93)	24 (83)
	Individual Dairy Foods****	6 (14)	0 (0)	6 (17)	1 (10)	5 (15)	1 (7)	5 (17)

328 ^a Percentages may not add to 100 due to rounding

329 * Follow up is not applicable for case control studies

330 ** Follow up for Johansson, I 2018 described the follow up as '8-12 years', we took the median of 10 years

331 *** This includes studies that looked at nutrients e.g calcium, fat & protein by measuring total dairy intake

332 ****Individual foods included milk, cheese & yogurt

333 **Risk of bias in included studies**

334 Every study was classified as having an overall high risk of bias, with 10 assessed as having a
335 serious risk of bias and 33 as having a critical risk of bias (Figure 2). Most studies were
336 assessed as having a critical risk of bias rating for the domain 'Bias due to confounding'. An
337 example of one of the several confounders we identified that studies needed to control for was
338 fruit and vegetable intake. If these confounders were not controlled for appropriately when
339 measuring the effect of dairy intake on a CVD outcome, the study was classified as having a
340 risk of bias for the confounding domain.

341
342 Studies without industry ties or without an author with a COI were more likely to have a
343 serious or critical risk of bias rating for 'Bias in classification of exposures'. For example, if a
344 study did not use a validated food frequency questionnaire to measure the dietary intake of
345 dairy, the study was classified as having a risk of bias for the domain of classification of
346 exposures. For all other domains, the risk of bias classifications were similarly distributed
347 across studies with industry ties, industry sponsorship or COI vs no industry ties, industry
348 sponsorship or COI, respectively (see Supplementary file 6).

350 **Favourable results - Statistical significance: Industry ties vs no industry ties; industry** 351 **sponsorship vs no sponsorship; COI v no COI**

352 There was no clear evidence of an association between the reporting of favourable results and
353 studies with industry ties (1/14) compared to those with no industry ties (8/29), RR= 0.26
354 (95% CI 0.04, 1.87; n=43 studies) (Supplementary file 7). When comparing studies with
355 industry sponsorship (1/8) with those with no industry sponsorship (8/35), there was no clear
356 evidence of an association, RR = 0.55 (95% CI 0.08, 3.77; n=43 studies). There was again no
357 clear evidence of an association between the reporting of favourable results and studies with
358 an author with a COI (0/10) than those with no COI (9/33), RR= 0.16 (95% CI 0.01, 2.57;
359 n=43 studies).

361 **Effect Size, Cardiovascular Disease: Industry ties v no industry ties; industry** 362 **sponsorship vs no industry sponsorship; COI v no COI**

363 For studies that quantified the association between dairy consumption and CVD outcomes
364 using a RR, we found no important difference in the magnitude of the effect in studies with
365 industry ties (RR = 0.89; n=3 studies) compared with those studies with no industry ties, (RR

1
2
3 366 = 0.99; n=7 studies) (ratio of RRs 0.90 (95% CI 0.74, 1.09)); P=0.27 (Supplementary file 8).
4
5 367 For studies that had quantified the association using HRs, we similarly did not find an
6
7 368 important difference in the magnitude of HRs between studies with industry ties, (HR=0.96;
8
9 369 n=7 studies) and those studies with no industry ties, (HR=0.95; n=14 studies) (ratio of HRs
10 370 1.01 (95% CI 0.90, 1.13)); P=0.86.
11

371

12
13 372 In our analysis comparing studies with industry sponsorship, (RR 0.83; n=2 studies) and
14 373 those with no industry sponsorship, (RR 0.97; n=8 studies) we again did not find an
15 374 important difference in the magnitude of RRs (ratio of RRs 0.86 (95% CI 0.44, 1.66));
16
17 375 P=0.65 (Supplementary file 8). However, when we compared industry sponsored studies,
18
19 376 (HR =0.78; n=3 studies) and non-industry sponsored studies, (HR=0.97; n=18 studies) that
20 377 measured the association using HRs, we found a statistically significant difference in the
21 378 magnitude of the HRs (ratio of HRs 0.80 (95%CI 0.66, 0.97)); P=0.03 (Figure 3).
22
23
24
25

379

26
27 380 In our analysis comparing studies with an author with a COI (RR 0.89; n=2 studies) and those
28 381 with no COI, (RR 0.99; n= 8 studies) we found no important difference in the magnitude of
29 382 RRs (ratio of RRs 0.90 (95% CI 0.76-1.07)); P=0.22 (Supplementary file 8). When we
30 383 compared studies with a COI, (HR =1.00; n= 5 studies) and studies with no COI, (HR=0.93;
31 384 n=16 studies) that measured the association using HRs, we again found no difference in the
32 385 magnitude of the HRs (ratio of HRs 1.08 (95% CI 0.99, 1.17)); P=0.12.
33
34
35
36
37

386

387 **Effect Size, Elevated Blood Pressure / Hypertension: Industry ties v no industry ties,**
388 **and industry sponsorship vs no sponsorship**

389 We found no important difference in the magnitude of the HRs for elevated blood pressure /
390 hypertension in studies with industry ties, (HR = 0.89; n =2) and those studies with no
391 industry ties, (HR = 0.78; n= 5) (ratio of HRs 1.14 (95% CI 0.88, 1.49); P=0.32
392 (Supplementary file 8).
393

394

395 All of these studies with industry ties also had industry sponsorship, so the ratio of HRs was
396 the same.

397

398 **Favourable conclusions: Industry ties vs no industry ties; industry sponsorship vs no
399 sponsorship; COI v no COI**

400

399 There was no clear evidence of an association between the reporting of favourable
400 conclusions and studies with industry ties (4/14) compared to those with no industry ties
401 (11/29), RR= 0.75 (95% CI 0.29, 1.95; n=43) (Supplementary file 7). When we compared
402 studies only by industry sponsorship, there was no clear evidence of an association between
403 industry sponsored studies (3/8), compared to studies with no sponsorship (12/35), RR = 1.09
404 (95% CI 0.40, 2.99; n=43). There was again no clear evidence of an association between the
405 reporting of favourable conclusions and studies with an author with a COI (2/10) than those
406 without a COI (13/33), RR= 0.51 (95% CI 0.14, 1.88; n=43 studies).

407

408 **Risk of Bias Assessment by Industry Ties**

409 As every study had an overall high (serious or critical) risk of bias rating, there was no
410 difference in the proportion of studies at a high risk of bias between those with industry ties,
411 industry sponsorship or COI and those without industry ties, sponsorship or COI.

412

413 **Concordance between study results and conclusions**

414 Six (of 43) studies, all with unfavorable results, overemphasized the benefits of the dairy
415 exposure in their conclusions and thus were coded as 'favourable' conclusions.

416 There was no clear evidence of an association between discordant results and conclusions and
417 studies with industry ties (3/14) than those with no industry ties (3/29), RR = 2.07 (95% CI
418 0.48, 8.99; n=43) (Supplementary file 7). There was no clear evidence of an association when
419 comparing studies with industry sponsorship (2/8) to those with no industry sponsorship
420 (4/35), RR = 2.19 (95% CI 0.48-9.94). There was again no clear evidence of an association
421 between studies with an author with a COI (2/10) than those with no COI (4/33), RR = 1.65
422 (95% CI 0.35, 7.72; n=43).

423

424 **DISCUSSION**

425 There was no clear evidence of an association between studies with food industry ties and the
426 reporting of favourable results and conclusions of observational studies measuring the
427 associations of dairy foods with cardiovascular disease outcomes. The 'mixed' group of
428 funders we identified in the industry sponsored studies may influence these results, as the
429 funding effect may be diluted by this heterogeneous group of sponsors. Unlike in drug

1
2
3 430 studies,¹² the funders in the studies included in this review were extremely diverse, with Big
4 431 Food and trade association jointly sponsoring several studies. Thus, dairy foods are not their
5 432 sole interest.

6
7
8
9 433 The meta-analysis of hazard ratios of CVD outcomes found that studies with industry
10 434 sponsorship showed a greater benefit from dairy than studies without industry sponsorship,
11 435 and this difference was statistically significant. The meta-analysis of risk ratios of CVD
12 436 outcomes found a similar estimate; however, this was not statistically significant. The likely
13 437 reason for this was that the meta-analysis of RRs had fewer studies, and so the ratio of RRs
14 438 could not be as precisely estimated. We found no evidence of a clinically important
15 439 difference in the magnitude of effect between studies with industry ties or authors with a COI
16 440 compared to those with no industry ties or no COI for other outcomes.

17 441

18 442 For every study, the overall risk of bias was classified as high (meaning either serious or
19 443 critical). Therefore, differences in the risk of bias across studies with and without industry
20 444 ties would not seem to provide an explanation for our findings. However, the version of the
21 445 ROBINS-E tool that we used may not have been able to adequately discriminate across the
22 446 studies, as perhaps is indicated by the uniformity in risk of bias classification.²⁶ Therefore, we
23 447 cannot rule out the possibility that differences in bias across studies with and without industry
24 448 ties may partly explain our findings.

25 449

26 450 **Strengths and limitations of this review**

27 451 Our review was prospectively registered in Prospero.¹⁹ We followed explicit inclusion and
28 452 exclusion criteria, conducted a comprehensive search across multiple databases and hand
29 453 searched reference lists for the included studies.

30 454

31 455 For those studies missing a funding or author COI disclosure, we did not contact the authors
32 456 and we therefore may be underestimating the number of studies with industry ties. The tool
33 457 that we used to assess the risk of bias is still under development, however it is unlikely any
34 458 future changes to the tool will affect the risk of bias ratings.²² We did not analyse studies of
35 459 low and full fat dairy or other types of dairy products separately. Industry ties may have
36 460 different effects on studies of low or full fat dairy foods or other foods and drinks.

37 461 **Agreements and disagreements with other studies or reviews**

1
2
3 462 The observed greater benefit of dairy on CVD outcomes in industry sponsored studies
4
5 463 compared to non-industry sponsored studies corroborates previous research that has
6
7 464 demonstrated studies sponsored by the food industry reported smaller harmful effect sizes for
8
9 465 soft drink consumption, compared with non-industry sponsored studies.¹⁷ It is not consistent,
10
11 466 however, with a recent meta-analysis funded by the Israel Dairy Board that found non
12
13 467 statistically significant differences in the estimated associations between industry and non-
14
15 468 industry funded studies.¹⁸ The differences in the results of our current review and this
16
17 469 previous study can be attributed to a number of important factors in how the studies were
18
19 470 conducted, including how the exposures were classified, the outcomes selected for the meta-
20
21 471 analyses and the analysis method used. For the exposures, our review included yogurt and
22
23 472 cheese, as well as ‘total dairy’ and milk, whereas the Dairy Board study included only ‘total
24
25 473 dairy’ and milk as exposures. We included all outcomes related to CVD, and the Dairy Board
26
27 474 study included only CVD and stroke, as well as Type 2 diabetes. For the analysis method, we
28
29 475 fitted separate meta-analyses for studies that had measured the association using HRs and
30
31 476 those that had used either RRs or ORs, while the Dairy Board study only measured the
32
33 477 associations using RRs.

34
35 478
36
37 479 The lack of difference in the risks of bias between studies with industry ties and those with no
38
39 480 industry ties, is consistent with a previous review that examined the association of industry
40
41 481 ties with outcomes of studies examining the effect of wholegrain foods on CVD and mortality
42
43 482 that used the same tool to assess risk of bias.¹⁶ These findings have also been shown in
44
45 483 pharmaceutical and tobacco research that have demonstrated industry sponsored studies are
46
47 484 of equal or better internal validity than studies with no sponsorship.^{12, 13, 15, 27, 28}

485 486 **Implications for clinicians, policy makers and future research**

487
488 As dietary guidelines depend on an evidence base that should be as free as possible of bias,
49
50 489 the difference in the magnitude of effects between industry sponsored studies compared to
51
52 490 non-industry sponsored studies is concerning. Therefore, the dairy intake recommendations
53
54 491 made in dietary guidelines should account for the potential influence of industry sponsorship
55
56 492 on evidence of health effects. Nutrition studies included in systematic reviews used in the
57
58 493 development of dietary guidelines should be assessed using empirical methods to identify
59
60 494 factors associated with study results. Current risk of bias tools should therefore be amended
or supplemented to include industry sponsorship and author COI as a separate risk of bias

1
2
3 495 domain. The University of California, San Francisco's Navigation Guide assesses both author
4
5 496 conflicts of interest and funding sources as a risk of bias in human and animal studies.²⁹ As
6
7 497 the study designs used in nutrition are the same as those used to evaluate the harms of an
8
9 498 exposure in environmental health, dietary guideline committees could consider adopting this
10
11 499 tool to evaluate the risk of bias of the studies included in the systematic reviews used to
12
13 500 develop dietary guidelines.

14 501

15 502 Industry sponsors may bias research via different mechanisms, including the design and
16
17 503 conduct of a study, the selective reporting of results, how they code events, analyse data, by
18
19 504 spinning conclusions,¹¹ as well as framing how the questions are asked.³⁰⁻³² It has been
20
21 505 suggested that the dairy industry may preferentially fund research on topics which will
22
23 506 provide them with more favourable outcomes.³³ The influence of the food industry on the
24
25 507 research agenda has been demonstrated in an examination of research topics covered by
26
27 508 samples of randomised controlled trials included in systematic reviews of nutrition studies
28
29 509 and obesity.³⁴ It was shown that most food industry studies focused on the manipulations of
30
31 510 specific nutrients, and not on dietary behaviours, therefore limiting the public health
32
33 511 relevance of rigorous evidence available for use in both systematic reviews and dietary
34
35 512 guidelines.³⁴ The topics examined in cohort studies on the relationship of nutrition and
36
37 513 obesity, which tend to focus on more complex exposures than trials, did not demonstrate a
38
39 514 similar influence of funding source. However, the disclosure of food industry sponsorship
40
41 515 was low, making a comparison difficult.³⁵

42 516

43 517 This present study has also demonstrated that there is significant funding for nutrition
44
45 518 research that comes from non-industry sources, including academia and government. In this
46
47 519 study, only eight studies had food industry sponsorship, while 34 had a non-food industry
48
49 520 sponsorship. A similar rate was seen in a study that assessed the association of industry ties
50
51 521 with outcomes of studies examining the effect of wholegrain foods on cardiovascular disease
52
53 522 and mortality, with only five industry sponsored studies and 17 non-industry sponsored
54
55 523 studies.¹⁶ To eliminate this risk of bias from nutrition research, investigators should use only
56
57 524 non-industry sources to fund their research.

58 525

59 526

60 527 **Conclusion**

1
2
3 528 There was no clear evidence of an association between studies with food industry ties and the
4 reporting of favourable results and conclusions compared with studies without industry ties.
5 529
6 However, the statistically significant difference in the magnitude of effects identified in
7 530
8 industry sponsored studies compared to non-industry sponsored studies is important in
9 531
10 532 quantifying industry influence on studies included in dietary guidelines.
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3 533 **Acknowledgements:** We thank Agnes Lau, University of California, San Francisco, for her
4 534 assistance with data collection.
5
6
7 535

8
9 536 **Contributors:** NC, AF and LB designed and wrote the review protocol. NC wrote the search
10 537 strategy and undertook the literature search. NC, AF and SMc, conducted the title and
11 538 abstract screening and full article screening for final study inclusion. NC, AF, JD, AL and
12 539 SMc conducted data collection and cleaning, LB supervised. NC and JMc undertook all data
13 540 analysis. LB advised on methods, statistical analyses, and interpretation of findings. All
14 541 authors contributed to the final manuscript. NC and LB are guarantors.
15
16
17
18
19

20 542
21
22 543 **Funding:** This work was supported by Australian Health and Medical Research Council
23 544 Project Grant APP 1139997. Nicholas Chartres is a recipient of the James Millner PhD
24 545 Scholarship in Pharmacy from the University of Sydney.
25
26
27
28
29

30 546
31 547 **Competing interests:** None declared.
32
33
34

35 549 **Data sharing statement:** Available from The University of Sydney data repository. DOI to
36 550 be determined.
37
38
39

40 551
41
42 552 **Patient consent for publication:** Not required.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Qin LQ, Xu JY, Han SF, et al. Dairy consumption and risk of cardiovascular disease: an updated meta-analysis of prospective cohort studies. *Asia Pac J Clin Nutr*. 2015;24(1):90-100.
2. Alexander DD, Bylsma LC, Vargas AJ, et al. Dairy consumption and CVD: a systematic review and meta-analysis. *Br J Nutr*. 2016;115(4):737-50.
3. Gholami F, Khoramdad M, Esmailnasab N, et al. The effect of dairy consumption on the prevention of cardiovascular diseases: A meta-analysis of prospective studies. *J Cardiovasc Thorac Res*. 2017;9(1):1-11.
4. Drouin-Chartier JP, Brassard D, Tessier-Grenier M, et al. Systematic Review of the Association between Dairy Product Consumption and Risk of Cardiovascular-Related Clinical Outcomes. *Adv Nutr*. 2016;7(6):1026-40.
5. Lee M, Lee H, Kim J. Dairy food consumption is associated with a lower risk of the metabolic syndrome and its components: a systematic review and meta-analysis. *Br J Nutr*. 2018;120(4):373-84.
6. National Health and Medical Research Council: Department of Health and Ageing. Australian Dietary Guidelines. Canberra, Commonwealth of Australia: NHMRC; 2013.
7. Public Health England. The Eatwell Guide. [Internet]. 2016. Available from: <https://www.gov.uk/government/publications/the-eatwell-guide>. Accessed 18 March, 2016.
8. Lexchin J. Those who have the gold make the evidence: how the pharmaceutical industry biases the outcomes of clinical trials of medications. *Sci Eng Ethics*.18(2):247-61.
9. Sismondo S. How pharmaceutical industry funding affects trial outcomes: causal structures and responses. *Social science & medicine* (1982). 2008;66(9):1909-14.
10. Boutron I, Dutton S, Ravaud P, et al. Reporting and interpretation of randomized controlled trials with statistically nonsignificant results for primary outcomes. *JAMA*. 2010;303(20):2058-64.
11. Odierna DH, Forsyth SR, White J, et al. The cycle of bias in health research: a framework and toolbox for critical appraisal training. *Account Res*. 2013;20(2):127-41.
12. Lundh A, Lexchin J, Mintzes B, et al. Industry sponsorship and research outcome. *Cochrane Database Syst Rev*. 2017;2:Mr000033.
13. Barnes DE, Bero LA. Industry-funded research and conflict of interest: an analysis of research sponsored by the tobacco industry through the Center for Indoor Air Research. *J Health Polit Policy Law*. 1996;21(3):515-42.
14. Yank V, Rennie D, Bero LA. Financial ties and concordance between results and conclusions in meta-analyses: retrospective cohort study. *BMJ*.335(7631):1202-5.
15. Chartres N, Fabbri A, Bero LA. Association of industry sponsorship with outcomes of nutrition studies: A systematic review and meta-analysis. *JAMA Intern Med*. 2016;176(12):1769-77.
16. Chartres N, Fabbri A, McDonald S, et al. Association of industry ties with outcomes of studies examining the effect of wholegrain foods on cardiovascular disease and mortality: systematic review and meta-analysis. *BMJ Open*. 2019;9(5):e022912.
17. Vartanian LR, Schwartz MB, Brownell KD. Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis. *Am J Public Health*. 2007;97(4):667-75.
18. Mishali M, Kisner M, Avrech T. Funding sources and outcomes of dairy consumption research – a meta-analysis of cohort studies: The case of type-2 diabetes and cardiovascular diseases. *Int Dairy J*. 2019.
19. National Institute for Health Research. International Prospective Register for Systematic Reviews [Internet]. 2015 [Available from: <http://www.crd.york.ac.uk/PROSPERO/>. Accessed 11 March, 2016.
20. Dietitians Association of Australia. A review of the evidence to address targeted questions to inform the revision of the Australian dietary guidelines 2009: Process Manual. 2011.
21. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355.

- 1
2
3 603 22. University of Bristol. The ROBINS-E tool (Risk Of Bias In Non-randomized Studies - of
4 604 Exposures) 2019 [Available from: [https://www.bristol.ac.uk/population-health-
6 606 sciences/centres/cresyda/barr/riskofbias/robins-e/](https://www.bristol.ac.uk/population-health-
5 605 sciences/centres/cresyda/barr/riskofbias/robins-e/).
7 607 23. Harris PA, Taylor R, Thielke R, et al. Research Electronic Data Capture (REDCap) - A
8 607 metadata-driven methodology and workflow process for providing translational research informatics
9 608 support. *J Biomed Inform X*. 2009;42(2):377-81.
10 609 24. Tierney JF, Stewart LA, Ghersi D, et al. Practical methods for incorporating summary time-to-
11 610 event data into meta-analysis. *Trials*. 2007;8:16.
12 611 25. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic
13 612 Cochrane Centre, The Cochrane Collaboration, 2014.
14 613 26. Bero L, Chartres N, Diong J, et al. The risk of bias in observational studies of exposures
15 614 (ROBINS-E) tool: concerns arising from application to observational studies of exposures. *Syst Rev*.
16 615 2018;7(1):242.
17 616 27. Mandrioli D, Kearns CE, Bero LA. Relationship between Research Outcomes and Risk of Bias,
18 617 Study Sponsorship, and Author Financial Conflicts of Interest in Reviews of the Effects of Artificially
19 618 Sweetened Beverages on Weight Outcomes: A Systematic Review of Reviews. *PLoS one*.
20 619 2016;11(9):e0162198.
21 620 28. Cho MK, Bero LA. The quality of drug studies published in symposium proceedings. *Ann*
22 621 *Intern Med*. 1996;124(5):485-9.
23 622 29. Woodruff TJ, Sutton P. The Navigation Guide systematic review methodology: a rigorous and
24 623 transparent method for translating environmental health science into better health outcomes.
25 624 *Environ Health Perspect*. 2014;122(10):1007-14.
26 625 30. Fabbri A, Lai A, Grundy Q, et al. The Influence of Industry Sponsorship on the Research
27 626 Agenda: A Scoping Review. *Am J Public Health*. 2018;108(11):e9-e16.
28 627 31. Psaty BM, Prentice RL. Minimizing bias in randomized trials: the importance of blinding.
29 628 *JAMA*. 2010;304(7):793-4.
30 629 32. Psaty BM, Kronmal RA. Reporting mortality findings in trials of rofecoxib for Alzheimer
31 630 disease or cognitive impairment: a case study based on documents from rofecoxib litigation. *JAMA*.
32 631 2008;299(15):1813-7.
33 632 33. Wilde P, Morgan E, Roberts J, et al. Relationship between funding sources and outcomes of
34 633 obesity-related research. *Physiol & Behav*. 2012;107(1):172-5.
35 634 34. Fabbri A, Chartres N, Bero LA. Study sponsorship and the nutrition research agenda: analysis
36 635 of cohort studies examining the association between nutrition and obesity. *Public Health Nutr*.
37 636 2017;20(17):3193-9.
38 637 35. Fabbri A, Chartres N, Bero LA. Study sponsorship and the nutrition research agenda: analysis
39 638 of cohort studies examining the association between nutrition and obesity. *Public Health Nutr*.
40 639 2017;20(17):3193-9.

640

641

642

643

644

645

646

647

1
2
3 648 **Figures**
4

5 649 **Figure 1. Study Flow Diagram**
6

7
8 650 **Figure 2. Risk of Bias in Included Studies**
9

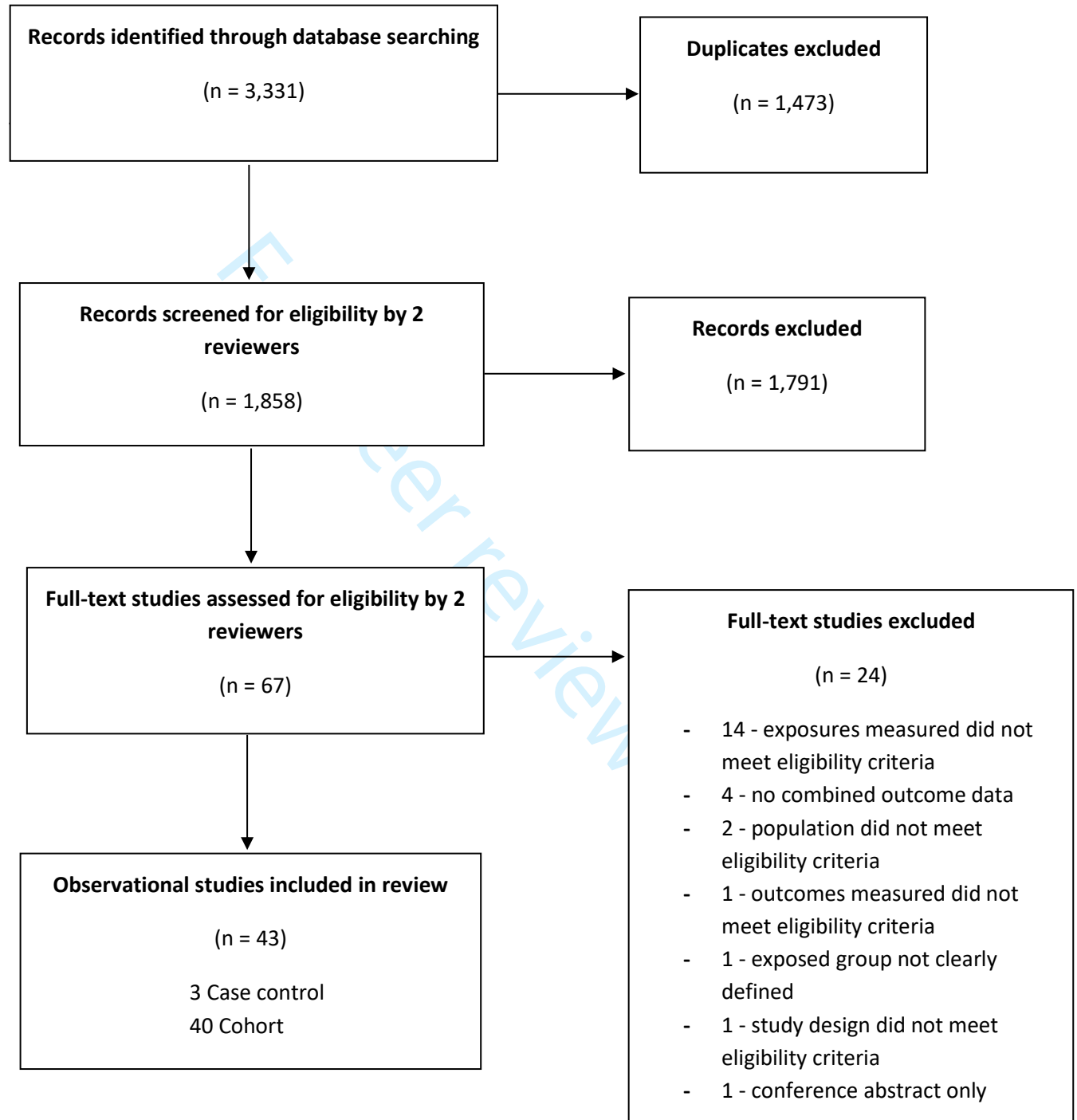
10 651 **Figure 3. Effect Size, Cardiovascular Disease: Industry sponsorship vs no industry**
11 **sponsorship, Hazard Ratio**
12
13

14
15 653
16

17 654
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Figure 1. Study Flow Diagram



BMJ Open

0-39036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Measurement of outcomes	Selection of the reported result	Overall bias
Aerde, M 2013	Red	Green	Green	Red	Red	Green	Red	Red
Al-Delaimy, WK 2003	Red	Green	Green	Green	Green	Green	Green	Red
Alonso A, 2005	Red	Green	Green	Green	Red	Green	Green	Red
Altorf-van der Kuil, W 2012	Red	Green	Green	Green	Red	Red	Green	Red
Avalos, EE 2013	Red	Red	Red	Red	Red	Red	Green	Red
Bernstein, AM 2012	Red	Green	Green	Green	Yellow	Green	Green	Red
Biong, A 2008	Red	Green	Red	Yellow	Green	Green	Red	Red
Bonthuis, M 2010	Red	Green	Green	Green	Green	Green	Green	Red
Buendia, JR 2018	Red	Green	Green	Green	Green	Red	Green	Red
Chen, M 2016	Red	Green	Green	Green	Green	Green	Green	Red
Dalmeijer, G 2013	Red	Green	Green	Red	Green	Green	Green	Red
Dauchet, L 2007	Red	Green	Green	Green	Yellow	Green	Green	Red
Dehghan, M 2018	Red	Green	Green	Red	Green	Green	Green	Red
Elwood, PC 2004	Red	Green	Green	Red	Green	Green	Green	Red
Engberink, MF 2009	Red	Green	Red	Green	Red	Green	Green	Red
Farvid, MS 2017	Red	Green	Green	Red	Green	Green	Green	Red
Haring, B 2014	Red	Green	Green	Red	Yellow	Green	Green	Red
He, K 2003	Red	Green	Red	Green	Yellow	Green	Green	Red
Heraclides, A 2012	Red	Red	Green	Red	Green	Green	Green	Red
Johansson, I 2018	Red	Green	Green	Green	Yellow	Red	Green	Red
Johansson, I 2019	Red	Green	Red	Red	Yellow	Green	Green	Red
Kim, D 2017	Red	Green	Green	Red	Yellow	Green	Green	Red

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41

Larsson, S 2009								
Larsson, SC 2012								
Li, K 2012								
Lin, PH 2013								
Lockheart, MSK 2007								
Louie, JCY 2013								
Mazidi, M, 2018								
Nettleton, J 2008								
Panagiotakos, D 2009								
Patterson, E 2013								
Praagman, J 2015								
Praagman, J 2015								
Sauvaget, C 2003								
Snijder, MB 2008								
Soedamah-Muthu, SS 2013								
Steffen, LM 2005								
Tavani, A 2002								
Um, C 2017								
Umesawa, M, 2008								
Wang, L 2008								

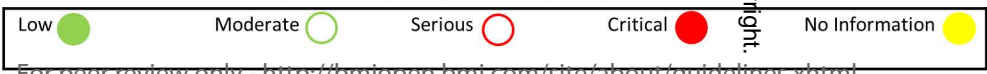
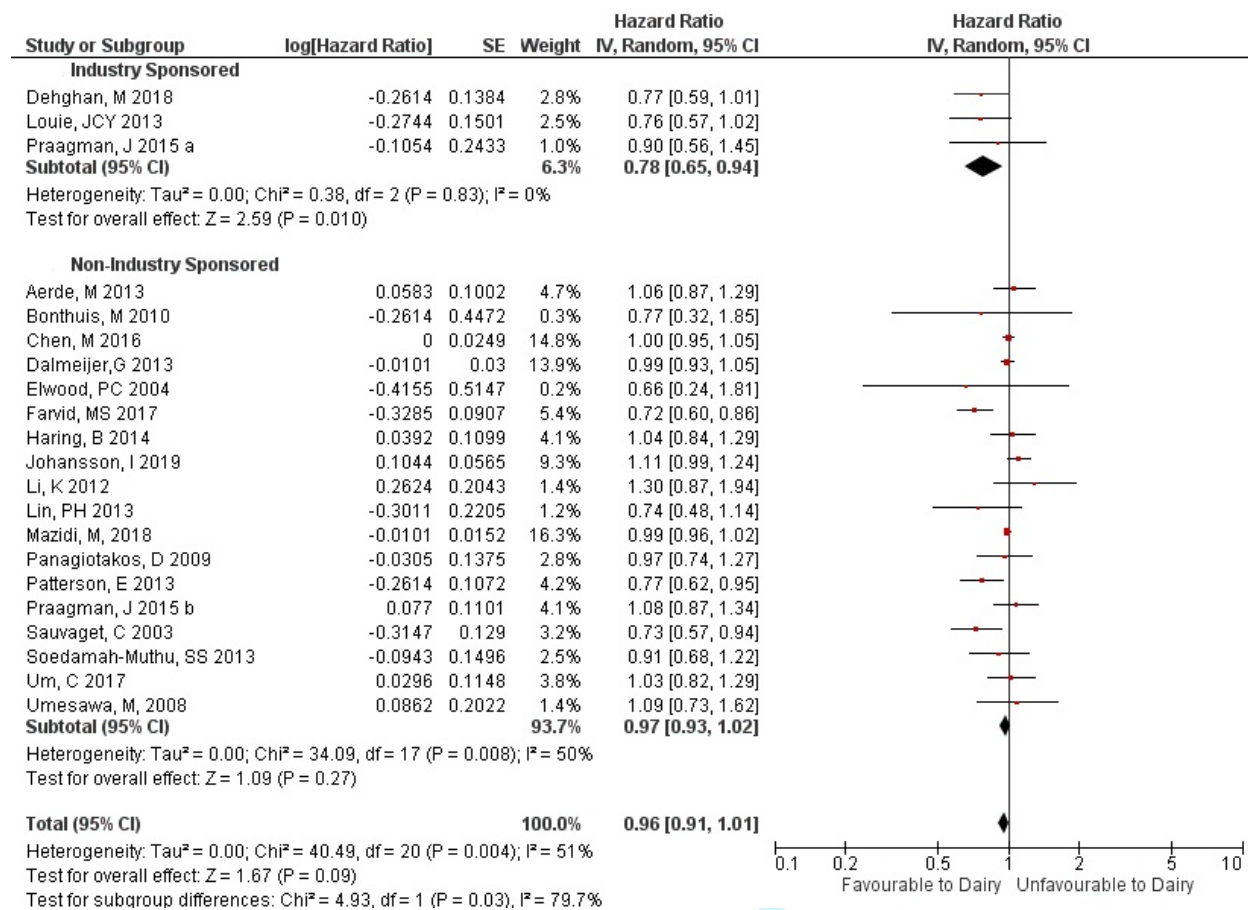


Figure 3. Effect Size, Cardiovascular Disease, Industry sponsorship vs no Industry sponsorship, Hazard Ratio



PROSPERO
International prospective register of systematic reviews

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

Please complete all mandatory fields below (marked with an asterisk *) and as many of the non-mandatory fields as you can then click *Submit* to submit your registration. You don't need to complete everything in one go, this record will appear in your *My PROSPERO* section of the web site and you can continue to edit it until you are ready to submit. Click *Show help* below or click on the icon to see guidance on completing each section.

This record cannot be edited because it has been rejected

1. * Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

The association of food industry ties with findings of studies examining the effect of dairy foods intake with cardiovascular disease and mortality: Systematic review and Meta-analysis: protocol registration:

2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. * Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

01/09/2016

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

01/06/2019

5. * Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.

Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.

This field should be updated when any amendments are made to a published record and on completion and publication of the review. If this field was pre-populated from the initial screening questions then you are not able to edit it until the record is published.

The review has not yet started: No

PROSPERO

International prospective register of systematic reviews

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	Yes	No
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

6. * Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Nicholas Chartres

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Mr Chartres

7. * Named contact email.

Give the electronic mail address of the named contact.

ngar0960@uni.sydney.edu.au

8. Named contact address

Give the full postal address for the named contact.

The University of Sydney, D17, the Hub, 6th Floor, Charles Perkins Centre | the University of Sydney | Nsw |
2006

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

02 8627 4328

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

University of Sydney

Organisation web address:

11. * Review team members and their organisational affiliations.

PROSPERO

International prospective register of systematic reviews

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country are now mandatory fields for each person.**

Mr Nicholas Chartres. University of Sydney
Dr Alice Fabbri. The University of Sydney
Agnes Lau. University of California
Dr Joanna Diong. The University of Sydney
Assistant/Associate Professor Joanne Mckenzie. Monash University
Professor Lisa Bero. The University of Sydney

12. * Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

Nicholas Chartres is a scholarship recipient (James Milner PhD scholarship in Pharmacy) from the University of Sydney.

Grant number(s)

13. * Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country are now mandatory fields for each person.**

15. * Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

The objective of this study is to determine if the presence of food industry sponsorship in primary nutrition studies examining the association of dairy foods with cardiovascular outcomes is associated with effect sizes, statistical significance of results and/ or conclusions that are favorable to the sponsor. We will also determine whether primary nutrition studies assessing the association of dairy foods with cardiovascular outcomes with industry sponsorship differ in their risk of bias compared with studies with no or other sources of sponsorship.

16. * Searches.

State the sources that will be searched. Give the search dates, and any restrictions (e.g. language or publication period). Do NOT enter the full search strategy (it may be provided as a link or attachment.)

We will search the following databases from 2000-March 2019: Ovid MEDLINE; CINAHL; PubMed;

Cochrane Library; and ScienceDirect. No language restrictions will be applied

PROSPERO**International prospective register of systematic reviews****17. URL to search strategy.**

Give a link to a published pdf/word document detailing either the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies), or upload your search strategy. Do NOT provide links to your search results.

https://www.crd.york.ac.uk/PROSPEROFILES/129659_STRATEGY_20190322.pdf

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

To determine whether industry sponsorship and/or study methods are associated with the results and/or conclusions of primary nutrition studies assessing the association of dairy foods and cardiovascular outcomes.

19. * Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

We will include primary research studies of any design that quantitatively examine the association of dairy foods with cardiovascular outcomes in healthy adults.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed.

- The study quantitatively measures the effects of dairy consumption in humans.
- The study evaluates the effectiveness, efficacy or harms of dairy consumption.
- The study compares dairy food to control OR dairy food to other foods OR different levels of dairy consumption
- The study evaluates cow, goat or sheep milk, yogurt, cheese or custard. We will include and use the studies definition of dairy it is broader than milk, yogurt, cheese or custard.
- The study evaluates skim, low or full fat dairy products
- The study evaluates the effect of nutrients, e.g calcium and vitamin D when consumed within a dairy product

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Dairy vs Dairy (different doses) Dairy vs Dairy (different fat content) Dairy vs No dairy Dairy vs Other food

PROSPERO

International prospective register of systematic reviews

Other (mixed intervention)

22. * Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

RCTs, Controlled Trials, Cohort, Case-control, Pre/Post, Other/Various

23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

- The study has a test of interest (e.g. risk ratio/hazard ratio) of cardiovascular mortality, nonfatal heart attack, stroke, etc.) and/or the surrogate outcomes of Blood Pressure (mmHg)

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

a. Primary Outcome 1 and 2

- o Statistical significance of results
- o Effect size of outcomes

For each study, the result reported for each primary outcome will be categorized as:

(1) Favourable if the result are statistically significant ($p < 0.05$ or 95% confidence interval [CI] excluding no difference) and in the direction of dairy being more efficacious, less harmful or no more harmful than the comparator;

(2) Unfavourable if the result was statistically significant (e.g. $P < 0.05$ or 95% confidence interval including the possibility of no difference) in the direction of the comparator being more efficacious or less harmful.

We will also extract the effect estimates for primary outcomes.

We will classify the results of the study as favourable if the stated primary outcome is reported as favourable.

If the study has multiple primary outcomes we will report the study as favourable if at least one of the outcomes is reported as favourable.

b. Primary Outcome 3 (Conclusions)

The conclusions reported in the published papers will be categorized as:

(1) Favourable if the dairy intervention was preferred to comparator

(2) Unfavourable if the comparator intervention was preferred to the test one OR if the test intervention

PROSPERO

International prospective register of systematic reviews

showed a risk increase.

* Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

As this is not relevant to our study, we have nothing to include.

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

We used the Cochrane Risk of Bias tool for randomised studies (15) to measure the methodological quality of randomized controlled trials. The tool assesses bias across 7 domains and each of these will be reported separately. To measure methodological quality in observational studies we will use the ROBINS-I tool for non-randomized studies (ROBINS-I)(16), which also measures bias across 7 domains.

d. Secondary Outcome 2 (Concordance between results and conclusions)

We will classify concordance between study results and conclusions as 'yes' if the authors' conclusions are supported by all outcomes. This will include the reporting of all significant and non-significant results.

Otherwise, concordance will be classified as 'no'

* Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

As this is not relevant to our study, we have nothing to include.

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Selection Process

Two investigators (NC & AF) will independently screen the titles and abstracts of all retrieved records for obvious exclusions. Two investigators (NC & AF) will then assess the remaining papers based on full text, applying the aforementioned inclusion criteria for included studies. Agreement will be reached on any discrepancies by consensus between the two assessors. If agreement cannot be reached, a third assessor (LB) will make a decision. The reasons for the eligible papers being excluded will be described in

PROSPERO

International prospective register of systematic reviews

'Characteristics of excluded papers' table.

Data collection process

- a) Title of the paper
- b) Year of publication
- c) Study design
- d) Comparisons:
- e) Sample size of study
- f) Mean age of participants
- g) Intervention or observation period
- h) Definition of intervention and exposure
- i) Risk of Bias
- j) Primary Hypothesis of the study (Verbatim)
- k) Primary outcomes measures
- l) Conclusion
- m) Concordance between conclusions and results
- n) Industry Sponsorship
- o) Role of the Funder: Information about the role of the sponsor as stated in the study
- p) The institutional affiliation of the corresponding author will be obtained from the article and classified into the following categories
- q) Country of origin (verbatim)
- r) Author COI

27. * Risk of bias (quality) assessment.

Describe the method of assessing risk of bias or quality assessment. State which characteristics of the studies will be assessed and any formal risk of bias tools that will be used.

We will use the Cochrane Risk of Bias tool for randomised studies (15) to measure the methodological quality of randomized controlled trials. The tool assesses bias across 7 domains and each of these will be reported separately. To measure methodological quality in observational studies we will use the ROBINS-I tool for non-randomized studies (ROBINS-I)(16), which also measures bias across 7 domains.

28. * Strategy for data synthesis.

Provide details of the planned synthesis including a rationale for the methods selected. This **must not be generic text** but should be **specific to your review** and describe how the proposed analysis will be applied to your data.

To test our hypothesis that studies with dairy industry sponsorship will be more likely to have favourable

PROSPERO

International prospective register of systematic reviews

results, we will compare the risk of dairy industry sponsored studies having a favourable result with the risk of non-dairy industry funded studies having a favorable result. Using Rev Manager we will calculate the pooled risk ratio (RR) and its 95% confidence interval using the Mantel-Haenszel fixed-effect model.

However, when substantial heterogeneity is observed, we will use an inverse variance DerSimonian-Laird random-effects model. We will assess heterogeneity using I^2 and use a random-effects model when statistical heterogeneity is substantial, defined as an I^2 50%.

To test our hypothesis that effect estimates will differ between studies with dairy industry sponsorship and those without sponsorship, we will compare the pooled effect estimates from dairy vs. non-dairy sponsored studies. We will pool the effect estimates of homogenous studies measuring dichotomous outcomes, (e.g. RR, HR, OR for all-cause mortality, CVD mortality, cardiovascular events, etc) calculating pooled risk ratios as described above. Blood pressure is a continuous outcome, so we will attempt to pool homogeneous studies and measure the mean difference from baseline measures.

To test our hypothesis that studies with dairy industry sponsorship would be more likely to have favourable conclusions we will compare the risk of dairy industry sponsored studies having favourable conclusions with the risk of non-dairy industry funded studies having a favorable conclusion. We will calculate the pooled risk ratio (RR) and its 95% confidence interval using the Mantel-Haenszel fixed-effect model. However, when substantial heterogeneity is observed, we will use an inverse variance DerSimonian-Laird random-effects model. We will assess heterogeneity using I^2 and use a random-effects model when statistical heterogeneity is substantial, defined as an I^2 50%.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

We will conduct an a priori subgroup analysis on low fat and full fat dairy products to determine if studies measuring the effects of low fat products have different results from studies that measure full fat dairy products.

We will conduct an a priori subgroup analysis by the risks of bias of the included studies to determine if studies that have a high risk of bias have different results from studies that have a low risk of bias. We hypothesize that industry sponsored studies will have the same level of risk of bias as non-industry sponsored studies.

30. * Type and method of review.

Select the type of review and the review method from the lists below. Select the health area(s) of interest for your review.

Type of review

Cost effectiveness

PROSPERO

International prospective register of systematic reviews

1
2
3
4 No
5 Diagnostic
6 No
7 Epidemiologic
8 No
9 Individual patient data (IPD) meta-analysis
10 No
11 Intervention
12 No
13
14 Meta-analysis
15 Yes
16 Methodology
17 No
18 Narrative synthesis
19 No
20
21 Network meta-analysis
22 No
23 Pre-clinical
24 No
25 Prevention
26 No
27 Prognostic
28 No
29 Prospective meta-analysis (PMA)
30 No
31
32 Review of reviews
33 No
34 Service delivery
35 No
36 Synthesis of qualitative studies
37 No
38
39 Systematic review
40 Yes
41 Other
42 No
43
44
45 **Health area of the review**
46 Alcohol/substance misuse/abuse
47 No
48
49 Blood and immune system
50 No
51 Cancer
52 No
53 Cardiovascular
54 Yes
55
56 Care of the elderly
57 No
58 Child health
59 No
60 Complementary therapies

PROSPERO**International prospective register of systematic reviews**

1 No
2
3
4 Crime and justice
5 No
6 Dental
7 No
8 Digestive system
9 No
10 Ear, nose and throat
11 No
12 Education
13 No
14 Endocrine and metabolic disorders
15 No
16 Eye disorders
17 No
18 General interest
19 No
20 Genetics
21 No
22 Health inequalities/health equity
23 No
24 Infections and infestations
25 No
26 International development
27 No
28 Mental health and behavioural conditions
29 No
30 Musculoskeletal
31 No
32 Neurological
33 No
34 Nursing
35 No
36 Obstetrics and gynaecology
37 No
38 Oral health
39 No
40 Palliative care
41 No
42 Perioperative care
43 No
44 Physiotherapy
45 No
46 Pregnancy and childbirth
47 No
48 Public health (including social determinants of health)
49 Yes
50 Rehabilitation
51 No
52 Respiratory disorders
53 No
54
55
56
57
58
59
60

PROSPERO

International prospective register of systematic reviews

Service delivery
No

Skin disorders
No

Social care
No

Surgery
No

Tropical Medicine
No

Urological
No

Wounds, injuries and accidents
No

Violence and abuse
No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

Australia

33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one

Give the link to the published protocol.

Alternatively, upload your published protocol to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

PROSPERO

International prospective register of systematic reviews

Do you intend to publish the review on completion?

Yes

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords will help users find the review in the Register (the words do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

Nutrition, Industry Sponsorship, Conflict of Interest, Bias, Food Industry

37. Details of any existing review of the same topic by the same authors.

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

CRD42017055841 The association of industry sponsorship with outcomes of studies examining the effect of intake of wholegrain foods with cardiovascular disease and mortality: protocol

38. * Current review status.

Review status should be updated when the review is completed and when it is published. For new registrations the review must be Ongoing.

Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information the review team feel is relevant to the registration of the review.

40. Details of final report/publication(s).

This field should be left empty until details of the completed review are available.

Give the link to the published review.

Supplementary file 2. Search Strategy OVID Medline: Dairy, CVD, Adults

1. Randomized controlled trial*.tw.
2. experimental design.tw.
3. intervention*.tw.
4. (RCT* or rct*).tw.
5. random* control* trial*.tw.
6. clinical trial*.tw.
7. field trial*.tw.
8. community trial*.tw.
9. controlled clinical trial*.tw.
10. pragmatic trial*.tw.
11. observational stud*.tw.
12. cohort stud*.tw.
13. prospective cohort*.tw.
14. retrospective cohort*.tw.
15. case control*.tw.
16. ecological stud*.tw.
17. time series analys?s*.tw.
18. before-after stud*.tw.
19. pre-post stud*.tw.
20. follow up stud*.tw.
21. comparative stud*.tw.
22. evaluation stud*.tw.
23. dairy.mp.
24. dairy intake*.mp.

- 1
- 2
- 3 25. dairy consumption.mp.
- 4
- 5 26. dairy food*.mp.
- 6
- 7 27. Dairy Products/ or dairy product*.mp.
- 8
- 9 28. dairy serv*.mp.
- 10
- 11 29. dairy type*.mp.
- 12
- 13 30. dairy source*.mp.
- 14
- 15
- 16 31. (calcium adj15 food sourc*).mp. [mp=title, abstract, original title, name of substance word,
- 17 subject heading word, keyword heading word, protocol supplementary concept word, rare
- 18 disease supplementary concept word, unique identifier]
- 19
- 20
- 21 32. (vitamin D adj15 food sourc*).mp. [mp=title, abstract, original title, name of substance word,
- 22 subject heading word, keyword heading word, protocol supplementary concept word, rare
- 23 disease supplementary concept word, unique identifier]
- 24
- 25
- 26 33. (milk and (cow or goat or sheep)).mp. [mp=title, abstract, original title, name of substance
- 27 word, subject heading word, keyword heading word, protocol supplementary concept word, rare
- 28 disease supplementary concept word, unique identifier]
- 29
- 30
- 31 34. yogurt.mp. or Yogurt/
- 32
- 33 35. cheese.mp. or Cheese/
- 34
- 35 36. custard.mp.
- 36
- 37 37. (milk and (skim or full fat or low fat)).mp. [mp=title, abstract, original title, name of
- 38 substance word, subject heading word, keyword heading word, protocol supplementary concept
- 39 word, rare disease supplementary concept word, unique identifier]
- 40
- 41
- 42 38. (yogurt and (skim or full fat or low fat)).mp. [mp=title, abstract, original title, name of
- 43 substance word, subject heading word, keyword heading word, protocol supplementary concept
- 44 word, rare disease supplementary concept word, unique identifier]
- 45
- 46
- 47 39. Milk/
- 48
- 49 40. 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or
- 50 39
- 51
- 52 41. cardiovascular disease.mp. or exp Cardiovascular Diseases/
- 53
- 54 42. coronary*.tw.
- 55
- 56
- 57
- 58
- 59
- 60

- 1
- 2
- 3 43. heart*.tw.
- 4
- 5 44. cardia*.tw.
- 6
- 7 45. cardio*.tw.
- 8
- 9 46. myocard*.tw.
- 10
- 11 47. isch?em*.tw.
- 12
- 13 48. angina*.tw.
- 14
- 15 49. ventric*.tw.
- 16
- 17 50. tachycardi*.tw.
- 18
- 19 51. pericard*.tw.
- 20
- 21 52. endocardi*.tw.
- 22
- 23 53. atrial fibrillat*.tw.
- 24
- 25 54. arrhythmi*.tw.
- 26
- 27 55. athero*.tw.
- 28
- 29 56. arterio*.tw.
- 30
- 31 57. exp Atherosclerosis/
- 32
- 33 58. exp Arteriosclerosis/
- 34
- 35 59. HDL.tw.
- 36
- 37 60. LDL.tw.
- 38
- 39 61. VLDL.tw.
- 40
- 41 62. lipid*.tw.
- 42
- 43 63. lipoprotein*.tw.
- 44
- 45 64. triacylglycerol*.tw.
- 46
- 47 65. exp Hyperlipidemias/
- 48
- 49 66. hyperlipid*.tw.
- 50
- 51 67. hypercholesterol*.tw.
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

- 1
- 2
- 3 68. hypercholester?emia*.tw.
- 4
- 5 69. hypertriglycerid?emia*.tw.
- 6
- 7 70. exp Cholesterol/
- 8
- 9 71. cholesterol*.tw.
- 10
- 11 72. exp Stroke/
- 12
- 13 73. stroke*.tw.
- 14
- 15 74. CVA.tw.
- 16
- 17 75. cerebrovasc*.tw.
- 18
- 19 76. "vascular accident".tw.
- 20
- 21 77. TIA.tw.
- 22
- 23 78. cerebral vascular.tw.
- 24
- 25 79. thrombo*.tw.
- 26
- 27 80. emboli*.tw.
- 28
- 29 81. apoplexy.tw.
- 30
- 31 82. (brain adj2 accident*).tw.
- 32
- 33 83. ((brain* or cerebral or lacunar) adj2 infarct*).tw.
- 34
- 35 84. Hypertension/
- 36
- 37 85. exp Blood Pressure/
- 38
- 39 86. hypertensi*.tw.
- 40
- 41 87. blood pressure*.tw.
- 42
- 43 88. systolic blood pressure.tw.
- 44
- 45 89. diastolic blood pressure.tw.
- 46
- 47 90. peripheral arter* disease*.tw.
- 48
- 49 91. (coronar\$ adj5 (bypas\$ or graft\$ or disease\$ or event\$)).tw.
- 50
- 51 92. (cerebrovasc\$ or cardiovasc\$ or mortal\$ or angina\$ or stroke or strokes).tw.
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

1
2
3 93. (myocardi\$ adj5 (infarct\$ or revascular\$ or ischaemi\$ or ischemi\$)).tw.
4

5 94. (morbid\$ adj5 (heart\$ or coronar\$ or ischaem\$ or ischem\$ or myocard\$)).tw.
6

7 95. (vascular\$ adj5 (peripheral\$ or disease\$ or complication\$)).tw.
8

9 96. (heart\$ adj5 (disease\$ or attack\$ or bypass\$)).tw.
10

11 97. 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or
12 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73
13 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or
14 90 or 91 or 92 or 93 or 94 or 95 or 96
15
16

17 98. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or
18 19 or 20 or 21 or 22
19
20

21 99. 40 and 97 and 98
22

23 100. limit 99 to yr="2000 - 2019"
24

25 101. limit 100 to humans
26

27 102. limit 101 to "all adult (19 plus years)"
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary File 3. List of confounders

Outcome	Confounders	Confounders (all outcomes)
1. CVD mortality	Fibre supplement (p) Red Meat (h) Sodium (Na+) (h)	Age Sex BMI
2. CVD events	Fibre supplement (p) Magnesium supplement (p)	Smoking Alcohol intake
3. CHD mortality (incident CVD)	Fibre supplement (p) Trans Fat (h) Polyunsaturated fat (n-6) (p) Sodium (+Na) (h)	History of co-morbidities Parenteral/Fhx MI < 60 yrs PA levels SES
4. CHD events (incident CHD)	Fibre supplement (p) Trans fat (h) Magnesium supplement (p) Polyunsaturated fat (n-6) (p)	Total energy intake Fruit & Vegetable intake <i>Specialised Confounders</i>
5. Total MI	Aspirin (p) Vitamin E supplement (p)	Hormone therapy
6. Fatal MI	Vitamin E supplement (p)	
7. Non-fatal MI	Aspirin (p)	
8. Total stroke	Potassium supplement (p) Red Meat (h) Sodium (+Na) (h)	
9. Ischemic stroke	Aspirin (p) Polyunsaturated fat (LC n-3) (p) Red meat (h)	
10. Haemorrhagic stroke	Aspirin (h)	
11. Systolic BP	Magnesium supplement (p) Sodium (-Na) (p) Polyunsaturated fat (supplement) (LC n-3) (p) Potassium supplement (p)	
12. Diastolic BP	Magnesium supplement (p) Sodium (-Na) (p) Polyunsaturated fat (supplement) (LC n-3) (p) Potassium supplement (p)	

p = protective, h = harmful

a) Not Confounders (inconclusive evidence)

Outcome	Not a confounder (inconclusive)
1. CVD mortality	Aspirin Dietary Saturated Fat Folate supplement Monounsaturated Fat Multivitamin Polyunsaturated Fat Total Dietary Fat Vitamin E supplement
2. CVD events	Folate supplement Monounsaturated Fat Multivitamin Polyunsaturated Fat Sodium Total Dietary Fat Vitamin E supplement
3. CHD mortality	Dietary Saturated Fat Magnesium supplement
4. CHD events	Dietary Saturated Fat Sodium Red Meat
5. Total MI	Dietary Saturated Fat Folate supplement Magnesium supplement Multivitamin Polyunsaturated Fat Total Dietary Fat
6. Fatal MI	Folate supplement Multivitamin
7. Non-fatal MI	Dietary Saturated Fat Folate supplement Multivitamin Polyunsaturated Fat Total Dietary Fat Vitamin E supplement

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

8. Total stroke	Aspirin Dietary Saturated Fat Folate supplement Monounsaturated Fat Multivitamin Polyunsaturated Fat Total Dietary Fat Vitamin E supplement
9. Ischemic stroke	Dietary Saturated Fat Trans Fat
10. Haemorrhagic stroke	Polyunsaturated Fat Red Meat
11. Systolic BP	Polyunsaturated Fat (dietary)
12. Diastolic BP	Polyunsaturated Fat (dietary)

Supplementary file 4: List of excluded studies and reasons for exclusion

Author	Title	Reason for Exclusion
Akbaraly, T 2013 ¹	Does overall diet in midlife predict future aging phenotypes? A cohort study	Dietary patterns only were assessed, not dairy foods
Anderson, LA 2011 ²	Dietary Patterns and Survival of Older Adults	No relevant outcomes were measured
Baylin, A 2003 ³	High 18:2 trans-fatty acids in adipose tissue are associated with increased risk of nonfatal acute myocardial infarction in Costa Rican adults	Effects of dairy foods not measured
Beydoun, MA 2018 ⁴	Dairy product consumption and its association with metabolic disturbance in a prospective study of urban adults	Groups exposed to dairy not clearly defined
Biong, AS 2006 ⁵	Intake of milk fat, reflected in adipose tissue fatty acids and risk of myocardial infarction: a case-control study	Effects of dairy foods not measured
Chen, y 2013 ⁶	Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh	Dietary patterns only were assessed, not dairy foods
Ding, M 2017 ⁷	Dairy consumption, systolic blood pressure, and risk of hypertension: Mendelian randomization study	Not an observational design study
Eguchi, E 2012 ⁸	Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study	Dietary patterns only were assessed, not dairy foods
Geleijnse, JM 2017 ⁹	Dietary Patterns in Relation to Cardiovascular Disease Incidence and Risk Markers in a Middle-Aged British Male Population: Data from the Caerphilly Prospective Study	Dietary patterns only were assessed, not dairy foods
Goldbohm, RA 2011 ¹⁰	Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in the Netherlands	No combined outcome data
Julián-Almárcegui, C 2016 ¹¹	Association of heart rate and blood pressure among European adolescents with usual food consumption: The HELENA study	Participants were adolescents, not adults
Larsson, SC 2018 ¹²	Dietary patterns, food groups, and incidence of aortic valve stenosis: A prospective cohort study	Dietary patterns only were assessed, not dairy foods
Lupton, BS 2003 ¹³	The Finnmark Intervention Study: is it possible to change CVD risk factors by community-based intervention in an Arctic village in crisis?	No combined outcome data
Meyer, J 2011 ¹⁴	Dietary patterns, subclinical inflammation, incident coronary heart disease and mortality	Dietary patterns only were assessed, not dairy foods

	in middle-aged men from the MONICA/KORA Augsburg cohort study	
Michaelsson, K 2013 ¹⁵	Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study	Dietary calcium only was assessed, not dairy foods
Oomen, CM 2000 ¹⁶	Arginine intake and risk of coronary heart disease mortality in elderly men	Effects of dairy foods not measured
Paillard, F 2015 ¹⁷	Cardiovascular risk and lifestyle habits of consumers of a phytosterol-enriched yogurt in a real-life setting	Yogurt was enriched with phytosterols
Praagman, J 2016 ¹⁸	The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort	Effects of dairy foods not measured
Streppel, MT 2014 ¹⁹	Nutrient-rich foods, cardiovascular diseases and all-cause mortality: the Rotterdam study	Dietary patterns only were assessed, not dairy foods
Umesawa, M 2006 ²⁰	Dietary intake of calcium in relation to mortality from cardiovascular disease: the JACC Study	No combined outcome data
van der Pols, J C 2009 ²¹	Childhood dairy and calcium intake and cardiovascular mortality in adulthood: 65-year follow-up of the Boyd Orr cohort	Participants were children, not adults
Warensjo, E 2009 ²²	Stroke and plasma markers of milk fat intake – a prospective nested case-control study	Effects of dairy foods not measured
Warensjo, E 2009 ²³	Milk Fat Biomarkers and the Risk of a First Ever Acute Myocardial Infarction - A Prospective Nested Case-Control Study. <i>Journal of the American Dietetic Association.</i> 2009;1	Poster presentation only, full study not available
Warensjo, E 2010 ²⁴	Biomarkers of milk fat and the risk of myocardial infarction in men and women: a prospective, matched case-control study	No combined outcome data

1. Akbaraly T, Sabia S, Hagger-Johnson G, et al. Does overall diet in midlife predict future aging phenotypes? A cohort study. *The American journal of medicine.* 2013;126(5):411-419.e413.
2. Anderson AL, Harris TB, Tylavsky FA, et al. Dietary Patterns and Survival of Older Adults. *Journal of the American Dietetic Association.* 2011;111(1):84-91.
3. Baylin A, Kabagambe EK, Ascherio A, et al. 18:2 trans-fatty acids in adipose tissue are associated with increased risk of nonfatal acute myocardial infarction in costa rican adults. *Journal of Nutrition.* 2003;133(4):1186-1191.
4. Beydoun MA, Fanelli-Kuczmarski MT, Beydoun HA, et al. Dairy product consumption and its association with metabolic disturbance in a prospective study of urban adults. *British Journal of Nutrition.* 2018;119(6):706-719.

5. Biong AS, Veierod MB, Ringstad J, et al. Intake of milk fat, reflected in adipose tissue fatty acids and risk of myocardial infarction: a case-control study. *European Journal of Clinical Nutrition*. 2006;60(2):236-244.
6. Chen Y, McClintock TR, Segers S, et al. Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh. *International Journal of Cardiology*. 2013;167(4):1495-1501.
7. Ding M, Huang T, Bergholdt HK, et al. Dairy consumption, systolic blood pressure, and risk of hypertension: Mendelian randomization study. *Bmj*. 2017;356:j1000.
8. Eguchi E, Iso H, Tanabe N, et al. Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study. *European heart journal*. 2012;33(4):467-477.
9. Geleijnse JM, Mertens E, Markey O, et al. Dietary Patterns in Relation to Cardiovascular Disease Incidence and Risk Markers in a Middle-Aged British Male Population: Data from the Caerphilly Prospective Study. *Nutrients*. 2017;9(1):75.
10. Goldbohm RA, Chorus AMJ, Galindo Garre F, et al. Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in the Netherlands. *American Journal of Clinical Nutrition*. 2011;93(3):615-627 613p.
11. Julián-Almárcegui C, Vandevijvere S, Gottrand F, et al. Association of heart rate and blood pressure among European adolescents with usual food consumption: The HELENA study. *Nutrition, Metabolism & Cardiovascular Diseases*. 2016;26(6):541-548.
12. Larsson SC, Wolk A, Bäck M. Dietary patterns, food groups, and incidence of aortic valve stenosis: A prospective cohort study. *International Journal of Cardiology*. 2018.
13. Lupton BS, Fonnebo V, Sogaard AJ, et al. The Finnmark Intervention Study: is it possible to change CVD risk factors by community-based intervention in an Arctic village in crisis? *Scandinavian Journal of Public Health*. 2003;31(3):178-186.
14. Meyer J, Doring A, Herder C, et al. Dietary patterns, subclinical inflammation, incident coronary heart disease and mortality in middle-aged men from the MONICA/KORA Augsburg cohort study. *European journal of clinical nutrition*. 2011;65(7):800-807.
15. Michaelsson K, Melhus H, Warensjo E, et al. Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study. *Bmj*. 2013;346:f228.
16. Oomen CM, van Erk MJ, Feskens EJ, et al. Arginine intake and risk of coronary heart disease mortality in elderly men. *Arteriosclerosis, thrombosis, and vascular biology*. 2000;20(9):2134-2139.
17. Paillard F, Bruckert E, Naelten G, et al. Cardiovascular risk and lifestyle habits of consumers of a phytosterol-enriched yogurt in a real-life setting. *Journal of Human Nutrition & Dietetics*. 2015;28(3):226-235 210p.
18. Praagman J, Beulens JW, Alsema M, et al. The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort. *American Journal of Clinical Nutrition*. 2016;103(2):356-365.
19. Streppel MT, Sluik D, van Yperen JF, et al. Nutrient-rich foods, cardiovascular diseases and all-cause mortality: the Rotterdam study. *European journal of clinical nutrition*. 2014;68(6):741-747.
20. Umesawa M, Iso H, Date C, et al. Dietary intake of calcium in relation to mortality from cardiovascular disease: the JACC Study. *Stroke*. 2006;37(1):20-26.
21. van der Pols JC, Gunnell D, Williams GM, et al. Childhood dairy and calcium intake and cardiovascular mortality in adulthood: 65-year follow-up of the Boyd Orr cohort. *Heart*. 2009;95(19):1600-1606.
22. Warensjo E, Smedman A, Stegmayr B, et al. Stroke and plasma markers of milk fat intake--a prospective nested case-control study. *Nutrition Journal*. 2009;8:21.

- 1
2
3 23. Warensjo E, Sjogren P, Cederholm T, et al. Milk Fat Biomarkers and the Risk of a First Ever
4 Acute Myocardial Infarction - A Prospective Nested Case-Control Study. *Journal of the*
5 *American Dietetic Association*. 2009;109(9, Supplement):A51.
6 24. Warensjö E, Jansson JH, Cederholm T, et al. Biomarkers of milk fat and the risk of myocardial
7 infarction in men and women: a prospective, matched case-control study. *American Journal of*
8 *Clinical Nutrition*. 2010;92(1):194-202 199p.
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Supplementary file 5: Characteristics of included studies

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Verbatim)	Funding Source	Disclosed author conflicts of interest
Aerde, M 2013 ⁽¹⁾	Cohort	12.4 years	1,956 men & women	61.6 years	Total Dairy, 271 g/day per SD of the mean intake for Total dairy (all dairy products except butter)		Total CVD	Non-Industry ¹	Yes ^a
Al-Delaimy, WK 2003 ⁽²⁾	Cohort	12 years	39,800 men	40-75 years	Dairy Calcium Q5, 819 mg/day (median) (dairy calcium intake summed the calcium intake from whole milk, skim or low-fat milk, yogurt, ice cream, cottage cheese, and other cheese was summed)	Q1, 106 mg/day	Total Ischemic Heart Disease	Non Industry ²	No ^b
Alonso A, 2005 ⁽³⁾	Cohort	27 months	5,880 men & women	37 years	Dairy Q 5, 798.8 g/day (whole-fat milk, partially skim milk, skim milk, condensed milk, whipped cream, yogurt, skim yogurt, milk-shake, cottage cheese or junket, petit Suisse cheese, spreadable cheese wedges, soft unripened cheese, other cheese, custard, and ice cream)	Q 1, 155.6 g/day	Hypertension	Non-industry ³	No ^c

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Altorf-van der Kuil, W2012 ⁽⁴⁾	Cohort	Mean follow up 7.5 years	3,588 men & women	44 years	Dairy Protein T3, ≥ 27 g/day (dairy protein was calculated as protein from milk, yogurt, coffee creamer, curd, pudding, porridge, custard, whipped cream and cheese)	T1, ≤ 19 g/day	Hypertension	Industry ⁴	Yes ^d
Avalos, EE 2013 ⁽⁵⁾	Cohort	Mean follow up 16.2 years	1,759 men & women	70.6 years men, 70.1 women	Whole Milk, Non-Fat Milk, Yogurt & Cheese, Sometimes/often (included daily, 4–6 times/week, 1–3 times/week and 1–3 times/months)	Rarely/never (included never & 1–11 times/year)	Incident CHD	Non-industry ⁵	No ^e
Bernstein, AM 2012 ⁽⁶⁾	2 Cohorts	26 and 22 years of follow-up in women and men, respectively	127,160 (43 150 men 84 010 women)	Men 40 to 75 years, Woman 30 to 55 years	Whole Fat Q 5, Men 2.55 servings/day, Woman 2.81 servings/day (whole milk, ice cream, hard cheese, full fat cheese, cream, sour cream, cream cheese, butter) Low Fat Q5, Men 2.64 servings/day, Women 2.20 servings/day (skim/low-fat milk, 1% and 2% milk, yogurt, cottage and ricotta cheeses, low-fat cheese, sherbet)	Q 1, Men 0.21 servings/day, Woman 0.34 servings/day. Low Fat Q1, Men 0.11 servings/day, Women 0.07 servings/day	Total Stroke	Non-industry ⁶	Yes ^f
Biong, A 2008 ⁽⁷⁾	Case Control		218 men & women	62.4 years	Dairy Fat, > 34.1 g/day	<14.6 g/day	First Myocardial Infarction	Industry ⁷	Yes ^g

36/bmjopen-2020-039136 on 4 December 2020. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Bonthuis, M 2010 ⁽⁸⁾	Cohort	Mean 14.4 years	1,529 men & women	25–78 years	Total Dairy T3, 599 g/day (median) ('low-fat dairy products was computed by adding daily servings (in grams) of skim milk, low-fat milk, low-fat yoghurt, cottage or ricotta cheese, whereas the food group 'high-fat/unmodified dairy' included whole milk, cream, ice cream, yoghurt, full-fat cheese and custard. Total dairy intake was the sum of intake of all these dairy foods)	T1, 174 g/day	Cardiovascular Disease Mortality	Non-Industry ⁸	No ^h
Buendia, JR 2018 ⁽⁹⁾	3 Cohorts	30 years of follow-up in NHS, 20 years in NHS II, 24 years in the HPFS	NHS (N=69298), NHS II (N=84368), HPFS (N=30512)	Mean baseline ages in the 3 cohorts were 44.6, 35.8, and 50.7 years, respectively	Total Dairy Q4, 3 - <6 servings/day (total dairy intake included: milk (skim, low-fat, whole), ice cream, sherbet/ frozen yogurt, cheese (cottage, ricotta, hard, sliced), and yogurt (all types)	Q1, <0.5 servings/day	High Blood Pressure	Industry ⁹	No ⁱ
Chen, M 2016 ⁽¹⁰⁾	3 Cohorts	24 years in the HPFS, 32 years NHS, 20 years in NHS II	222,234 - 43,652 men HPFS, 87,907 women NHS, 90,675 women NHS II	40–75 years HPFS, 30–55 years NHS, 25–42 y NHS II	Dairy Fat, Q5	Q1	CVD	Non-Industry ¹⁰	No ^j

36/bmjopen-2020-039136 on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Dalmeijer, G 2013 ⁽¹¹⁾	Cohort	13 years	33,625 men & women	49.0 years	Total dairy and its subtypes were evaluated as continuous variables per standard deviation of the mean intake which is 265 g/d for total dairy (total dairy included all dairy food products except for butter and ice cream. Milk and milk products included all kinds of milk, yogurt, coffee creamers, curd, pudding, porridge, custard, and whipping cream)		Incident of Coronary Heart Disease & Incident Stroke	Non-Industry ¹¹	Yes ^k
Dauchet, L 2007 ⁽¹²⁾	Cohort	5.4 years	2,341 men & women	Men 52.7 years, Women 46.9 years	Dairy Q4, 456 g/day (dairy products including milk, cheese, yogurt, and other dairy products)	Q1, 84 g/day	Systolic & Diastolic Blood Pressure	Non-Industry ¹²	No ^l

36/bmjopen-2020-039136 on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Deign	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Dehghan, M 2018 ⁽¹³⁾	Cohort	9.1 yrs	136,384 men & women	50-1 years	Dairy Q4, >2 servings/day (median) (dairy comprised milk, yoghurt, various types of cheese, yoghurt drink, and mixed dishes prepared with dairy. Mixed dishes prepared with dairy were dis- aggregated into their constituents and a proportional weight was assigned to each component. Then each component was included in the related dairy group.	Q1, 0 servings/day	Cardiovascular Mortality or Major Events	Industry ¹³	No ^m
Elwood, PC 2004 ⁽¹⁴⁾	Cohort	20-24 years	2,403 men	45-59 years	Milk Q4, >1 pint per day	Q1, None	ascular Event	Non-Industry ¹⁴	No disclosure

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (verbatim)	Funding Source	Disclosed author conflicts of interest
Engberink, MF 2009 ⁽¹⁵⁾	Cohort	6 years	2,245 men & women	>55 years	Dairy Q4, 691 g/day (i.e. 4.5 servings/day) (median intake) (calculated total dairy intake by summing the intake of individual dairy items, except butter and ice cream. The category "milk and milk products" included all kinds of milk, yogurt, coffee creamer, curd, pudding, porridge, custard, and whipped cream. The category "cheese" included all kinds of cheese products, ie, soft cheese, hard cheese, and cheese spreads)	Q1, 164 g/day (i.e. 1 serving/day) (median intake)	Hypertension	No disclosure	No ^a
Farvid, MS 2017 ⁽¹⁶⁾	Cohort	8 years	42,403 men & women	51.6 years	Total Dairy Q5, 2.4 servings/day (median) (total dairy product items listed in the food frequency questionnaire included milk, cheese, yogurt, liquid yogurt (doogh), dried yogurt paste (kashk), and cream)	Q1, 0.4 servings/day (median)	Cardiovascular Disease Mortality	Non-Industry ¹⁵	No ^o
Haring, B 2014 ⁽¹⁷⁾	Cohort	22 years (median)	12,066 men & women	45-64 years	Dairy Protein Q5, 2.9 servings/day	Q1, 0.1 median servings/day	Coronary Heart Disease	Non-Industry ¹⁶	No ^p
He, K 2003 ⁽¹⁸⁾	Cohort	14 years	43,732 men	40-75 years	High Fat Dairy Q5, ≥1/day	Q1, <1/week	Ischaemic & Haemorrhagic Stroke	Non-Industry ¹⁷	No ^q

36/bmjopen-2020-039136 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Heraclides, A 2012 ⁽¹⁹⁾	Cohort	10 years	1,750 men & women	Men 43 years, Women 53 years	Total Dairy T3, 309.0 g/day (median) (full-fat milk; semi-skimmed milk; skimmed milk; milk-containing beverages (full fat, semi-skimmed and skimmed); full-fat cheese; low-fat cheese; full-fat yoghurt; low-fat yoghurt; fruit-flavoured yoghurt (full fat and low fat); and milk-based puddings)	T1, 224.1 g/day	Incident Hypertension	Non-Industry ¹⁸	Yes ^r
Johansson, I 2018 ⁽²⁰⁾	Cohort	8-12 years	27,682 men & women	29-65 years	Dairy Q 5, 7.1 servings/day (median)	Q1, 1.6 servings/day (median)	Blood Pressure	Non-Industry ¹⁹	No ^s
Johansson, I 2019 ⁽²¹⁾	Cohort	14.2 years	108,065 men & women	calculated mean = 52.5 years *	High Fat & Low Fat Non-Fermented Milk & Cheese Q 4, high dose	Q1, low dose	Myocardial Infarction & Stroke	Non-Industry ²⁰	No ^t
Kim, D 2017 ⁽²²⁾	Cohort	67-4 months	4,335 men & women	40-69 years	Total Dairy Q 5, >7 servings/week	Q 1, <1 servings/week	Blood Pressure	Non-Industry ²¹	No ^u
Larsson,S 2009 ⁽²³⁾	Cohort	13.6 years	26,556 men	50-69 years	Dairy Q5, 1295.6 g/day (median) (including low-fat milk, whole milk, sour milk, yogurt, cheese, cream, ice cream, and butter)	Q1 286.5 g/day	Cerebral Infarction, Intracerebral Haemorrhage, Subarachnoid Hemorrhage	Non-Industry ²²	No disclosure

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (verbatim)	Funding Source	Disclosed author conflicts of interest
Larsson, SC 2012 ⁽²⁴⁾	Cohort	10.2 years	74,961 men & women	45-83 years	Dairy Q5, 9.3 servings/day (median) (dairy foods included low-fat milk (0.5% fat), medium-fat milk (1.5% fat), full-fat milk (3% fat), milk in pancakes, low-fat sour milk/yogurt (0.5% fat), full-fat sour milk/yogurt (3% fat), cottage cheese (4% fat), low-fat cheese (10%-17% fat), full-fat cheese (approximately 28% fat), ice cream, cream, and creme fraiche)	Q1, 2.3 servings/day	Total Stroke	Non-Industry ²³	No ^v
Li, K 2012 ⁽²⁵⁾	Cohort	11 years	23,980 men & women	35-64 years	Dairy Calcium Q4, 780 mg/day	Q1, 188 mg/day	CVD Mortality	Non-Industry ²⁴	No ^w
Lin, PH 2013 ⁽²⁶⁾	Cohort	12 years	2,061 men & women	45.8 years (no information for stroke group)	Dairy T3, (dairy milk of any kind, cheese, yogurt).	T1	Total Stroke	Non-Industry ²⁵	No ^x
Lockheart, MSK 2007 ⁽²⁷⁾	Case Control		211 men & women	62.5 years cases and 62.2 years controls	Low Fat Dairy T3, 618 g/day (Low-fat milk, skimmed milk, light sour cream)	T 1, 48 g/day	First Myocardial Infarction	Industry ²⁶	No disclosure
Louie, JCY 2013 ⁽²⁸⁾	Cohort	15 years	2,625 men & women	49-97 years	Total Dairy T3, 2.9 servings/day (median) (included all dairy foods)	T1, 0.6 servings/day	Total CVD	Industry ²⁷	No disclosure
Mazidi, M, 2018 ⁽²⁹⁾	Cohort	76.4 months	24,474 men & women	47.6 years	Total Dairy Q4, 3.08 cup equivalent servings/day (total dairy, milk, cheese, and yogurt)	Q1, 0.25 cup equivalent servings/day	CHD Mortality Cerebrovascular Disease mortality	Non-Industry ²⁸	No ^y

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Ness, AR 2001 ⁽³⁰⁾	Cohort	25 years	5,765 men	35-64 years	Milk T3, > 1 pint (= 0.568 liters)	T1, None	Cardiovascular Disease Deaths	Non-Industry ²⁹	No ^z
Nettleton, J 2008 ⁽³¹⁾	Cohort	13.3 years	14,153 men & women	45 to 64 years	High Fat Dairy, per 1 daily serving difference in food group intake		Ischemic Heart Failure	Non Industry ³⁰	No ^{aa}
Panagiotakos, D 2009 ⁽³²⁾	Cohort	5 years	3,042 men & women	18-89 years	Low Fat Dairy, 1-unit increase in components' scores (0%, 2% or total fat), like cheese, yogurt, milk)		CVD Events	Non-Industry ³¹	No disclosure
Patterson, E 2013 ⁽³³⁾	Cohort	11.6 years	33,636 women	48-83 years	Total Dairy, Q5 8.4 servings/day (median) (total dairy intake was the sum of milk [full-fat ($\geq 3.0\%$ fat), semi-skimmed ($\leq 1.5\%$ fat), skimmed (0.5% fat), and pancakes], cultured milk/yogurt [full-fat ($\geq 3.0\%$ fat) and low-fat ($\leq 1.5\%$ fat)], cheese [full-fat ($> 17\%$ fat), low-fat ($\leq 17\%$ fat), and cottage cheese/ quark], cream and creme fariche (full fat and low fat) intakes)	Q1, 2.2 servings/day	Myocardial Infarction	Non Industry ³²	No ^{bb}
Praagman, J 2015 (a) ⁽³⁴⁾	Cohort	13.3 years (median)	4,235 men & women	66.9 years	Total Dairy, T3 >400g/day (total dairy included milk, buttermilk, yogurt, coffee creamer, curd, pudding, porridge, custard, whipped cream, ice cream, and cheese, but not butter)	Total Dairy, T 1 <200 g/day	Fatal Stroke & Fatal CHD	Industry ³³	Yes ^{cc}

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Praagman, J 2015 (b) ⁽³⁵⁾	Cohort	15 years	34,409 men & women	Men 51 years & women 43 years	Total Yogurt & Cheese Q4, (fermented dairy foods)	Q1	CVD Mortality	Non-Industry ³⁴	Yes ^{dd}
Sauvaget, C 2003 ⁽³⁶⁾	Cohort	16 years	37,130 men & women	56 years	Dairy Q4, Almost Daily (dairy products (butter and cheese, excluding margarine))	Q1, Never	Total Stroke	Non-Industry ³⁵	No disclosure
Snijder, MB 2008 ⁽³⁷⁾	Cohort	6.4 years	1,124 men & women	50–75 years	Dairy Q4, 5.75-17.24 servings/day (range) (total dairy consumption was categorized as low-fat dairy ($\leq 2\%$ fat) or high-fat dairy ($> 2\%$ fat). The variable dairy desserts included yoghurt, curds, and custard. The variable milk included low-fat, skim, and, whole milk. The variable yoghurt included all low-fat, skim, and whole yoghurts)	Q1 0-2.97 servings/day (range)	Systolic & Diastolic Blood Pressure	Industry ³⁶	Yes ^{ee}
Soedamah-Muthu, SS 2013 ⁽³⁸⁾	Cohort	10.8 years	4,255 men & women	56 years	Dairy, T3 575 g/day (median) (all dairy products, except butter and ice cream)	T1, 246 g/day (median)	Fatal & Non-Fatal CHD	Non-Industry ³⁷	Yes ^{ff}
Steffen, LM 2005 ⁽³⁹⁾	Cohort	15 years	4,304 men & women	18-30 years	Dairy Foods Q5, > 3.4 times/day (dairy foods, including milk, cheese, yogurt, and dairy desserts)	Q1, < 1.1 times/day	Blood Pressure	Non-Industry ³⁸	No ^{gg}

36/bmjopen-2020-039139 on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Tavani, A 2002 ⁽⁴⁰⁾	Case Control		985 men & women	61 years (median)	Total milk >7 cups/week, Yogurt >= 7 portions/week, Cheese >=350g/week	Total milk 0 cups/week, Yogurt 0 portions/week, Cheese <200g/week	Acute Myocardial Infarction	Non-Industry ³⁹	No ^{hh}
Um, C 2017 ⁽⁴¹⁾	Cohort	5.7 years of follow-up	21,427 men & women	calculated mean = 64.8 years**	Total Dairy Q5, 17.8 servings/day (dairy products (milk, cream, fermented dairy products, ice cream, butter, cheeses))	Q1, 0.9 servings/day	CVD Mortality	Non-Industry ⁴⁰	No ⁱⁱ
Umesawa, M, 2008 ⁽⁴²⁾	Cohort	12.9-year follow-up	41,526 men & women	40-59 years	Dairy Calcium, Q5, 116 mg/day (median) (to calculate dairy calcium intake, we specified 2 kinds of dairy products, ie, cheese and dairy products except cheese, for the baseline questionnaire, and 4 kinds, ie, whole milk, low fat milk, cheese, and yogurt, for the 5-year follow-up questionnaire)	Q1, 0 mg/day	Total Stroke & CHD	Non-Industry ⁴¹	No ^{jj}

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

36/bmjopen-2020-039138 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Deign	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or ‘yes’ to dairy foods)	Comparison (lowest tertile/quartile/quintile or ‘no’ to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Wang,L 2008 ⁽⁴³⁾	Cohort	10 years	28,886 women	53.8 years	Total Dairy Q5, 3.69 servings/day (median) (total dairy product intake was calculated by summing the intake of individual dairy items: low-fat dairy items include skim or low-fat milk, sherbet, yogurt, and cottage/ricotta cheese, high-fat dairy items include whole milk, cream, sour cream, ice cream, cream cheese, and other cheese)	Q1, 0.56 servings/day (median)	Hypertension	Non-Industry ⁴²	No ^{kk}

* We calculated the mean age score of participants by summing Non-cases, T2D, MI and stroke cases at baseline and dividing them by 4

**We calculated the mean age score of participants by summing all quintiles 1, 3, & 5 (they were the only ones available) at baseline and dividing them by 5

Description of Funding Source (Verbatim)

1. The Hoorn Study has been made possible by the Vrije Universiteit Amsterdam and the VU University Medical Center, and by grants from the Dutch Diabetes Research Foundation, the Dutch Organization for Scientific Research, the Netherlands Heart Foundation, and the Health Research and Development Council of the Netherlands.
2. Supported by research grants HL24074, HL34594, DK36798, and CA87969 from the National Institutes of Health.
3. Supported by the Spanish Ministry of Health (grants PI040233 and G03-140), the Navarra Regional Government (141-2005), and the University of Navarra (línea especial Nutricio LE-97). AA was supported partially by a Fulbright fellowship and an MMA Foundation grant.
4. The Doetinchem Cohort Study was financially supported by the Ministry of Health, Welfare and Sport of the Netherlands and the National Institute for Public Health and the Environment. For the present analysis, Wageningen University was supported by the Top Institute Food and Nutrition, which is a public/private partnership that generates vision on scientific breakthroughs in food and nutrition, resulting in the development of innovative products and technologies. Partners are major Dutch Food companies and research organisations.
5. The study was supported by grants AG007181 and AG028507 from the National Institutes of Health/National Institute on Aging, and by grant DK31801 from the National Institute of Diabetes and Digestive and Kidney Diseases.
6. This study was supported by grant P01CA087969 from the National Institutes of Health, Department of Health and Human Services. A.M.B. was supported through the Harvard Human Nutrition Program.
7. The study was supported financially by the Research Council of Norway, Throne Holst's Foundation for Nutrition Research, The Norwegian Association of Margarine Producers, DeNoFa Fabrikker A/S and Tine BA. Tine BA is a dairy company.
8. This study was supported by the National Health and Medical Research Council of Australia.
9. Funding sources: The Nurses' Health Study and Health Professionals Follow-up Study cohorts are supported by grants UM1 CA186107, UM1 CA176726, and UM1 CA167552 from the National Institutes of Health. The current analyses were supported by small grants from the National Dairy Council, the General Mills Bell Institute for Health and Nutrition, and the Boston Nutrition and Obesity Research Center.
10. Supported by the NIH (grants R01 HL034594, UM1 CA176726, UM1 CA186107, R01 HL35464, R01 HL088521, R01 CA67262, HL60712, and UM1 CA167552).
11. This research was supported by a personal Dr. Dekker postdoctoral grant (2008T062) from The Netherlands Heart Foundation (JWJ Beulens).
12. The SU.VI.MAX study is supported by the Direction Générale de la Santé, the Ministère de la Santé, and the Institut Virtuel de Recherche en Santé Publique (groupe cohorte) INSERM.
13. The PURE Study is an investigator-initiated study that is funded by the Population Health Research Institute, the Canadian Institutes of Health Research (CIHR), Heart and Stroke Foundation of Ontario, support from CIHR's Strategy for Patient Oriented Research (SPOR) through the Ontario SPOR Support Unit, as well as the Ontario Ministry of Health and Long-Term Care and through unrestricted grants from several pharmaceutical companies, with major contributions from AstraZeneca (Canada), Sanofi-Aventis (France and Canada), Boehringer Ingelheim (Germany and Canada), Servier, and GlaxoSmithKline, and additional contributions from Novartis and King Pharma and from various

- national or local organisations in participating countries. These include Brazil: Unilever Health Institute, Brazil; South Africa: The SA Sugar Association (SASA).
14. The Medical Research Council, the University of Wales College of Medicine and Bristol University, Food Standards Agency.
 15. This work was supported by Tehran University of Medical Sciences (grant 82-603); Cancer Research UK (grant C20/A5860); the Intramural Research Program of the National Cancer Institute, US National Institutes of Health (grant Z01 CP000185-03); and various collaborative research agreements with the International Agency for Research on Cancer. M.F. was supported by a Takemi Fellowship from the Japan Pharmaceutical Manufacturers Association.
 16. The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C).
 17. This work was supported by the research grant HL35464 and CA55075 from the National Institutes of Health.
 18. The study was funded by the Medical Research Council, and some aspects of the analysis were funded by The European Commission, Quality of Life and Management of Living Resources Programme, contract number QLGI-CT-2000–01643.
 19. The present study was supported by the Swedish Research Council for Health, Working Life and Welfare (FORTE).
 20. This research was funded by The Swedish Research Council for Health, Working Life and Welfare (FORTE), grant number 2016-00960. The Northern Sweden Diet Database has been supported by the Swedish Research Council for Health, Working Life and Welfare (FORTES) and The Swedish Research Council.
 21. This research was supported by the Basic Science Research Program of the National Research Foundation of Korea (NRF), funded by the Ministry of Education, Science, and Technology (NRF2016R1D1A1B03931307).
 22. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study was supported by Public Health Service contracts N01-CN-45165, N01-RC-45035 and N01-RC-37004 from the US National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Md. Dr. Larsson's research at the National Public Health Institute in Helsinki, Finland, was supported by a grant from the Swedish Council for Working Life and Social Research.
 23. This study was supported by a research grant from the Swedish Council for Working Life and Social Research (FA), the Swedish Research Council, and by a Research Fellow grant from Karolinska Institutet (to Dr Larsson).
 24. This work was supported by supported by the Deutsche Krebshilfe (grant-No70-488-Ha I) and the Graduiertenkolleg 793: Epidemiology of communicable and chronic non-communicable disease and their inter-relationships.
 25. Data collection was supported by the Department of Health in Taiwan.
 26. The present study was supported by NIH NRSA T32HL007779, CVD Epidemiology and Prevention, American Heart Association – Greater Midwest Affiliate, Throne Holst's Foundation for Nutrition Research, The Norwegian Association of Margarine Producers, DeNoFa Fabriker A/S and Tine Norwegian Dairies.
 27. This study was funded by Dairy Australia.

28. This manuscript was written independently; no company or institution supported it financially.
29. Funding: this study was provided with funding by a grant from the NHS Management Executive Cardiovascular Disease and Stroke Research and Development Initiative.
30. This research was supported by the National Institutes of Health grant HL73366, training grant T32 HL07779, and contracts N01-HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, and N01-HC-55022 from the National Heart, Lung, and Blood Institute.
31. The ATTICA study was supported by research grants from the Hellenic Cardiological Society (HCS2002).
32. Supported by research grants from the Swedish Council for Working Life and Social Research and from the Swedish Research Council/Infrastructure Medicine.
33. This study was supported by an unrestricted grant from the Dutch Dairy Organization (NZO) for epidemiological analyses on dairy intake and cardiovascular diseases.
34. The present study was supported by a personal Dr Dekker postdoctoral grant (2008T062) from the Netherlands Heart Foundation (J. W. J. B.).
35. This publication is based on research performed at the Radiation Effects Research Foundation (RERF), Hiroshima and Nagasaki, Japan. RERF is a private nonprofit foundation funded equally by the Japanese Ministry of Health, Labor and Welfare and the US Department of Energy through the National Academy of Sciences.
36. This particular study has been supported by a grant from the Dutch Dairy Association (NZO).
37. The Whitehall II study was supported by grants from the Medical Research Council (G0902037), the British Heart Foundation (RG/07/008/23674), the Stroke Association, the National Heart Lung and Blood Institute (5RO1 HL036310), the National Institute on Aging (5RO1AG13196) and the Agency for Health Care Policy Research (5RO1AG034454).
38. The CARDIA Study is supported by National Heart, Lung, and Blood Institute contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95095.
39. Funding: partly supported by the Italian Ministry of Health (Programmi Speciali).
40. The REGARDS research project is supported by a cooperative agreement U01 NS041588 from the National Institute of Neurological Disorders and Stroke, National Institutes of Health, Department of Health and Human Service. Additional support provided by the Franklin Foundation.
41. This study was supported by grants-in-aid for cancer research and by the Third Term Comprehensive Ten-Year Strategy for Cancer Control from the Ministry of Health, Labor and Welfare of Japan.
42. This work was supported by research grants CA-047988 and HL-080467 from the National Institutes of Health, Bethesda, Md.

Description of Author Disclosure Statement (Verbatim)

- a) Sabita S. Soedamah-Muthu and Johanna M. Geleijnse obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out meta-analyses on the association between dairy products and CVD.
- b) None of the authors had any conflict of interest from a financial, personal, or professional aspect in relation to the findings of this study.
- c) None of the authors had any conflicts of interest.
- d) Altorf-van der Kuil W, Engberink MF, Geleijnse JM - Top Institute Food and Nutrition, PO Box 557, 6700 AN, Wageningen, The Netherlands.
- e) The authors have no conflicts of interest.
- f) D.M. received research grants for studying the effects of diet on cardiometabolic diseases from the National Institutes of Health; the Searle Scholar Award from the Searle Funds at The Chicago Community Trust; the Genes and Environment Initiative at the Harvard School of Public Health; and the Gates Foundation/World Health Organization Global Burden of Diseases, Injuries, and Risk Factors Study; and from GlaxoSmithKline, Sigma Tau, Pronova, and the National Institutes of Health for an investigator-initiated, not-for-profit clinical trial of fish oil and postsurgical complications. He also received ad hoc travel reimbursement and/or honoraria for research presentations from the Chicago Council, International Life Sciences Institute, Aramark, Unilever, SPRIM, Nutrition Impact, Norwegian Seafood Export Council, United Nations Food and Agricultural Organization, World Health Organization, US Food and Drug Administration, and several universities. He received ad hoc consulting fees from Foodminds and royalties from UpToDate for an online chapter on fish oil.
- g) A. S. Biong is employed as a Ph.D. student in a research project funded jointly by TINE BA, a Norwegian dairy company, and the Norwegian Research Council.
- h) The authors declare no conflict of interest.
- i) There are no conflicts of interest.
- j) None of the authors reported a conflict of interest related to the study.
- k) SS-Mand MG obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out meta-analyses on the association between dairy products and cardiovascular diseases.
- l) None of the authors had any personal or financial conflicts of interest.
- m) We declare no competing interests.
- n) There were no conflicts of interest.
- o) Conflict of interest: none declared
- p) The authors have declared that no competing interests exist.
- q) Competing interests: None declared.
- r) SSM, JMG and AH and were supported by an unrestricted grant from the Dutch dairy industry (NZO).
- s) The authors declare that they have no competing interests.
- t) The authors declare no conflict of interest
- u) The authors have no conflicts of interest to declare.

- 1
2
3 v) Disclosures: None.
4 w) Competing interests None.
5 x) AUTHOR DISCLOSURES None.
6 y) All authors have nothing to declare in relation to the subject of this paper.
7 z) Conflicts of interest: none.
8
9 aa) The authors have no conflicts of interest to report.
10 bb) Author disclosures: E. Patterson, S. C. Larsson, A. Wolk, and A. A kesson, no conflicts of interest.
11 cc) J.M.G and S.S.S.M received an unrestricted grant from the Dutch Dairy Organization (NZO) for epidemiological analyses on dairy intake and
12 cardiovascular diseases.
13 dd) S. S. S. M. received an unrestricted research grant from the Global Dairy Platform, Dairy Research Institute and Dairy Australia for a meta-
14 analysis project on the effect of cheese on lipids.
15 ee) Gerrit J. Hiddink - Dutch Dairy Association (NZO), Zoetermeer, The Netherlands.
16 ff) S. S. S.-M., L. V. and J. M. G. obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out meta-analyses on the
17 association between dairy products.
18 gg) None of the authors had any conflicts of interest.
19 hh) Conflicts of interest: none.
20 ii) Conflict of Interests: None.
21 jj) Disclosures: None.
22 kk) Disclosures: None.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

References

1. Aerde M, Soedamah-Muthu S, Geleijnse J, et al. Dairy intake in relation to cardiovascular disease mortality and all-cause mortality: the Hoorn Study. *European Journal of Nutrition*. 2013;52(2):609-16 8p.
2. Al-Delaimy WK, Rimm E, Willett WC, et al. A prospective study of calcium intake from diet and supplements and risk of ischemic heart disease among men. *American Journal of Clinical Nutrition*. 2003;77(4):814-8 5p.
3. Alonso A, Beunza JJ, Delgado-Rodriguez M, et al. Low-fat dairy consumption and reduced risk of hypertension: the Seguimiento Universidad de Navarra (SUN) cohort. *American Journal of Clinical Nutrition*. 2005;82(5):972-9.
4. Altorf-van der Kuil W, Engberink MF, Geleijnse JM, et al. Sources of dietary protein and risk of hypertension in a general Dutch population. *British Journal of Nutrition*. 2012;108(10):1897-903 7p.
5. Avalos EE, Barrett-Connor E, Kritiz-Silverstein D, et al. Is dairy product consumption associated with the incidence of CHD? *Public health nutrition*. 2013;16(11):2055-63.
6. Bernstein AM, Pan A, Rexrode KM, et al. Dietary protein sources and the risk of stroke in men and women. *Stroke*. 2012;43(3):637-44.
7. Biong AS, Rebord HM, Fimreite RL, et al. Intake of dairy fat and dairy products, and risk of myocardial infarction: A case-control study. *International Journal of Food Sciences and Nutrition*. 2008;59(2):155-65.
8. Bonthuis M, Hughes MCB, Ibiebele TI, et al. Dairy consumption and patterns of mortality of Australian adults. *European journal of clinical nutrition*. 2010;64(6):569-77.
9. Buendia JR, Yanping L, Hu FB, et al. Long-term yogurt consumption and risk of incident hypertension in adults. *Journal of Hypertension*. 2018;36(8):1671-9.
10. Chen M, Li Y, Sun Q, et al. Dairy fat and risk of cardiovascular disease in 3 cohorts of US adults. *American Journal of Clinical Nutrition*. 2016;104(5):1209-17.
11. Dalmeijer GW, Struijk EA, van der Schouw YT, et al. Dairy intake and coronary heart disease or stroke—A population-based cohort study. *International Journal of Cardiology*. 2013;167(3):925-9.
12. Dauchet L, Kesse-Guyot E, Czernichow S, et al. Dietary patterns and blood pressure change over 5-y follow-up in the SU.VI.MAX cohort. *The American journal of clinical nutrition*. 2007;85(6):1650-6.
13. Dehghan M, Mente A, Rangarajan S, et al. Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. *Lancet*. 2018;392 North American Edition(10161):2288-97.
14. Elwood PC, Pickering JE, Fehily AM, et al. Milk drinking, ischaemic heart disease and ischaemic stroke I. Evidence from the Caerphilly cohort. *European Journal of Clinical Nutrition*. 2004;58(5):711-7.
15. Engberink MF, Hendriksen MA, Schouten EG, et al. Inverse association between dairy intake and hypertension: the Rotterdam Study. *The American journal of clinical nutrition*. 2009;89(6):1877-83.
16. Farvid MS, Malekshah AF, Pourshams A, et al. Dairy Food Intake and All-Cause, Cardiovascular Disease, and Cancer Mortality. *American Journal of Epidemiology*. 2017;185(8):697-711.

17. Haring B, Gronroos N, Nettleton JA, et al. Dietary Protein Intake and Coronary Heart Disease in a Large Community Based Cohort: Results from the Atherosclerosis Risk in Communities (ARIC) Study. *PloS one*. 2014;9(10):e109552.
18. He K, Merchant A, Rimm EB, Rosner BA, et al. Dietary fat intake and risk of stroke in male US healthcare professionals: 14 year prospective cohort study. *BMJ*. 2003;327(7418):777-82.
19. Heraclides A, Mishra GD, Hardy RJ, et al. Dairy intake, blood pressure and incident hypertension in a general British population: the 1946 birth cohort. *European journal of nutrition*. 2012;51(5):583-91.
20. Johansson I, Nilsson LM, Esberg A, et al. Dairy intake revisited - associations between dairy intake and lifestyle related cardio-metabolic risk factors in a high milk consuming population. *Nutrition Journal*. 2018;17(1):N.PAG-N.PAG.
21. Johansson I, Esberg A, Nilsson LM, et al. Dairy Product Intake and Cardiometabolic Diseases in Northern Sweden: A 33-Year Prospective Cohort Study. *Nutrients*. 2019;11(2):284.
22. Kim D, Kim J. Dairy consumption is associated with a lower incidence of the metabolic syndrome in middle-aged and older Korean adults: the Korean Genome and Epidemiology Study (KoGES). *British Journal of Nutrition*. 2017;117(1):148-60.
23. Larsson SC, Männistö S, Virtanen MJ, et al. Dairy foods and risk of stroke. *Epidemiology (Cambridge, Mass)* [Internet]. 2009; 20(3):[355-60 pp.]. Available from: <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/629/CN-00701629/frame.html>.
24. Larsson SC, Virtamo J, Wolk A. Dairy consumption and risk of stroke in Swedish women and men. *Stroke*. 2012;43(7):1775-80.
25. Li K, Kaaks R, Linseisen J, et al. Associations of dietary calcium intake and calcium supplementation with myocardial infarction and stroke risk and overall cardiovascular mortality in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition study (EPIC-Heidelberg). *Heart*. 2012;98(12):920-5.
26. Lin PH, Yeh WT, Svetkey LP, et al. Dietary intakes consistent with the DASH dietary pattern reduce blood pressure increase with age and risk for stroke in a Chinese population. *Asia Pacific journal of clinical nutrition*. 2013;22(3):482-91.
27. Lockheart MSK, Steffen LM, Rebnord HM, et al. Dietary patterns, food groups and myocardial infarction: a case-control study. *British Journal of Nutrition*. 2007;98(2):380-7.
28. Louie JCY, Flood VM, Burlutsky G, et al. Dairy consumption and the risk of 15-year cardiovascular disease mortality in a cohort of older Australians. *Nutrients*. 2013;5(2):441-54.
29. Mazidi M, Mikhailidis DP, Sattar N, et al. Consumption of dairy product and its association with total and cause specific mortality - A population-based cohort study and meta-analysis. *Clin Nutr*. 2018.
30. Ness AR, Smith GD, Hart C. Milk, coronary heart disease and mortality. *Journal of Epidemiology & Community Health*. 2001;55(6):379-82.
31. Nettleton JA, Steffen LM, et al. Incident heart failure is associated with lower whole-grain intake and greater high-fat dairy and egg intake in the Atherosclerosis Risk in Communities (ARIC) study. *Journal of the American Dietetic Association*. 2008;108(11):1881-7.
32. Panagiotakos D, Pitsavos C, Chrysohoou C, et al. Dietary patterns and 5-year incidence of cardiovascular disease: A multivariate analysis of the ATTICA study. *Nutrition, Metabolism and Cardiovascular Diseases*. 2009;19(4):253-63.
33. Patterson E, Larsson SC, Wolk A, et al. Association between dairy food consumption and risk of myocardial infarction in women differs by type of dairy food. *The Journal of nutrition*. 2013;143(1):74-9.

- 1
2
3 34. Praagman J, Franco OH, Ikram MA, et al. Dairy products and the risk of stroke and coronary heart disease: the Rotterdam Study. *European journal of nutrition*. 2015;54(6):981-90.
- 4
5 35. Praagman J, Dalmeijer GW, van der Schouw YT, et al. The relationship between fermented food intake and mortality risk in the European
6 Prospective Investigation into Cancer and Nutrition-Netherlands cohort. *British Journal of Nutrition*. 2015;113(3):498-506.
- 7
8 36. Sauvaget C, Nagano J, Allen N, et al. Intake of animal products and stroke mortality in the Hiroshima/Nagasaki Life Span Study.
9 *International journal of epidemiology*. 2003;32(4):536-43.
- 10 37. Snijder MB, van Dam RM, Stehouwer CD, et al. A prospective study of dairy consumption in relation to changes in metabolic risk factors:
11 the Hoorn Study. *Obesity (Silver Spring, Md)*. 2008;16(3):706-9.
- 12 38. Soedamah-Muthu SS, Masset G, Verberne L, Geleijnse JM, et al. Consumption of dairy products and associations with incident diabetes,
13 CHD and mortality in the Whitehall II study. *The British journal of nutrition*. 2013;109(4):718-26.
- 14 39. Steffen LM, Kroenke CH, Yu X, et al. Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood
15 pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *American Journal of Clinical
16 Nutrition*. 2005;82(6):1169-77; quiz 363-4.
- 17 40. Tavani A, Gallus S, Negri E, et al. Milk, dairy products, and coronary heart disease. *Journal of Epidemiology & Community Health*.
18 2002;56(6):471-2.
- 19 41. Um CY, Judd SE, Flanders WD, et al. Associations of Calcium and Dairy Products with All-Cause and Cause-Specific Mortality in the
20 REasons for Geographic and Racial Differences in Stroke (REGARDS) Prospective Cohort Study. *Nutrition & Cancer*. 2007;69(8):1185-95.
- 21 42. Umesawa M, Iso H, Ishihara J, et al. Dietary calcium intake and risks of stroke, its subtypes, and coronary heart disease in Japanese: the
22 JPHC Study Cohort I. *Stroke*. 2008;39(9):2449-56.
- 23 43. Wang L, Manson JE, Buring JE, et al. Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged
24 and older women. *Hypertension*. 2008;51(4):1073-9.
- 25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Supplementary File 6. Risk of bias in included studies

Funding Source, n (%^a)

Characteristic	Category	Total N = 43	Sponsorship		COI		Industry Ties	
			Industr y N= 8	Non- Industry N=35	COI N =10	No COI N=33	Industry /COI N = 14	Non- Industry/ No COI N = 29
Risk of Bias Assessment								
	Serious/Critical Bias due to confounding	43 (100)	8 (100)	35 (100)	10 (100)	33 (100)	14 (100)	29 (100)
	Serious/Critical Bias in selection of participants into the study	6 (14)	1 (13)	5 (14)	1 (10)	5 (15)	2 (14)	4 (14)
	Serious/Critical Bias in classification of exposures	16 (37)	3 (38)	13 (37)	2 (20)	14 (42)	3 (21)	13 (44)
	Serious/Critical Bias due to deviations from exposures	21 (49)	3 (38)	18 (51)	6 (60)	15 (45)	7 (50)	14 (48)
	Serious/Critical Bias due to missing data	10 (23)	2 (25)	8 (23)	3 (30)	7 (21)	3 (21)	7 (24)

	Serious/Critical Bias in measurement of outcomes	6 (14)	2 (25)	4 (11)	1 (10)	5 (15)	2 (14)	4 (14)
	Serious/Critical Bias in selection of reported results	4 (9)	1 (13)	3 (9)	2 (20)	2 (6)	2 (14)	2 (7)
	Serious/Critical overall risk of bias	43 (100)	8 (100)	35 (100)	10 (100)	33 (100)	14 (100)	29 (100)

^a Percentages may not add to 100 due to rounding

Supplementary File 7: Favorable Outcomes by Industry Ties v No Industry Ties, Industry Sponsorship v No Industry Sponsorship and Conflicts of Interest v No Conflicts of Interest

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
Aerde, M 2013	Non-Industry	Yes	U	U	Al-Delaimy, WK 2003	Non Industry	No	U	U
Altorf-van der Kuil, W2012	Industry	Yes	U	U	Alonso A, 2005	Non-industry	No	U	U
Bernstein, AM 2012	Non-industry	Yes	U	U	Avalos, EE 2013	Non-industry	No	U	U
Biong, A 2008	Industry	Yes	U	F	Bonthuis, M 2010	Non-Industry	No	U	U
Buendia, JR 2018	Industry	No	F	F	Chen, M 2016	Non-Industry	No	U	F
Dalmeijer, G 2013	Non-Industry	Yes	U	F	Dauchet, L 2007	Non-Industry	No	U	U
Dehghan, M 2018	Industry	No	U	F	Elwood, PC 2004	Non-Industry	No disclosure	U	U
Heraclides, A 2012	Non-Industry	Yes	U	U	Engberink, MF 2009	No disclosure	No	U	F
Lockheart, MSK 2007	Industry	No disclosure	U	U	Farvid, MS 2017	Non-Industry	No	F	F
Louie, JCY 2013	Industry	No disclosure	U	U	Haring, B 2014	Non-Industry	No	U	U
Praagman, J 2015	Industry	Yes	U	U	He, K 2003	Non-Industry	No	U	U

36/bmjopen-2020-019036 on 14 September 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
Praagman J, 2015	Non-Industry	Yes	U	U	Johansson, I 2018	Non-Industry	No	U	U
Snijder, MB 2008	Industry	Yes	U	U	Johansson, I 2019	Non-Industry	No	U	U
Soedamah-Muthu, SS 2013	Non-Industry	Yes	U	U	Kim, D 2017	Non-Industry	No	F	F
					Larsson,S 2009	Non-Industry	No disclosure	U	U
					Larsson, SC 2012	Non-Industry	No	U	U
					Li, K 2012	Non-Industry	No	U	U
					Lin, PH 2013	Non-Industry	No	U	U
					Mazidi, M, 2018	Non-Industry	No	F	F
					Ness, AR 2001	Non-Industry	No	U	U
					Nettleton, J 2008	Non-Industry	No	U	U
					Panagiotakos, D 2009	Non-Industry	No disclosure	U	U
					Patterson, E 2013	Non-Industry	No	F	F
					Sauvaget, C 2003	Non-Industry	No disclosure	F	F
					Steffen, LM 2005	Non-Industry	No	U	U

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
					Tavani, A 2002	Non-Industry	No	F	F
					Um, C 2017	Non-Industry	No	U	F
					Umesawa, M, 2008	Non-Industry	No	F	F
					Wang,L 2008	Non-Industry	No	F	F

Favourable results - Statistical significance: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no COI

Industry Ties

	Industry/COI	Non-Industry/No COI
Favourable	1	8
Unfavourable	13	21

RR= 0.26 (95% CI 0.04, 1.87)

Industry Sponsorship

	Industry	Non-Industry
Favourable	1	8
Unfavourable	7	27

RR = 0.55 (95% CI 0.08, 3.77)

Conflicts of Interest

	COI	No/COI
Favourable	0	9
Unfavourable	10	24

RR= 0.16 (95% CI 0.01, 2.57)

Favourable conclusions: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no COI

Industry Ties

	Industry/COI	Non-Industry/NO COI
Favourable	4	11
Unfavourable	10	18

RR = 0.75 (95% CI 0.29, 1.95)

Industry Sponsorship

	Industry	Non-Industry
Favourable	3	12
Unfavourable	5	23

RR= 1.09 (95% CI 0.40, 2.99)

Conflicts of Interest

	COI	No COI
Favourable	2	13
Unfavourable	8	20

RR =0.51 (95% 0.14, 1.88)

Concordance between study results and conclusions: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no

COI Industry Ties

Industry Ties

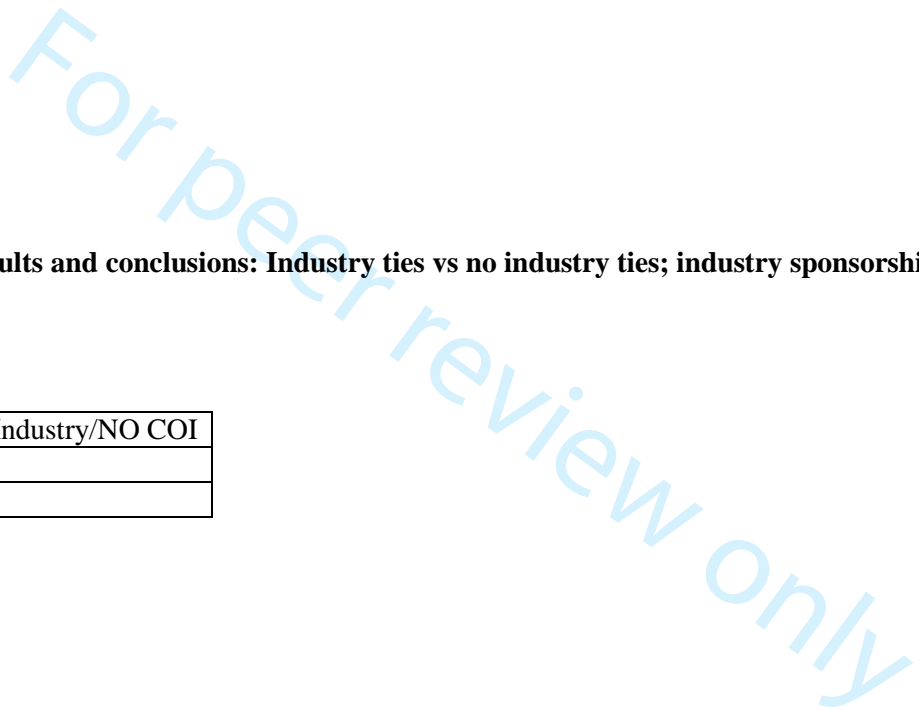
	Industry/COI	Non-Industry/NO COI
Discord	3	3
Concord	11	26

RR = 2.07 (95% CI 0.48, 8.99)

Industry Sponsorship

	Industry	Non-Industry
Discord	2	4
Concord	6	31

RR = 2.19 (95% CI 0.48, 9.94)



Conflicts of Interest

	COI	No/COI
Favourable	2	4
Unfavourable	8	29

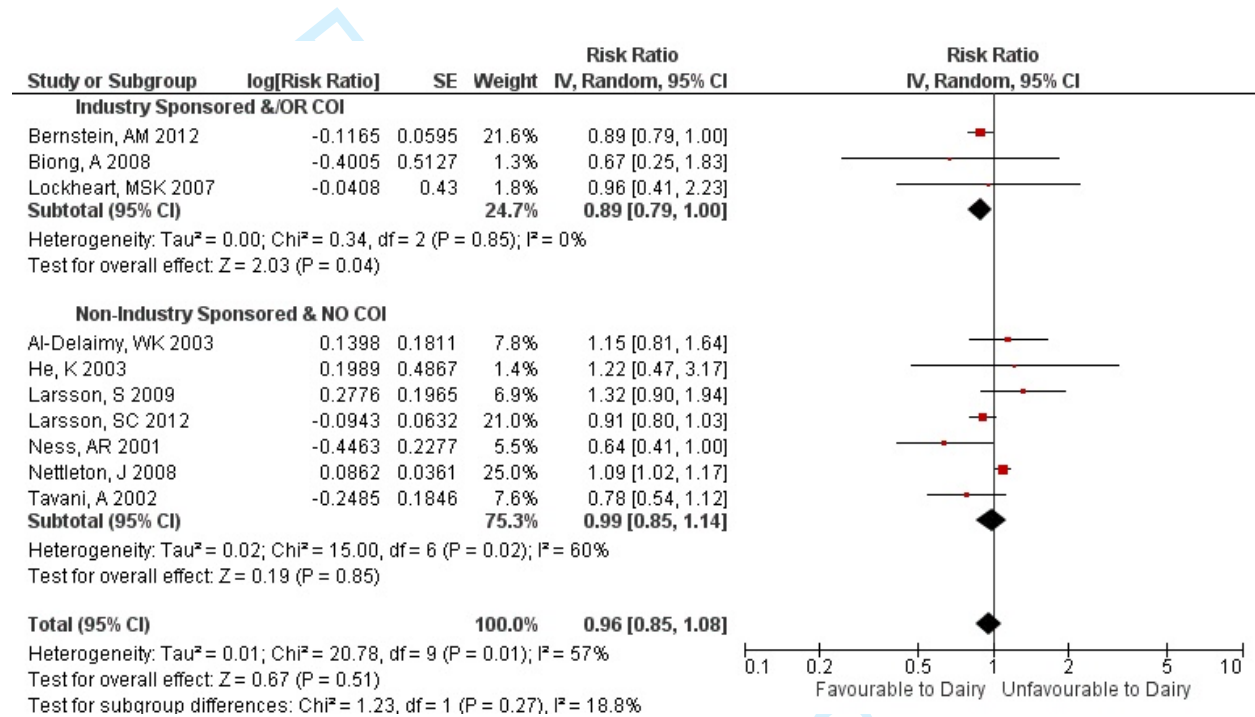
RR = 1.65 (95% CI 0.35, 7.72)

For peer review only

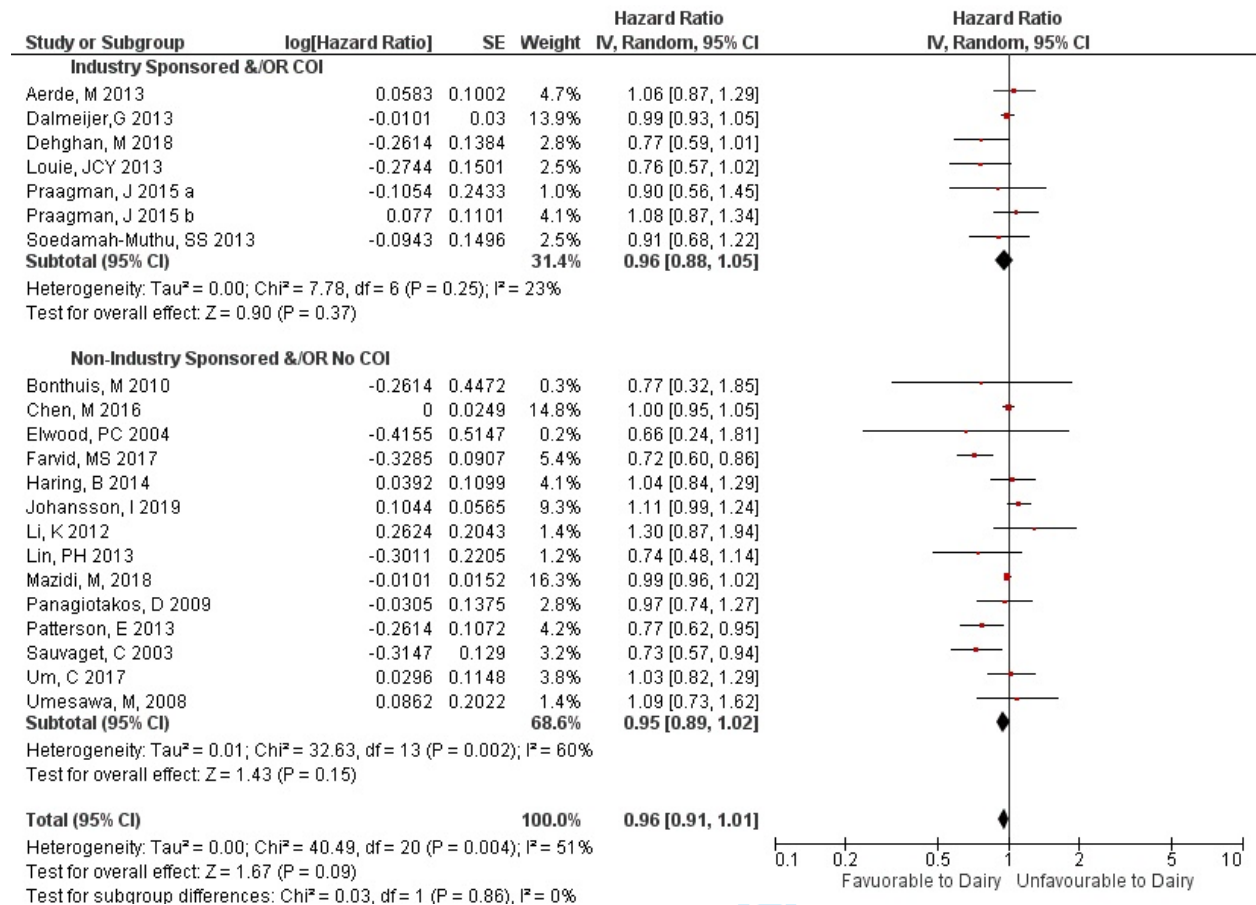
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Supplementary File 8. Results for each of the meta-analyses conducted

Effect Size, Cardiovascular Disease: Industry ties v no industry ties, Risk Ratio

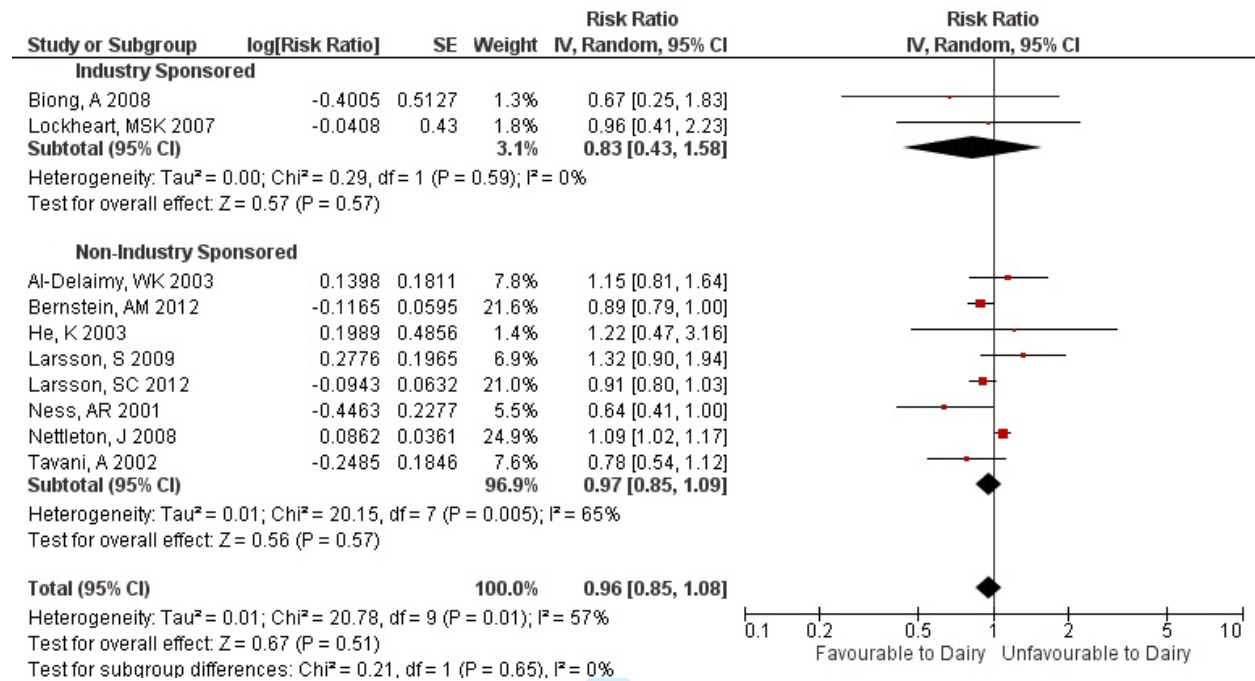


Effect Size, Cardiovascular Disease: Industry ties v no industry ties, Hazard Ratio

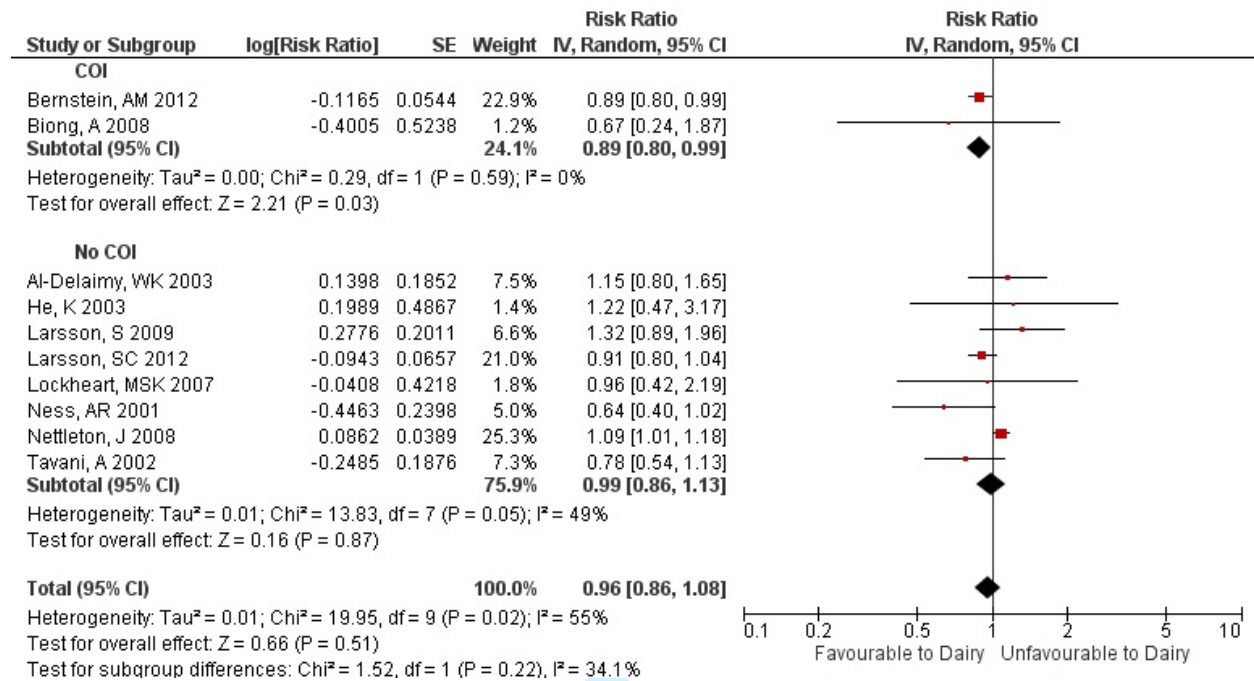


BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Effect Size, Cardiovascular Disease: Industry sponsorship vs no industry sponsorship, Risk Ratio

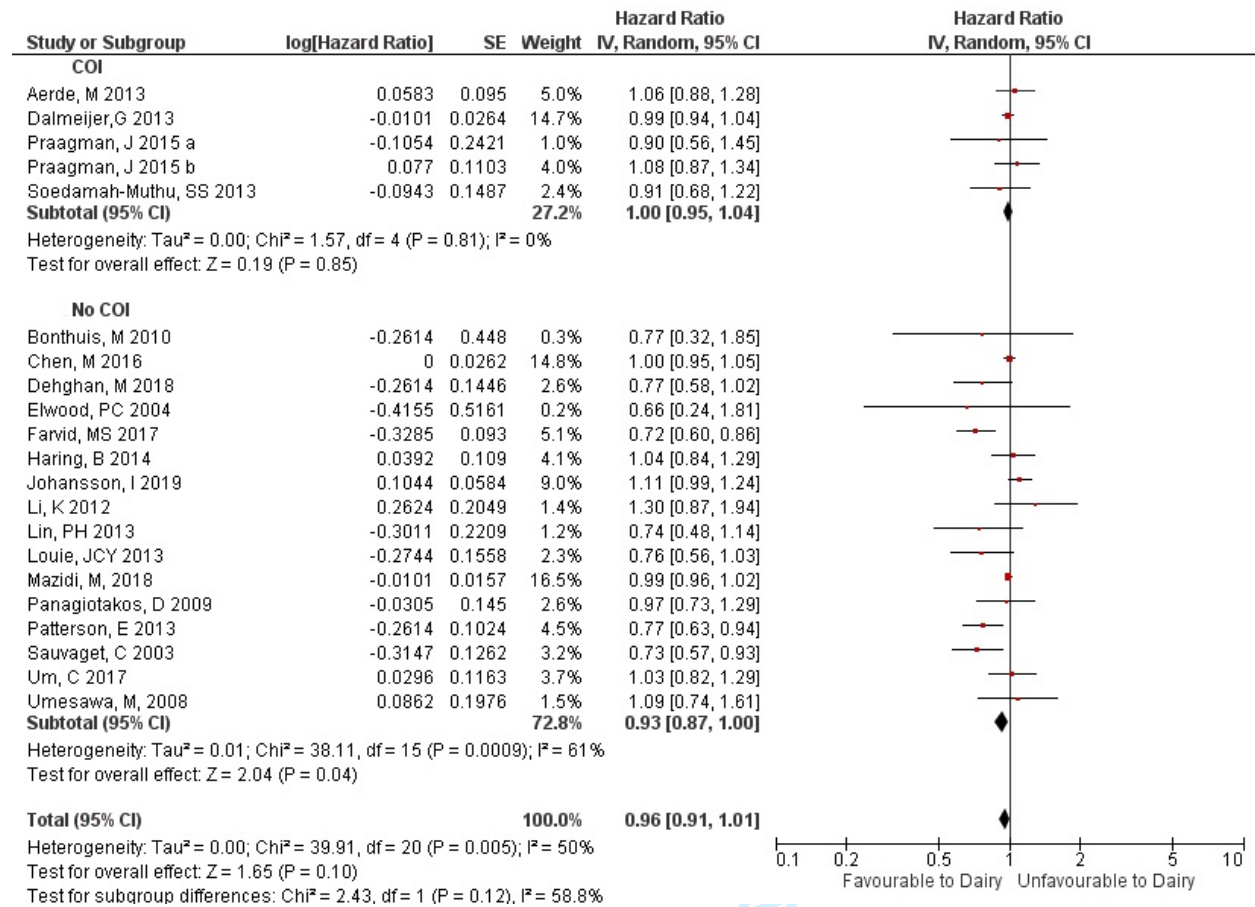


Effect Size, Cardiovascular Disease: COI vs No COI, Risk Ratio

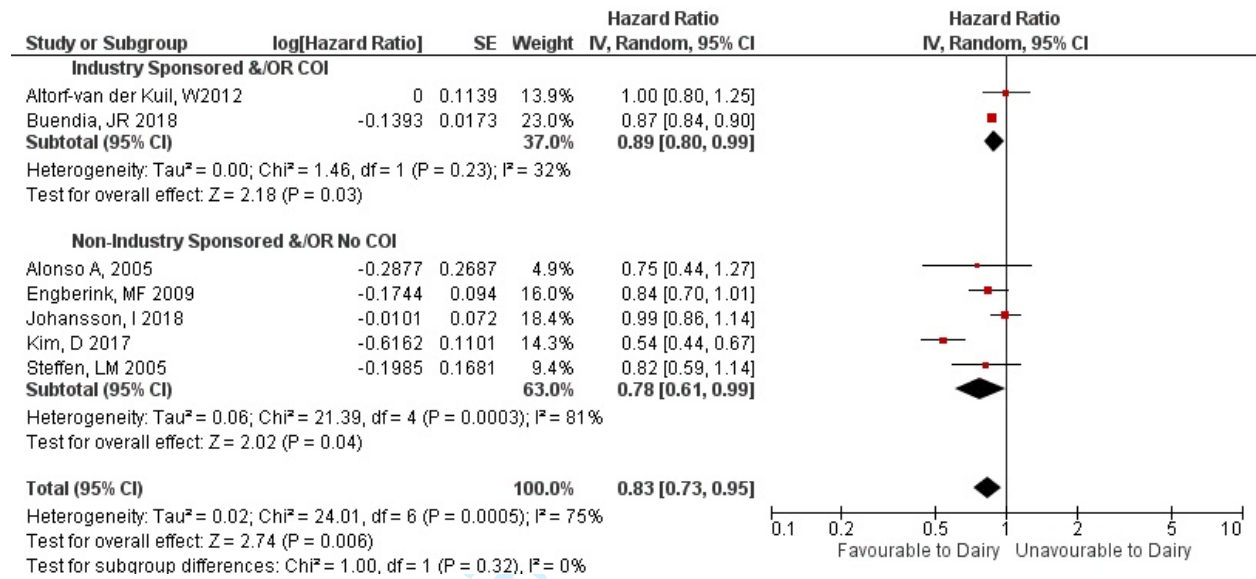


BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Effect Size, Cardiovascular Disease: COI vs no COI, Hazard Ratio



Effect Size, Elevated Blood Pressure / Hypertension: Industry ties v no industry ties



BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3&5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5, Supp file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7 & 11
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6 & 10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2 for each meta-analysis).	10 -11



PRISMA 2009 Checklist

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10-11
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11, Figure 1, Supp file 4
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICO(S), follow-up period) and provide the citations.	Supp file 5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	13, Supp File 6, Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13-15
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	13-15, Supp file 7 & 8, Figure 3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	13, Supp file 6, Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16



PRISMA 2009 Checklist

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data), role of funders for the systematic review.	3&20

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Page 2 of 2

For peer review only

36/bmjopen-2020-033036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

BMJ Open

The association of food industry ties with findings of studies examining the effect of dairy foods intake on cardiovascular disease and mortality: Systematic review and Meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-039036.R2
Article Type:	Original research
Date Submitted by the Author:	13-Oct-2020
Complete List of Authors:	Chartres, Nicholas; The University of Sydney, Charles Perkins Centre Fabbri, Alice; University of Insubria, Centre for Research in Medical Pharmacology McDonald, Sally ; The University of Sydney, ; the University of Sydney Diong, Joanna; The University of Sydney Faculty of Medicine and Health McKenzie, Joanne; Monash University Bero, Lisa; University of Sydney Faculty of Health Sciences, Pharmacy
Primary Subject Heading:	Research methods
Secondary Subject Heading:	Public health, Epidemiology, Health policy, Nutrition and metabolism
Keywords:	STATISTICS & RESEARCH METHODS, NUTRITION & DIETETICS, PUBLIC HEALTH

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 1 **The association of food industry ties with findings of studies examining the effect of**
4 **dairy foods intake on cardiovascular disease and mortality: Systematic review and**
5 **Meta-analysis**
6
7
8
9 4

10
11 5 **Authors:** Nicholas Chartres¹, Alice Fabbri¹, Sally McDonald¹, Joanna Diong², Joanne
12 Mckenzie³, Lisa Bero¹
13
14
15 7

- 16
17 8 1. The University of Sydney, D17, The Hub, 6th floor, Charles Perkins Centre, The
18 University of Sydney, New South Wales, 2006, Australia
19 9
20 10 2. The University of Sydney, School of Medical Sciences, Faculty of Medicine and
21 Health, The University of Sydney, New South Wales, 2006, Australia
22 11
23 12 3. Monash University, 553 St Kilda Road, Melbourne, Victoria, 3004, Australia
24
25
26 13

27
28 14 **Corresponding author:** Lisa Bero, The University of Sydney, D17, The Hub, 6th floor,
29 Charles Perkins Centre, The University of Sydney, New South Wales, 2006, Australia, email
30 lisa.bero@sydney.edu.au; Telephone +612 8627
31
32
33

34 17
35
36 18 **Word Count: 5064**
37
38 19
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

20 Abstract

21 **Objective:** To determine if the association of dairy foods with cardiovascular disease
22 outcomes differs between studies with food industry ties versus those without industry ties.

23 To determine whether studies with or without industry ties differ in their risk of bias.

24 **Eligibility criteria:** We included cohort and case control studies that estimated the
25 association of dairy foods with cardiovascular disease (CVD) outcomes in healthy adults.

26 **Information sources:** We searched eight databases on February 1, 2019 from 2000-2019 and
27 hand searched reference lists

28 **Risk of bias:** We used the Risk of Bias in Non-Randomized Studies-of Exposure (ROBINS-
29 E) tool.

30 **Included studies:** 43 studies (3 case controls, 40 cohorts).

31 **Synthesis of results:** There was no clear evidence of an association between studies with
32 industry ties (1/14) vs. no industry ties (8/29) and the reporting of favourable results, RR=
33 0.26 (95% CI 0.04, 1.87; n=43 studies) and studies with industry ties (4/14) vs. no industry
34 ties (11/29) and favourable conclusions, RR= 0.75 (95% CI 0.29, 1.95; n=43).. Studies with
35 industry sponsorship, (HR =0.78; n= 3 studies) showed a decreased magnitude of risk of
36 CVD outcomes compared to studies with no industry sponsorship (HR=0.97; n=18) (ratio of
37 HRs 0.80 (95% CI 0.66, 0.97)) P=0.03.

38 **Strengths and Limitations of evidence:** Every study had an overall high risk of bias rating;
39 this was primarily due to confounding.

40 **Interpretation:** There was no clear evidence of an association between studies with food
41 industry ties and the reporting of favourable results and conclusions compared with studies
42 without industry ties. The statistically significant difference in the magnitude of effects
43 identified in industry sponsored studies compared to non-industry sponsored studies,
44 however, is important in quantifying industry influence on studies included in dietary
45 guidelines.

46 **Funding:** This work was supported by Australian Health and Medical Research Council
47 Project Grant APP 1139997.

48 **Registration:** Prospero ID CRD42019129659

51 **Keywords:** Industry Sponsorship, Conflicts of Interest, Bias, Dietary Guidelines

53 **Strengths and limitations of this study**

- 1
2
3
4 54 • This is the first systematic review and meta-analysis to evaluate the association of
5 55 food industry ties (industry sponsorship and / or author conflicts of interest (COI))
6 56 with the results, conclusions and risk of bias of primary nutrition studies examining
7 57 the association of dairy foods with cardiovascular disease outcomes and mortality.
8
9 58 • We conducted a comprehensive search and followed explicit and well-defined
10 59 inclusion and exclusion criteria for the included studies.
11
12 60 • For studies missing a funding or author COI disclosure, we did not contact the
13 61 authors; thus we may be underestimating the number of studies with industry ties.
14
15 62 • The tool that we used to assess the risk of bias is still under modification, however it
16 63 is unlikely any future changes to the tool will affect the risk of bias ratings.
17
18 64 • We did not analyse studies of low and full fat dairy separately. Industry ties may have
19 65 different effects on studies of low or full fat dairy foods.
20
21
22
23
24 66

67 INTRODUCTION

68 The effect of dairy foods on cardiovascular disease (CVD) is unclear. Recent systematic
69 reviews and meta-analyses of observational studies have reported conflicting results between
70 the association of total dairy consumption and risk of CVD, with some showing decreased
71 risk and some showing no clear evidence.¹⁻⁴ The beneficial effects of decreasing blood
72 pressure, however, appear more consistent.^{4,5} Further, dairy intake recommendations made in
73 dietary guidelines around the world vary. Although the Australian Dietary Guidelines
74 concluded that there is a probable association between dairy food consumption and a reduced
75 risk of cardiovascular events,⁶ recent amendments to the Eatwell guidelines by Public Health
76 England recommend a significant reduction in the daily intake of dairy foods.⁷

77

78 Food industry sponsors and authors with a conflict of interest (COI) with the food industry
79 may gain financially from finding that dairy foods have health benefits, since such a finding
80 can be used to market dairy products. Such a driver may lead industry sponsors to magnify
81 (or bias) the health benefits of dairy foods by influencing the research agenda, design and
82 conduct of the study, or reporting of the results.⁸⁻¹¹ Prior examinations of pharmaceutical and
83 tobacco research have identified that even when controlling for methodological biases,
84 studies sponsored by industry were more likely to have results that favoured the sponsor than
85 studies with other sources of sponsorship.¹²⁻¹⁴

86

87 The effects of food industry sponsorship or author COI with the food industry on study
88 results needs further examination.¹⁵ A systematic review assessing the association of
89 wholegrain foods with CVD and mortality found that studies with food industry ties more
90 often have favourable results and conclusions compared to those with no industry ties, but the
91 association was uncertain.¹⁶ One study has demonstrated an association of food industry
92 sponsorship with the magnitude of effect estimates.¹⁷ In this examination, studies of soft
93 drink consumption sponsored by the food industry reported significantly smaller harm effect
94 estimates than those with no food industry sponsorship. A recent dairy industry funded meta-
95 analysis of observational studies found that studies without food industry sponsorship showed
96 that dairy consumption was associated with a statistically significant decreased risk of
97 developing CVD and Type 2 diabetes, while studies with food industry sponsorship did not.¹⁸

1
2
3 98 The primary objective of this systematic review and meta-analysis is to determine whether:
4

- 5 99 • Studies of observational design examining the associations of dairy foods with CVD
6
7 100 with food industry ties (industry sponsorship and / or authors with a COI) are more
8
9 101 likely to have results and / or conclusions that are favourable to industry than those
10
11 102 with no industry ties.
12
13

14 104 The secondary objectives of this review are to determine whether observational studies with
15
16 105 food industry ties compared with no industry ties:

- 17
18 106 I. differ in their risk of bias;
19
20 107 II. have a higher level of discordance between study results and conclusions, with the
21
22 108 conclusions more likely to be favourable compared to the results.
23
24
25 109

26 27 110 **METHODS**

28
29 111 We conducted a systematic review of observational studies examining the effect of dairy
30
31 112 consumption on CVD. Our study is registered with Prospero ID CRD42019129659 (see
32
33 113 Supplementary file 1).¹⁹
34
35 114

36 115 **Search Strategy**

37
38 116 The search included terms to locate observational studies and randomised control trials, the
39
40 117 latter of which are for a separate systematic review. The search used was based on the
41
42 118 Process Manual used to develop the 2013 Australian Dietary Guidelines and the guidance of
43
44 119 an information specialist.²⁰ The search dates used were to ensure that we identified the
45
46 120 studies used to inform the recommendations in these guidelines. We therefore searched the
47
48 121 following databases from January 2000-February 2019: MEDLINE; CINAHL; PubMed;
49
50 122 PreMEDLINE; Cochrane Library; PsycINFO; Science Direct; and ERIC. The search strategy
51
52 123 used for Ovid MEDLINE on February 1, 2019 is shown in Supplementary file 2. We adapted
53
54 124 this strategy for the other databases. We hand searched references lists of the identified
55
56 125 studies and reviews.
57
58 126
59 127
60 128

129 **Eligibility Criteria**

130 We included studies of cohort or case control designs that estimated the effects of dairy
131 consumption on CVD outcomes in healthy adults. We focused on these study designs as they
132 are often used to assess the association of diet with long term health outcomes.

133
134 We included studies with no restriction on the authors' definition of dairy. For example, some
135 authors' defined dairy as milk, yogurt and cheese, while others defined dairy as 'whole fat'
136 milk, yogurt and cheese. We included studies that compared dairy foods to other foods or
137 compared various levels of dairy consumption.

138
139 We included studies that measured any clinical outcome of CVD, defined as either mortality
140 related to specific CVD events, and / or CVD events, (e.g., first myocardial infarction, total
141 stroke etc.) or incidence of elevated blood pressure / hypertension.

142
143 We excluded conferences presentations, opinion pieces and letters to the editor. We had no
144 language restrictions.

145

146 **Types of Outcome Measures**

147 **Primary Outcomes**

148 We hypothesized that studies with food industry sponsorship and / or authors with a COI with
149 the food industry would be more likely to have favourable findings than those with no
150 industry ties. We assessed three primary outcomes:

151 1. Statistical significance of results favourable to dairy

152 Favourable results were defined as those that were in the direction of showing a health
153 benefit of dairy product(s), and were statistically significant at the 0.05 level (two tailed),
154 such as a statistically significant decreased risk of CVD compared to the comparator (i.e.
155 another food or lower dairy consumption). Otherwise, results were classified as unfavourable.
156 In the circumstance where a study reported multiple results (e.g. first myocardial infarction
157 and total stroke), only one result needed to be 'favourable' for the study as a whole to be
158 classified as 'favourable'.

159

160 2. Effect size of results

161 Effect size was defined as the risk ratio (RR), hazard ratio (HR) or odds ratio (OR) between
162 dairy foods tested versus comparator on the CVD outcome.

163

3. Conclusions

Conclusions that suggested that the dairy consumption was beneficial to health by decreasing CVD were considered favourable. Otherwise, the conclusions were considered unfavourable.

In the circumstance where a study reported multiple results (e.g. first myocardial infarction and total stroke), only one conclusion needed to be 'favourable' for the study as a whole to be classified as 'favourable'.

170

Secondary Outcomes

We assessed two secondary outcomes:

1. The risk of bias of the included studies

To evaluate the risk of bias of included observational studies, we used an adapted version of the Cochrane Collaboration's 'Risk of Bias in Non-Randomized Studies-of Interventions' (ROBINS-I) tool,²¹ the ROBINS-E²². Bias is assessed across seven domains ('Bias due to confounding', 'Bias in selection of participants', 'Bias in classification of exposures', 'Bias due to deviations from exposures', 'Bias due to missing data', 'Bias in measurement of outcomes', 'Bias in selection of reported results'), with each domain classified low, moderate, serious, critical risk of bias, or no information. The first step in using the ROBINS-E tool is to identify all possible confounders that a study should control. We developed this list of confounders by searching the literature for the most recent systematic reviews on possible confounders and having this list reviewed by expert Professors in nutrition at The University of Sydney (see Supplementary file 3 for list of confounder). An overall risk of bias rating for the study is given based on the domain with the highest risk of bias rating. For example, if a study is rated as being at a 'critical' risk of bias in one domain, the overall risk of bias rating is 'critical.' In the circumstance where a study reported multiple results (e.g. stroke and myocardial infarction), the risk of bias was only assessed for one randomly selected outcome.

190

2. Concordance between study results and conclusions

Results unfavourable to the sponsor with conclusions favourable to the sponsor, were considered discordant. Otherwise, the results and conclusions were considered concordant.

194

Selection of studies

195

1
2
3 196 Three investigators (NC, SMC & AF), working independently in pairs, screened the titles and
4
5 197 abstracts of all records for obvious exclusions. If both investigators agreed on excluding the
6
7 198 study, the full text was not retrieved. Three investigators (NC, SMC & AF) working
8
9 199 independently in pairs, assessed the full text of potentially eligible studies against the
10
11 200 inclusion criteria. If agreement could not be reached, a fourth investigator (LB) resolved the
12
13 201 conflict.

202

203 **Selection of results for meta-analysis**

17 204 If total dairy consumption had been assessed in the study, we included this as our only
18
19 205 exposure. If total dairy consumption had not been assessed, we included any type of dairy
20
21 206 consumption (e.g. milk, yogurt, and cheese; or low fat, high fat) other than fermented milk as
22
23 207 our exposure. We included the results comparing the highest level of dairy consumption to
24
25 208 the lowest level of dairy consumption (e.g., 'yes' to dairy consumption vs. 'no' to dairy
26
27 209 consumption, tertile 3 vs. tertile 1, quartile 4 vs. quartile 1, quintile 5 vs. quintile 1). For the
28
29 210 meta-analyses if our pre-specified rules for selecting results did not allow us to uniquely
30
31 211 identify one exposure for inclusion, we randomly selected one result.

212

32
33 213 If 'cardiovascular disease mortality/death/s' (verbatim) had been assessed, we included this
34
35 214 as our only outcome. If not, we included any type of CVD mortality (e.g., coronary heart
36
37 215 disease mortality, stroke mortality etc.) as our outcome. If there were no mortality outcomes
38
39 216 assessed in the study, we included any CVD event or incidence of elevated blood pressure /
40
41 217 hypertension as our outcome. If a study used a composite outcome, which was a combination
42
43 218 of multiple outcomes, the result pertaining to the composite outcome was selected. For the
44
45 219 meta-analyses if our pre-specified rules for selecting results did not allow us to uniquely
46
47 220 identify one outcome for inclusion, we randomly selected one result.

221

222 **Data Collection**

223 From each study we extracted:

- 51 224 • Year of publication
- 53 225 • Study design (cohort or case control)
- 55 226 • Sample size of study
- 57 227 • Age of participants (combined or if reported, separately)
- 59 228 • Exposure duration or observation period

60

- 1
2
3 229 • How the study defined dairy (verbatim)
4
5 230 • Disclosure of funding source (no disclosure, yes and there is a sponsor, the authors
6 state they received no funding for their work)
7 231
8 232 • Name of the funders of the study (verbatim)
9
10 233 • Role of the funders (role of the sponsor not mentioned, sponsor not involved in study
11 design and analyses, sponsor involved, N/A)
12 234
13 235 • Disclosure of author COI (no disclosure, yes (if at least 1 author had a COI), the authors
14 state they had no conflicts of interest to declare)
15 236
16 237 • Authors COI statement (verbatim)
17
18 238 • Outcomes assessed in the study (any CVD death and/or event or blood
19 pressure/hypertension)
20 239
21 240 • The numerical results of the study (e.g., OR, HR, RR)
22
23 241

24
25 242 All extracted data from the included studies was stored in REDcap, a secure web-based
26 application for the collection and management of data.²³ Five investigators (NC, SMc, AF,
27 AL & JD) working independently in pairs extracted data from the included studies.
28 243
29 244 Discrepancies in data extraction were resolved by consensus. If agreement could not be
30 reached, a sixth investigator (LB) resolved the discrepancy.
31 245
32 246
33 247

248 **Classification of industry sponsorship and author conflicts of interest**

249 Sponsorship was categorized as 1) industry or 2) non-industry. Industry sponsored studies
250 were defined as those that declared any sponsorship from the food industry, including 'Big
251 Food' (i.e. Danone, Kraft, Unilever etc), trade associations (i.e. dairy associations and
252 organisations) and dairy industry (i.e. primary producers). Studies with food industry
253 sponsorship plus any other sponsorship were classified as industry. Any study that did not
254 contain a funding disclosure statement was classified as 'non-industry'.
255

256 Studies with at least one author with any disclosed financial tie with the food industry were
257 classified as having a conflict of interest (COI). Author COI were categorised as 1) COI or 2)
258 no COI. Studies with no authors with disclosed financial ties with the food industry were
259 classified as 'no conflict of interest'.
260

1
2
3 261 Since the number of studies with industry sponsorship or author COI was small, we also
4 262 categorized studies as having “industry ties” for analysis. Studies classified as having an
5 263 industry tie were industry sponsored and / or had an author COI. Otherwise, they were
6 264 classified as having no industry ties.
7
8
9

10 265

11 266 **Analysis**

12 267 We report the frequencies and percentages of the study characteristics across all studies, and
13 268 separately, by sponsorship, COI and industry ties. We visually present the risk of bias rating
14 269 for each domain and overall across each study.
15
16
17
18

19 270

20 271 To quantify the association between industry ties, food industry sponsorship, or authors with
21 272 a conflict of interest with the food industry and (i) favourable results, (ii) favourable
22 273 conclusions, (iii) overall risk of bias across each study, and (iv) level of concordance, we
23 274 calculated RR (and 95% confidence intervals). To analyse the risk of bias rating for each
24 275 study, we dichotomised the overall risk of bias ratings as low (low or moderate) or high
25 276 (serious or critical).
26
27
28
29
30

31 277

32 278 We conducted meta-analysis to examine whether studies with food industry ties, food
33 279 industry sponsorship, or authors with a conflict of interest with the food industry modified the
34 280 magnitude of effect of dairy on CVD outcomes.. For each outcome, we combined effect
35 281 estimates using a random effects meta-analysis model using the inverse variance method.
36 282 DerSimonian and Laird’s method of moments estimator was used to estimate between study
37 283 heterogeneity. We fitted separate meta-analyses for studies that had measured the association
38 284 using HRs and those that had used either RRs or ORs. It is not recommended to combine HRs
39 285 with RRs and ORs in a meta-analysis, as HRs represent instantaneous risk over the study time
40 286 period, whereas RRs and ORs estimate risk/odds at a fixed time point.²⁴ We considered that
41 287 the ORs approximated RRs given CVD events were rare.
42
43
44
45
46
47
48
49

50 288

51 289 We undertook a fixed-effects test for subgroup differences (defined by industry sponsorship /
52 290 authors conflict of interest) using the Chi² test and calculated the ratio of RRs (ORs) or HRs
53 291 along with 95% confidence intervals. Analyses were undertaken in Review Manager 5.3.²⁵
54
55
56
57
58
59
60

292

1
2
3 293 We planned to use sensitivity analysis to assess the influence of risk of bias by restricting the
4 294 analysis to studies at ‘low risk of bias’ overall (i.e. an overall risk of bias rating of low or
5 295 moderate). However, as the overall risk of bias was high across all studies, this was not
6 296 undertaken.
7
8
9

10 297

11 298 **Patient and Public Involvement**

12 299 No patient involved
13
14
15

16 300

17 301 **RESULTS**

18 302 As shown in Figure 1, there were 1, 858 studies screened for inclusion and 43 studies were
19 303 included (3 case controls, 40 cohorts). See Supplementary file 4 for ‘List of excluded studies
20 304 and reasons for exclusion’.
21
22
23

24 305

25 306 **Characteristics of included Studies**

26 307 All studies were published between 2001 and 2019. All but one contained a funding
27 308 disclosure. Eight studies disclosed food industry sponsorship, but only two of these studies
28 309 described the role of the sponsor. Six studies did not contain an author COI disclosure
29 310 statement. Ten studies contained an author with a COI with the food industry. Fourteen
30 311 studies were classified as having industry ties, disclosing food industry sponsorship and / or
31 312 an author with a COI.
32
33
34
35
36
37

38 313

39 314 As shown in Table 1, most characteristics were similarly distributed across studies with
40 315 industry ties or no industry ties. Studies with industry ties (64%) were more likely to have
41 316 sample sizes <5000 than non-industry sponsored studies (34%). A greater proportion of
42 317 industry sponsored studies (100%) than non-industry sponsored studies (83%) focused on
43 318 total dairy intake rather than a specific food. Details of the individual studies are in
44 319 Supplementary file 5.
45
46
47
48
49

50 320

51 321

52 322

53 323

54 324

55
56
57
58
59
60

325 **Table 1. Characteristics of the included studies by sponsorship, author conflict of**
 326 **interest and industry ties**

327 Funding Source, n (%^a)

Characteristic	Category	Total N = 43	Sponsorship		COI		Industry Ties	
			Industr y N= 8	Non- Industry N=35	COI N =10	No COI N=33	Industry /COI N = 14	Non- Industry/ No COI N = 29
Sex	Male	5 (12)	0 (0)	5 (14)	0 (0)	5 (15)	0 (0)	5 (17)
	Female	2 (5)	0 (0)	2 (6)	0 (0)	2 (6)	0 (0)	2 (7)
	Both	36 (84)	8 (100)	28 (80)	10 (100)	26 (79)	14 (100)	22 (76)
Sample Size	<5000	19 (44)	6 (75)	13 (37)	7 (70)	12 (36)	9 (64)	10 (34)
	5000-50,000	18 (42)	0 (0)	18 (51)	2 (20)	16 (48)	2 (14)	16 (55)
	>50,000	6 (14)	2 (25)	4 (11)	1 (10)	5 (15)	3 (21)	3 (10)
Length of Follow up	N/A*	3 (7)	2 (25)	1 (3)	1 (10)	2 (6)	2 (14)	1 (3)
	<10 years	11 (26)	3 (38)	8 (23)	2 (20)	9 (27)	3 (21)	8 (28)
	10-15 years	21 (49)	2 (25)	19 (54)**	6 (60)	15 (45)**	7 (50)	14 (48)
	>15 years	8 (19)	1 (13)	7 (20)	1 (10)	7 (21)	2 (14)	6 (21)
Type of Dairy	Total Dairy Intake***	37 (86)	8 (100)	29 (83)	9 (90)	28 (85)	13 (93)	24 (83)
	Individual Dairy Foods****	6 (14)	0 (0)	6 (17)	1 (10)	5 (15)	1 (7)	5 (17)

328 ^a Percentages may not add to 100 due to rounding

329 * Follow up is not applicable for case control studies

330 ** Follow up for Johansson, I 2018 described the follow up as '8-12 years', we took the median of 10 years

331 *** This includes studies that looked at nutrients e.g calcium, fat & protein by measuring total dairy intake

332 ****Individual foods included milk, cheese & yogurt

333 **Risk of bias in included studies**

334 Every study was classified as having an overall high risk of bias, with 10 assessed as having a
335 serious risk of bias and 33 as having a critical risk of bias (Figure 2). Most studies were
336 assessed as having a critical risk of bias rating for the domain 'Bias due to confounding'. An
337 example of one of the several confounders we identified that studies needed to control for was
338 fruit and vegetable intake. If these confounders were not controlled for appropriately when
339 measuring the effect of dairy intake on a CVD outcome, the study was classified as having a
340 risk of bias for the confounding domain.

341
342 Studies without industry ties or without an author with a COI were more likely to have a
343 serious or critical risk of bias rating for 'Bias in classification of exposures'. For example, if a
344 study did not use a validated food frequency questionnaire to measure the dietary intake of
345 dairy, the study was classified as having a risk of bias for the domain of classification of
346 exposures. For all other domains, the risk of bias classifications were similarly distributed
347 across studies with industry ties, industry sponsorship or COI vs no industry ties, industry
348 sponsorship or COI, respectively (see Supplementary file 6).

350 **Favourable results - Statistical significance: Industry ties vs no industry ties; industry** 351 **sponsorship vs no sponsorship; COI v no COI**

352 There was no clear evidence of an association between the reporting of favourable results and
353 studies with industry ties (1/14) compared to those with no industry ties (8/29), RR= 0.26
354 (95% CI 0.04, 1.87; n=43 studies) (Supplementary file 7). When comparing studies with
355 industry sponsorship (1/8) with those with no industry sponsorship (8/35), there was no clear
356 evidence of an association, RR = 0.55 (95% CI 0.08, 3.77; n=43 studies). There was again no
357 clear evidence of an association between the reporting of favourable results and studies with
358 an author with a COI (0/10) than those with no COI (9/33), RR= 0.16 (95% CI 0.01, 2.57;
359 n=43 studies).

361 **Effect Size, Cardiovascular Disease: Industry ties v no industry ties; industry** 362 **sponsorship vs no industry sponsorship; COI v no COI**

363 For studies that quantified the association between dairy consumption and CVD outcomes
364 using a RR, we found no important difference in the magnitude of the effect in studies with
365 industry ties (RR = 0.89; n=3 studies) compared with those studies with no industry ties, (RR

1
2
3 366 = 0.99; n=7 studies) (ratio of RRs 0.90 (95% CI 0.74, 1.09)); P=0.27 (Supplementary file 8).
4
5 367 For studies that had quantified the association using HRs, we similarly did not find an
6
7 368 important difference in the magnitude of HRs between studies with industry ties, (HR=0.96;
8
9 369 n=7 studies) and those studies with no industry ties, (HR=0.95; n=14 studies) (ratio of HRs
10 370 1.01 (95% CI 0.90, 1.13)); P=0.86.
11

371

12
13 372 In our analysis comparing studies with industry sponsorship, (RR 0.83; n=2 studies) and
14 373 those with no industry sponsorship, (RR 0.97; n=8 studies) we again did not find an
15 374 important difference in the magnitude of RRs (ratio of RRs 0.86 (95% CI 0.44, 1.66));
16
17 375 P=0.65 (Supplementary file 8). However, when we compared industry sponsored studies,
18
19 376 (HR =0.78; n=3 studies) and non-industry sponsored studies, (HR=0.97; n=18 studies) that
20 377 measured the association using HRs, we found a statistically significant difference in the
21 378 magnitude of the HRs (ratio of HRs 0.80 (95%CI 0.66, 0.97)); P=0.03 (Figure 3).
22
23
24
25

379

26
27 380 In our analysis comparing studies with an author with a COI (RR 0.89; n=2 studies) and those
28 381 with no COI, (RR 0.99; n= 8 studies) we found no important difference in the magnitude of
29 382 RRs (ratio of RRs 0.90 (95% CI 0.76-1.07)); P=0.22 (Supplementary file 8). When we
30 383 compared studies with a COI, (HR =1.00; n= 5 studies) and studies with no COI, (HR=0.93;
31 384 n=16 studies) that measured the association using HRs, we again found no difference in the
32 385 magnitude of the HRs (ratio of HRs 1.08 (95% CI 0.99, 1.17)); P=0.12.
33
34
35
36
37

386

387 **Effect Size, Elevated Blood Pressure / Hypertension: Industry ties v no industry ties,**
388 **and industry sponsorship vs no sponsorship**

389 We found no important difference in the magnitude of the HRs for elevated blood pressure /
390 hypertension in studies with industry ties, (HR = 0.89; n =2) and those studies with no
391 industry ties, (HR = 0.78; n= 5) (ratio of HRs 1.14 (95% CI 0.88, 1.49); P=0.32
392 (Supplementary file 8).
393

394

395 All of these studies with industry ties also had industry sponsorship, so the ratio of HRs was
396 the same.
397

398

399 **Favourable conclusions: Industry ties vs no industry ties; industry sponsorship vs no**
400 **sponsorship; COI v no COI**

399 There was no clear evidence of an association between the reporting of favourable
400 conclusions and studies with industry ties (4/14) compared to those with no industry ties
401 (11/29), RR= 0.75 (95% CI 0.29, 1.95; n=43) (Supplementary file 7). When we compared
402 studies only by industry sponsorship, there was no clear evidence of an association between
403 industry sponsored studies (3/8), compared to studies with no sponsorship (12/35), RR = 1.09
404 (95% CI 0.40, 2.99; n=43). There was again no clear evidence of an association between the
405 reporting of favourable conclusions and studies with an author with a COI (2/10) than those
406 without a COI (13/33), RR= 0.51 (95% CI 0.14, 1.88; n=43 studies).

407

408 **Risk of Bias Assessment by Industry Ties**

409 As every study had an overall high (serious or critical) risk of bias rating, there was no
410 difference in the proportion of studies at a high risk of bias between those with industry ties,
411 industry sponsorship or COI and those without industry ties, sponsorship or COI.

412

413 **Concordance between study results and conclusions**

414 Six (of 43) studies, all with unfavorable results, overemphasized the benefits of the dairy
415 exposure in their conclusions and thus were coded as 'favourable' conclusions.

416 There was no clear evidence of an association between discordant results and conclusions and
417 studies with industry ties (3/14) than those with no industry ties (3/29), RR = 2.07 (95% CI
418 0.48, 8.99; n=43) (Supplementary file 7). There was no clear evidence of an association when
419 comparing studies with industry sponsorship (2/8) to those with no industry sponsorship
420 (4/35), RR = 2.19 (95% CI 0.48-9.94). There was again no clear evidence of an association
421 between studies with an author with a COI (2/10) than those with no COI (4/33), RR = 1.65
422 (95% CI 0.35, 7.72; n=43).

423

424 **DISCUSSION**

425 There was no clear evidence of an association between studies with food industry ties and the
426 reporting of favourable results and conclusions of observational studies measuring the
427 associations of dairy foods with cardiovascular disease outcomes. The 'mixed' group of
428 funders we identified in the industry sponsored studies may influence these results, as the
429 funding effect may be diluted by this heterogeneous group of sponsors. Unlike in drug

1
2
3 430 studies,¹² the funders in the studies included in this review were extremely diverse, with Big
4
5 431 Food and trade association jointly sponsoring several studies. Thus, dairy foods are not their
6
7 432 sole interest.

8
9 433 The meta-analysis of hazard ratios of CVD outcomes found that studies with industry
10
11 434 sponsorship showed a greater benefit from dairy than studies without industry sponsorship,
12
13 435 and this difference was statistically significant. The meta-analysis of risk ratios of CVD
14
15 436 outcomes found a similar estimate; however, this was not statistically significant. The likely
16
17 437 reason for this was that the meta-analysis of RRs had fewer studies, and so the ratio of RRs
18
19 438 could not be as precisely estimated. We found no evidence of a clinically important
20
21 439 difference in the magnitude of effect between studies with industry ties or authors with a COI
22
23 440 compared to those with no industry ties or no COI for other outcomes.
24

25 441
26 442 For every study, the overall risk of bias was classified as high (meaning either serious or
27
28 443 critical). Therefore, differences in the risk of bias across studies with and without industry
29
30 444 ties would not seem to provide an explanation for our findings. However, the version of the
31
32 445 ROBINS-E tool that we used may not have been able to adequately discriminate across the
33
34 446 studies, as perhaps is indicated by the uniformity in risk of bias classification.²⁶ Therefore, we
35
36 447 cannot rule out the possibility that differences in bias across studies with and without industry
37
38 448 ties may partly explain our findings.
39

40 450 **Strengths and limitations of this review**

41
42 451 Our review was prospectively registered in Prospero.¹⁹ We followed explicit inclusion and
43
44 452 exclusion criteria, conducted a comprehensive search across multiple databases and hand
45
46 453 searched reference lists for the included studies.
47

48 454
49 455 For those studies missing a funding or author COI disclosure, we did not contact the authors
50
51 456 and we therefore may be underestimating the number of studies with industry ties. The tool
52
53 457 that we used to assess the risk of bias is still under development, however it is unlikely any
54
55 458 future changes to the tool will affect the risk of bias ratings.²² We did not analyse studies of
56
57 459 low and full fat dairy or other types of dairy products separately. Industry ties may have
58
59 460 different effects on studies of low or full fat dairy foods or other foods and drinks. A final
60
61 461 limitation of our study is that we relied on definitions of exposures and outcomes that were

1
2
3 462 used in the original studies included in our analyses. Using finer categorizations of exposures
4 and outcomes would not provide a sufficient sample size to do our analyses. However, future
5 463 studies, using additional data and finer categorizations, may have different results.
6
7 464
8
9 465

466 **Agreements and disagreements with other studies or reviews**

12 467 The observed greater benefit of dairy on CVD outcomes in industry sponsored studies
13 compared to non-industry sponsored studies corroborates previous research that has
14 468 demonstrated studies sponsored by the food industry reported smaller harmful effect sizes for
15 soft drink consumption, compared with non-industry sponsored studies.¹⁷ It is not consistent,
16 469 however, with a recent meta-analysis funded by the Israel Dairy Board that found non
17 statistically significant differences in the estimated associations between industry and non-
18 470 industry funded studies.¹⁸ The differences in the results of our current review and this
19 previous study can be attributed to a number of important factors in how the studies were
20 471 conducted, including how the exposures were classified, the outcomes selected for the meta-
21 472 analyses and the analysis method used. For the exposures, our review included yogurt and
22 cheese, as well as ‘total dairy’ and milk, whereas the Dairy Board study included only ‘total
23 473 dairy’ and milk as exposures. We included all outcomes related to CVD, and the Dairy Board
24 study included only CVD and stroke, as well as Type 2 diabetes. For the analysis method, we
25 474 fitted separate meta-analyses for studies that had measured the association using HRs and
26 those that had used either RRs or ORs, while the Dairy Board study only measured the
27 475 associations using RRs.
28
29 482

30 483
31 484 The lack of difference in the risks of bias between studies with industry ties and those with no
32 industry ties, is consistent with a previous review that examined the association of industry
33 485 ties with outcomes of studies examining the effect of wholegrain foods on CVD and mortality
34 that used the same tool to assess risk of bias.¹⁶ These findings have also been shown in
35 486 pharmaceutical and tobacco research that have demonstrated industry sponsored studies are
36 of equal or better internal validity than studies with no sponsorship.^{12, 13, 15, 27, 28}
37
38
39 489

491 **Implications for clinicians, policy makers and future research**

492 As dietary guidelines depend on an evidence base that should be as free as possible of bias,
493 the difference in the magnitude of effects between industry sponsored studies compared to
494 non-industry sponsored studies is concerning. Therefore, the dairy intake recommendations

1
2
3 495 made in dietary guidelines should account for the potential influence of industry sponsorship
4
5 496 on evidence of health effects. Nutrition studies included in systematic reviews used in the
6
7 497 development of dietary guidelines should be assessed using empirical methods to identify
8
9 498 factors associated with study results. Current risk of bias tools should therefore be amended
10
11 499 or supplemented to include industry sponsorship and author COI as a separate risk of bias
12
13 500 domain. The University of California, San Francisco's Navigation Guide assesses both author
14
15 501 conflicts of interest and funding sources as a risk of bias in human and animal studies.²⁹ As
16
17 502 the study designs used in nutrition are the same as those used to evaluate the harms of an
18
19 503 exposure in environmental health, dietary guideline committees could consider adopting this
20
21 504 tool to evaluate the risk of bias of the studies included in the systematic reviews used to
22
23 505 develop dietary guidelines.

24 506
25 507 Industry sponsors may bias research via different mechanisms, including the design and
26
27 508 conduct of a study, the selective reporting of results, how they code events, analyse data, by
28
29 509 spinning conclusions,¹¹ as well as framing how the questions are asked.³⁰⁻³² It has been
30
31 510 suggested that the dairy industry may preferentially fund research on topics which will
32
33 511 provide them with more favourable outcomes.³³ The influence of the food industry on the
34
35 512 research agenda has been demonstrated in an examination of research topics covered by
36
37 513 samples of randomised controlled trials included in systematic reviews of nutrition studies
38
39 514 and obesity.³⁴ It was shown that most food industry studies focused on the manipulations of
40
41 515 specific nutrients, and not on dietary behaviours, therefore limiting the public health
42
43 516 relevance of rigorous evidence available for use in both systematic reviews and dietary
44
45 517 guidelines.³⁴ The topics examined in cohort studies on the relationship of nutrition and
46
47 518 obesity, which tend to focus on more complex exposures than trials, did not demonstrate a
48
49 519 similar influence of funding source. However, the disclosure of food industry sponsorship
50
51 520 was low, making a comparison difficult.³⁵

52 521
53 522 This present study has also demonstrated that there is significant funding for nutrition
54
55 523 research that comes from non-industry sources, including academia and government. In this
56
57 524 study, only eight studies had food industry sponsorship, while 34 had a non-food industry
58
59 525 sponsorship. A similar rate was seen in a study that assessed the association of industry ties
60
526 with outcomes of studies examining the effect of wholegrain foods on cardiovascular disease
527
528 and mortality, with only five industry sponsored studies and 17 non-industry sponsored

1
2
3 528 studies.¹⁶ To eliminate this risk of bias from nutrition research, investigators should use only
4
5 529 non-industry sources to fund their research.
6

7 530

8 531

9
10 532 **Conclusion**

11
12 533 There was no clear evidence of an association between studies with food industry ties and the
13
14 534 reporting of favourable results and conclusions compared with studies without industry ties.

15 535 However, the statistically significant difference in the magnitude of effects identified in
16
17 536 industry sponsored studies compared to non-industry sponsored studies is important in
18
19 537 quantifying industry influence on studies included in dietary guidelines.
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 538 **Acknowledgements:** We thank Agnes Lau, University of California, San Francisco, for her
4
5 539 assistance with data collection.
6
7 540

8
9 541 **Contributors:** NC, AF and LB designed and wrote the review protocol. NC wrote the search
10
11 542 strategy and undertook the literature search. NC, AF and SMc, conducted the title and
12
13 543 abstract screening and full article screening for final study inclusion. NC, AF, JD, AL and
14
15 544 SMc conducted data collection and cleaning, LB supervised. NC and JMc undertook all data
16
17 545 analysis. LB advised on methods, statistical analyses, and interpretation of findings. All
18
19 546 authors contributed to the final manuscript. NC and LB are guarantors.
20
21 547

22
23 548 **Funding:** This work was supported by Australian Health and Medical Research Council
24
25 549 Project Grant APP 1139997. Nicholas Chartres is a recipient of the James Millner PhD
26
27 550 Scholarship in Pharmacy from the University of Sydney.
28
29 551

30
31 552 **Competing interests:** None declared.
32
33 553

34
35 554 **Data sharing statement:** Available from The University of Sydney data repository. DOI to
36
37 555 be determined.
38
39 556

40
41
42 557 **Patient consent for publication:** Not required.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 **References**

- 4 559 1. Qin LQ, Xu JY, Han SF, et al. Dairy consumption and risk of cardiovascular disease: an
5 560 updated meta-analysis of prospective cohort studies. *Asia Pac J Clin Nutr*. 2015;24(1):90-100.
- 6 561 2. Alexander DD, Bylsma LC, Vargas AJ, et al. Dairy consumption and CVD: a systematic review
7 562 and meta-analysis. *Br J Nutr*. 2016;115(4):737-50.
- 8 563 3. Gholami F, Khoramdad M, Esmailnasab N, et al. The effect of dairy consumption on the
9 564 prevention of cardiovascular diseases: A meta-analysis of prospective studies. *J Cardiovasc Thorac*
10 565 *Res*. 2017;9(1):1-11.
- 11 566 4. Drouin-Chartier JP, Brassard D, Tessier-Grenier M, et al. Systematic Review of the
12 567 Association between Dairy Product Consumption and Risk of Cardiovascular-Related Clinical
13 568 Outcomes. *Adv Nutr*. 2016;7(6):1026-40.
- 14 569 5. Lee M, Lee H, Kim J. Dairy food consumption is associated with a lower risk of the metabolic
15 570 syndrome and its components: a systematic review and meta-analysis. *Br J Nutr*. 2018;120(4):373-
16 571 84.
- 17 572 6. National Health and Medical Research Council: Department of Health and Ageing. Australian
18 573 Dietary Guidelines. Canberra, Commonwealth of Australia: NHMRC; 2013.
- 19 574 7. Public Health England. The Eatwell Guide. [Internet]. 2016. Available from:
20 575 <https://www.gov.uk/government/publications/the-eatwell-guide>. Accessed 18 March, 2016.
- 21 576 8. Lexchin J. Those who have the gold make the evidence: how the pharmaceutical industry
22 577 biases the outcomes of clinical trials of medications. *Sci Eng Ethics*.18(2):247-61.
- 23 578 9. Sismondo S. How pharmaceutical industry funding affects trial outcomes: causal structures
24 579 and responses. *Social science & medicine* (1982). 2008;66(9):1909-14.
- 25 580 10. Boutron I, Dutton S, Ravaud P, et al. Reporting and interpretation of randomized controlled
26 581 trials with statistically nonsignificant results for primary outcomes. *JAMA*. 2010;303(20):2058-64.
- 27 582 11. Odierna DH, Forsyth SR, White J, et al. The cycle of bias in health research: a framework and
28 583 toolbox for critical appraisal training. *Account Res*. 2013;20(2):127-41.
- 29 584 12. Lundh A, Lexchin J, Mintzes B, et al. Industry sponsorship and research outcome. *Cochrane*
30 585 *Database Syst Rev*. 2017;2:Mr000033.
- 31 586 13. Barnes DE, Bero LA. Industry-funded research and conflict of interest: an analysis of research
32 587 sponsored by the tobacco industry through the Center for Indoor Air Research. *J Health Polit Policy*
33 588 *Law*. 1996;21(3):515-42.
- 34 589 14. Yank V, Rennie D, Bero LA. Financial ties and concordance between results and conclusions
35 590 in meta-analyses: retrospective cohort study. *BMJ*.335(7631):1202-5.
- 36 591 15. Chartres N, Fabbri A, Bero LA. Association of industry sponsorship with outcomes of
37 592 nutrition studies: A systematic review and meta-analysis. *JAMA Intern Med*. 2016;176(12):1769-77.
- 38 593 16. Chartres N, Fabbri A, McDonald S, et al. Association of industry ties with outcomes of studies
39 594 examining the effect of wholegrain foods on cardiovascular disease and mortality: systematic review
40 595 and meta-analysis. *BMJ Open*. 2019;9(5):e022912.
- 41 596 17. Vartanian LR, Schwartz MB, Brownell KD. Effects of soft drink consumption on nutrition and
42 597 health: a systematic review and meta-analysis. *Am J Public Health*. 2007;97(4):667-75.
- 43 598 18. Mishali M, Kisner M, Avrech T. Funding sources and outcomes of dairy consumption
44 599 research – a meta-analysis of cohort studies: The case of type-2 diabetes and cardiovascular
50 600 diseases. *Int Dairy J*. 2019.
- 51 601 19. National Institute for Health Research. International Prospective Register for Systematic
52 602 Reviews [Internet]. 2015 [Available from: <http://www.crd.york.ac.uk/PROSPERO/>. Accessed 11
53 603 March, 2016.
- 54 604 20. Dietitians Association of Australia. A review of the evidence to address targeted questions to
55 605 inform the revision of the Australian dietary guidelines 2009: Process Manual. 2011.
- 56 606 21. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-
57 607 randomised studies of interventions. *BMJ*. 2016;355.

- 1
2
3 608 22. University of Bristol. The ROBINS-E tool (Risk Of Bias In Non-randomized Studies - of
4 609 Exposures) 2019 [Available from: [https://www.bristol.ac.uk/population-health-
6 611 sciences/centres/cresyda/barr/riskofbias/robins-e/](https://www.bristol.ac.uk/population-health-
5 610 sciences/centres/cresyda/barr/riskofbias/robins-e/).
7 612 23. Harris PA, Taylor R, Thielke R, et al. Research Electronic Data Capture (REDCap) - A
8 613 metadata-driven methodology and workflow process for providing translational research informatics
9 614 support. *J Biomed Inform X*. 2009;42(2):377-81.
10 615 24. Tierney JF, Stewart LA, Ghersi D, et al. Practical methods for incorporating summary time-to-
11 616 event data into meta-analysis. *Trials*. 2007;8:16.
12 617 25. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic
13 618 Cochrane Centre, The Cochrane Collaboration, 2014.
14 619 26. Bero L, Chartres N, Diong J, et al. The risk of bias in observational studies of exposures
15 620 (ROBINS-E) tool: concerns arising from application to observational studies of exposures. *Syst Rev*.
16 621 2018;7(1):242.
17 622 27. Mandrioli D, Kearns CE, Bero LA. Relationship between Research Outcomes and Risk of Bias,
18 623 Study Sponsorship, and Author Financial Conflicts of Interest in Reviews of the Effects of Artificially
19 624 Sweetened Beverages on Weight Outcomes: A Systematic Review of Reviews. *PLoS one*.
20 625 2016;11(9):e0162198.
21 626 28. Cho MK, Bero LA. The quality of drug studies published in symposium proceedings. *Ann
22 627 Intern Med*. 1996;124(5):485-9.
23 628 29. Woodruff TJ, Sutton P. The Navigation Guide systematic review methodology: a rigorous and
24 629 transparent method for translating environmental health science into better health outcomes.
25 630 *Environ Health Perspect*. 2014;122(10):1007-14.
26 631 30. Fabbri A, Lai A, Grundy Q, et al. The Influence of Industry Sponsorship on the Research
27 632 Agenda: A Scoping Review. *Am J Public Health*. 2018;108(11):e9-e16.
28 633 31. Psaty BM, Prentice RL. Minimizing bias in randomized trials: the importance of blinding.
29 634 *JAMA*. 2010;304(7):793-4.
30 635 32. Psaty BM, Kronmal RA. Reporting mortality findings in trials of rofecoxib for Alzheimer
31 636 disease or cognitive impairment: a case study based on documents from rofecoxib litigation. *JAMA*.
32 637 2008;299(15):1813-7.
33 638 33. Wilde P, Morgan E, Roberts J, et al. Relationship between funding sources and outcomes of
34 639 obesity-related research. *Physiol & Behav*. 2012;107(1):172-5.
35 640 34. Fabbri A, Chartres N, Bero LA. Study sponsorship and the nutrition research agenda: analysis
36 641 of cohort studies examining the association between nutrition and obesity. *Public Health Nutr*.
37 642 2017;20(17):3193-9.
38 643 35. Fabbri A, Chartres N, Bero LA. Study sponsorship and the nutrition research agenda: analysis
39 644 of cohort studies examining the association between nutrition and obesity. *Public Health Nutr*.
40 645 2017;20(17):3193-9.
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 653 **Figures**
4

5 654 **Figure 1. Study Flow Diagram**
6

7 655 **Figure 2. Risk of Bias in Included Studies**
8

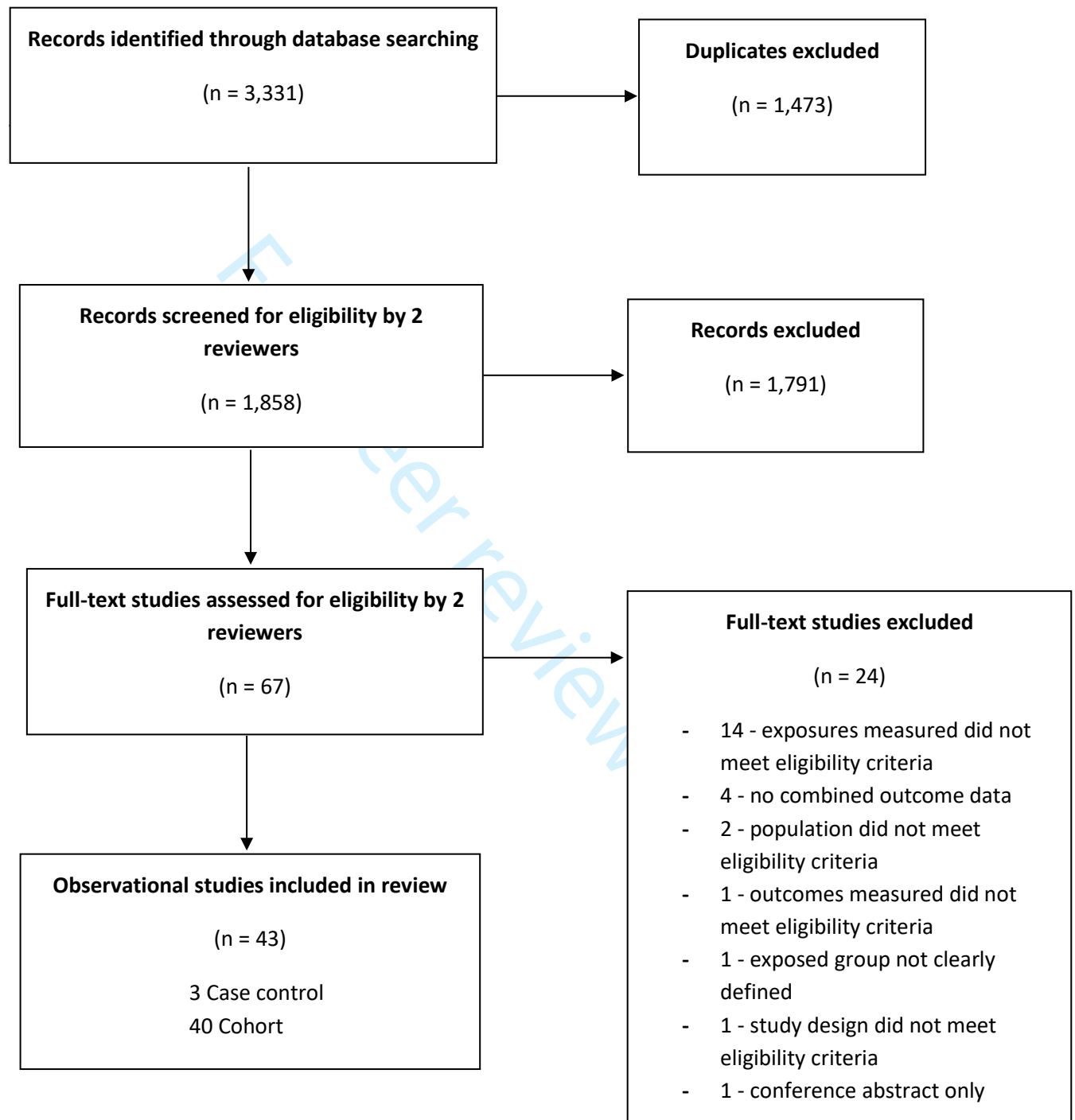
9 656 **Figure 3. Effect Size, Cardiovascular Disease: Industry sponsorship vs no industry**
10 **sponsorship, Hazard Ratio**
11
12
13

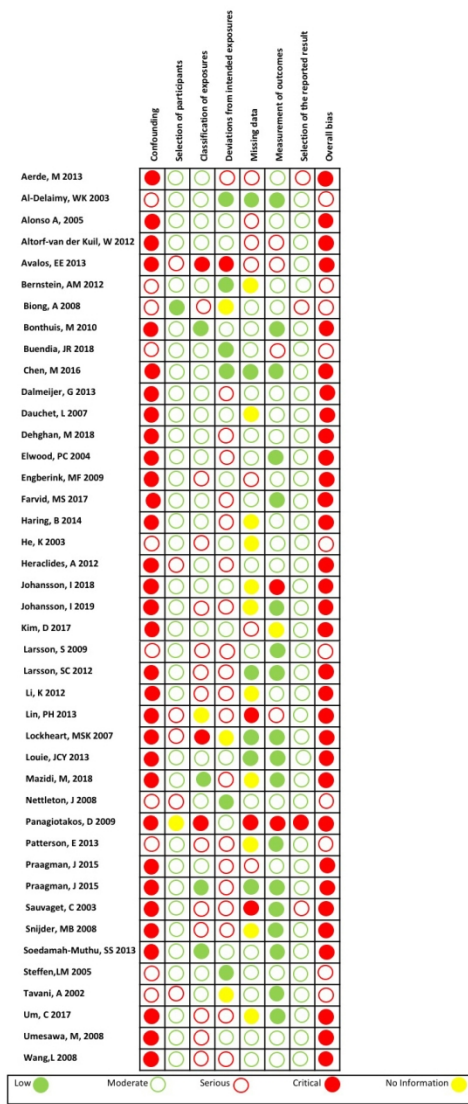
14 658
15

16 659
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

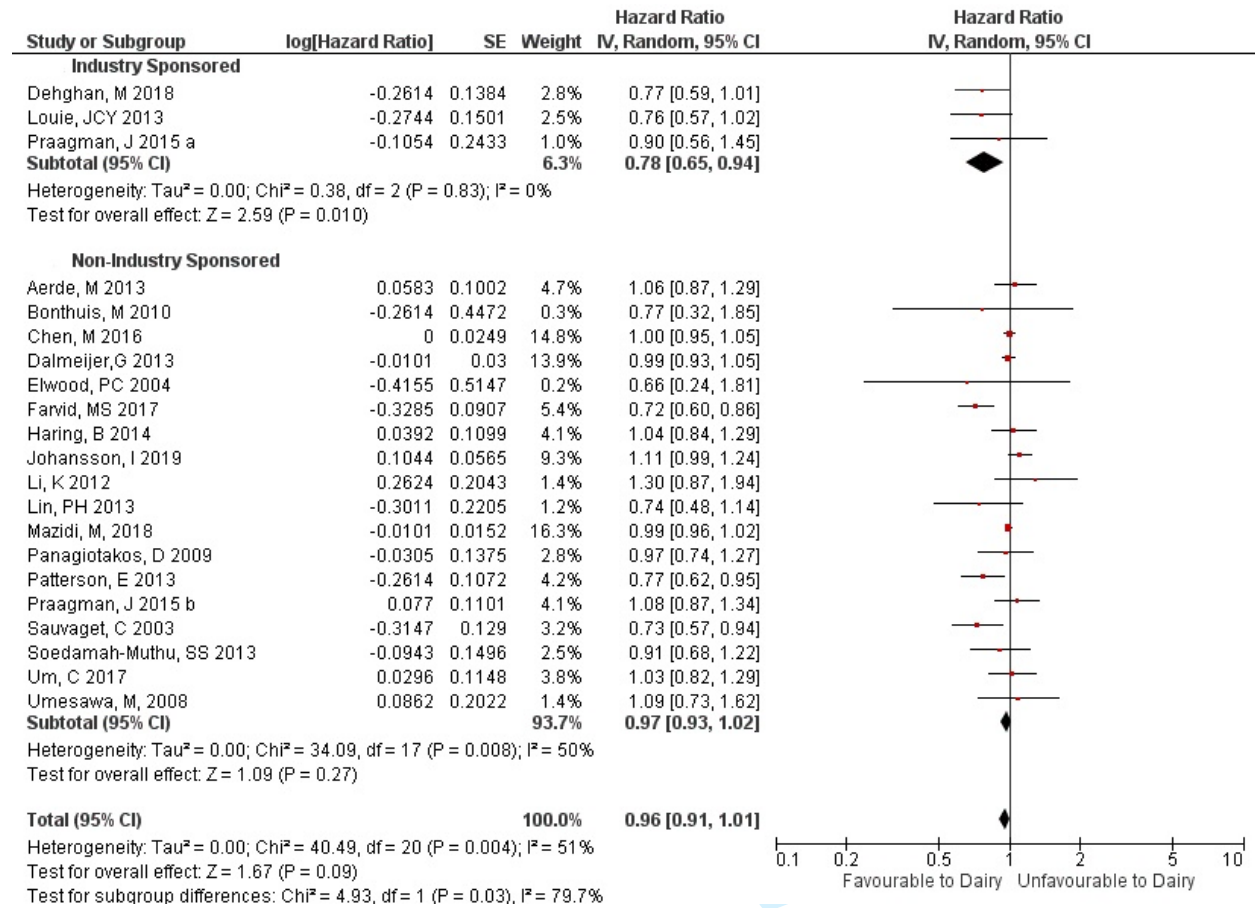
Figure 1. Study Flow Diagram





122x161mm (300 x 300 DPI)

Figure 3. Effect Size, Cardiovascular Disease, Industry sponsorship vs no Industry sponsorship, Hazard Ratio



PROSPERO**International prospective register of systematic reviews**

UNIVERSITY of York
Centre for Reviews and Dissemination

Systematic review

Please complete all mandatory fields below (marked with an asterisk *) and as many of the non-mandatory fields as you can then click *Submit* to submit your registration. You don't need to complete everything in one go, this record will appear in your *My PROSPERO* section of the web site and you can continue to edit it until you are ready to submit. Click *Show help* below or click on the icon to see guidance on completing each section.

This record cannot be edited because it has been rejected

1. * Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

The association of food industry ties with findings of studies examining the effect of dairy foods intake with cardiovascular disease and mortality: Systematic review and Meta-analysis: protocol registration:

2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. * Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

01/09/2016

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

01/06/2019

5. * Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.

Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.

This field should be updated when any amendments are made to a published record and on completion and publication of the review. If this field was pre-populated from the initial screening questions then you are not able to edit it until the record is published.

The review has not yet started: No

PROSPERO

International prospective register of systematic reviews

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	Yes	No
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

6. * Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record.

Nicholas Chartres

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Mr Chartres

7. * Named contact email.

Give the electronic mail address of the named contact.

ngar0960@uni.sydney.edu.au

8. Named contact address

Give the full postal address for the named contact.

The University of Sydney, D17, the Hub, 6th Floor, Charles Perkins Centre | the University of Sydney | Nsw |
2006

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

02 8627 4328

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

University of Sydney

Organisation web address:

11. * Review team members and their organisational affiliations.

PROSPERO

International prospective register of systematic reviews

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country are now mandatory fields for each person.**

Mr Nicholas Chartres. University of Sydney

Dr Alice Fabbri. The University of Sydney

Agnes Lau. University of California

Dr Joanna Diong. The University of Sydney

Assistant/Associate Professor Joanne Mckenzie. Monash University

Professor Lisa Bero. The University of Sydney

12. * Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

Nicholas Chartres is a scholarship recipient (James Milner PhD scholarship in Pharmacy) from the University of Sydney.

Grant number(s)

13. * Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country are now mandatory fields for each person.**

15. * Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

The objective of this study is to determine if the presence of food industry sponsorship in primary nutrition studies examining the association of dairy foods with cardiovascular outcomes is associated with effect sizes, statistical significance of results and/ or conclusions that are favorable to the sponsor. We will also determine whether primary nutrition studies assessing the association of dairy foods with cardiovascular outcomes with industry sponsorship differ in their risk of bias compared with studies with no or other sources of sponsorship.

16. * Searches.

State the sources that will be searched. Give the search dates, and any restrictions (e.g. language or publication period). Do NOT enter the full search strategy (it may be provided as a link or attachment.)

We will search the following databases from 2000-March 2019: Ovid MEDLINE; CINAHL; PubMed;

Cochrane Library; and ScienceDirect. No language restrictions will be applied

PROSPERO

International prospective register of systematic reviews

17. URL to search strategy.

Give a link to a published pdf/word document detailing either the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies), or upload your search strategy. Do NOT provide links to your search results.

https://www.crd.york.ac.uk/PROSPEROFILES/129659_STRATEGY_20190322.pdf

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

To determine whether industry sponsorship and/or study methods are associated with the results and/or conclusions of primary nutrition studies assessing the association of dairy foods and cardiovascular outcomes.

19. * Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

We will include primary research studies of any design that quantitatively examine the association of dairy foods with cardiovascular outcomes in healthy adults.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed.

- The study quantitatively measures the effects of dairy consumption in humans.
- The study evaluates the effectiveness, efficacy or harms of dairy consumption.
- The study compares dairy food to control OR dairy food to other foods OR different levels of dairy consumption
- The study evaluates cow, goat or sheep milk, yogurt, cheese or custard. We will include and use the studies definition of dairy it is broader than milk, yogurt, cheese or custard.
- The study evaluates skim, low or full fat dairy products
- The study evaluates the effect of nutrients, e.g calcium and vitamin D when consumed within a dairy product

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Dairy vs Dairy (different doses) Dairy vs Dairy (different fat content) Dairy vs No dairy Dairy vs Other food

PROSPERO

International prospective register of systematic reviews

Other (mixed intervention)

22. * Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

RCTs, Controlled Trials, Cohort, Case-control, Pre/Post, Other/Various

23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

- The study evaluates clinical outcomes (e.g. risk ratio/hazard ratio/odds ratio (RR/HR/OR) of cardiovascular mortality, nonfatal heart attack, stroke, etc.) and/or the surrogate outcomes of Blood Pressure (mmHg)

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

a. Primary Outcome 1 and 2

- o Statistical significance of results
- o Effect size of outcomes

For each study, the result reported for each primary outcome will be categorized as:

(1) Favourable if the result are statistically significant ($p < 0.05$ or 95% confidence interval [CI] excluding no difference) and in the direction of dairy being more efficacious, less harmful or no more harmful than the comparator;

(2) Unfavourable if the result was statistically significant (e.g. $P < 0.05$ or 95% confidence interval including the possibility of no difference) in the direction of the comparator being more efficacious or less harmful.

We will also extract the effect estimates for primary outcomes.

We will classify the results of the study as favourable if the stated primary outcome is reported as favourable.

If the study has multiple primary outcomes we will report the study as favourable if at least one of the outcomes is reported as favourable.

b. Primary Outcome 3 (Conclusions)

The conclusions reported in the published papers will be categorized as:

(1) Favourable if the dairy intervention was preferred to comparator

(2) Unfavourable if the comparator intervention was preferred to the test one OR if the test intervention

PROSPERO

International prospective register of systematic reviews

showed a risk increase.

* Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

As this is not relevant to our study, we have nothing to include.

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

We used the Cochrane Risk of Bias tool for randomised studies (15) to measure the methodological quality of randomized controlled trials. The tool assesses bias across 7 domains and each of these will be reported separately. To measure methodological quality in observational studies we will use the ROBINS-I tool for non-randomized studies (ROBINS-I)(16), which also measures bias across 7 domains.

d. Secondary Outcome 2 (Concordance between results and conclusions)

We will classify concordance between study results and conclusions as 'yes' if the authors' conclusions are supported by all outcomes. This will include the reporting of all significant and non-significant results.

Otherwise, concordance will be classified as 'no'

* Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

As this is not relevant to our study, we have nothing to include.

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Selection Process

Two investigators (NC & AF) will independently screen the titles and abstracts of all retrieved records for obvious exclusions. Two investigators (NC & AF) will then assess the remaining papers based on full text, applying the aforementioned inclusion criteria for included studies. Agreement will be reached on any discrepancies by consensus between the two assessors. If agreement cannot be reached, a third assessor (LB) will make a decision. The reasons for the eligible papers being excluded will be described in

PROSPERO

International prospective register of systematic reviews

'Characteristics of excluded papers' table.

Data collection process

- a) Title of the paper
- b) Year of publication
- c) Study design
- d) Comparisons:
- e) Sample size of study
- f) Mean age of participants
- g) Intervention or observation period
- h) Definition of intervention and exposure
- i) Risk of Bias
- j) Primary Hypothesis of the study (Verbatim)
- k) Primary outcomes measures
- l) Conclusion
- m) Concordance between conclusions and results
- n) Industry Sponsorship
- o) Role of the Funder: Information about the role of the sponsor as stated in the study
- p) The institutional affiliation of the corresponding author will be obtained from the article and classified into the following categories
- q) Country of origin (verbatim)
- r) Author COI

27. * Risk of bias (quality) assessment.

Describe the method of assessing risk of bias or quality assessment. State which characteristics of the studies will be assessed and any formal risk of bias tools that will be used.

We will use the Cochrane Risk of Bias tool for randomised studies (15) to measure the methodological quality of randomized controlled trials. The tool assesses bias across 7 domains and each of these will be reported separately. To measure methodological quality in observational studies we will use the ROBINS-I tool for non-randomized studies (ROBINS-I)(16), which also measures bias across 7 domains.

28. * Strategy for data synthesis.

Provide details of the planned synthesis including a rationale for the methods selected. This **must not be generic text** but should be **specific to your review** and describe how the proposed analysis will be applied to your data.

To test our hypothesis that studies with dairy industry sponsorship will be more likely to have favourable

PROSPERO

International prospective register of systematic reviews

results, we will compare the risk of dairy industry sponsored studies having a favourable result with the risk of non-dairy industry funded studies having a favorable result. Using Rev Manager we will calculate the pooled risk ratio (RR) and its 95% confidence interval using the Mantel-Haenszel fixed-effect model.

However, when substantial heterogeneity is observed, we will use an inverse variance DerSimonian-Laird random-effects model. We will assess heterogeneity using I^2 and use a random-effects model when statistical heterogeneity is substantial, defined as an I^2 50%.

To test our hypothesis that effect estimates will differ between studies with dairy industry sponsorship and those without sponsorship, we will compare the pooled effect estimates from dairy vs. non-dairy sponsored studies. We will pool the effect estimates of homogenous studies measuring dichotomous outcomes, (e.g. RR, HR, OR for all-cause mortality, CVD mortality, cardiovascular events, etc) calculating pooled risk ratios as described above. Blood pressure is a continuous outcome, so we will attempt to pool homogeneous studies and measure the mean difference from baseline measures.

To test our hypothesis that studies with dairy industry sponsorship would be more likely to have favourable conclusions we will compare the risk of dairy industry sponsored studies having favourable conclusions with the risk of non-dairy industry funded studies having a favorable conclusion. We will calculate the pooled risk ratio (RR) and its 95% confidence interval using the Mantel-Haenszel fixed-effect model. However, when substantial heterogeneity is observed, we will use an inverse variance DerSimonian-Laird random-effects model. We will assess heterogeneity using I^2 and use a random-effects model when statistical heterogeneity is substantial, defined as an I^2 50%.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

We will conduct an a priori subgroup analysis on low fat and full fat dairy products to determine if studies measuring the effects of low fat products have different results from studies that measure full fat dairy products.

We will conduct an a priori subgroup analysis by the risks of bias of the included studies to determine if studies that have a high risk of bias have different results from studies that have a low risk of bias. We hypothesize that industry sponsored studies will have the same level of risk of bias as non-industry sponsored studies.

30. * Type and method of review.

Select the type of review and the review method from the lists below. Select the health area(s) of interest for your review.

Type of review

Cost effectiveness

PROSPERO

International prospective register of systematic reviews

1
2
3
4 No
5 Diagnostic
6 No
7 Epidemiologic
8 No
9 Individual patient data (IPD) meta-analysis
10 No
11 Intervention
12 No
13
14 Meta-analysis
15 Yes
16 Methodology
17 No
18 Narrative synthesis
19 No
20
21 Network meta-analysis
22 No
23 Pre-clinical
24 No
25 Prevention
26 No
27 Prognostic
28 No
29
30 Prospective meta-analysis (PMA)
31 No
32 Review of reviews
33 No
34 Service delivery
35 No
36
37 Synthesis of qualitative studies
38 No
39 Systematic review
40 Yes
41 Other
42 No
43
44
45 **Health area of the review**
46 Alcohol/substance misuse/abuse
47 No
48
49 Blood and immune system
50 No
51 Cancer
52 No
53 Cardiovascular
54 Yes
55
56 Care of the elderly
57 No
58 Child health
59 No
60 Complementary therapies

PROSPERO**International prospective register of systematic reviews**

1
2
3
4 No
5 Crime and justice
6 No
7 Dental
8 No
9 Digestive system
10 No
11 Ear, nose and throat
12 No
13 Education
14 No
15 Endocrine and metabolic disorders
16 No
17 Eye disorders
18 No
19 General interest
20 No
21 Genetics
22 No
23 Health inequalities/health equity
24 No
25 Infections and infestations
26 No
27 International development
28 No
29 Mental health and behavioural conditions
30 No
31 Musculoskeletal
32 No
33 Neurological
34 No
35 Nursing
36 No
37 Obstetrics and gynaecology
38 No
39 Oral health
40 No
41 Palliative care
42 No
43 Perioperative care
44 No
45 Physiotherapy
46 No
47 Pregnancy and childbirth
48 No
49 Public health (including social determinants of health)
50 Yes
51 Rehabilitation
52 No
53 Respiratory disorders
54 No
55
56
57
58
59
60

PROSPERO

International prospective register of systematic reviews

Service delivery

No

Skin disorders

No

Social care

No

Surgery

No

Tropical Medicine

No

Urological

No

Wounds, injuries and accidents

No

Violence and abuse

No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.

English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

Australia

33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one

Give the link to the published protocol.

Alternatively, upload your published protocol to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences.

PROSPERO

International prospective register of systematic reviews

Do you intend to publish the review on completion?

Yes

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords will help users find the review in the Register (the words do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

Nutrition, Industry Sponsorship, Conflict of Interest, Bias, Food Industry

37. Details of any existing review of the same topic by the same authors.

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

CRD42017055841 The association of industry sponsorship with outcomes of studies examining the effect of intake of wholegrain foods with cardiovascular disease and mortality: protocol

38. * Current review status.

Review status should be updated when the review is completed and when it is published. For new registrations the review must be Ongoing.

Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information the review team feel is relevant to the registration of the review.

40. Details of final report/publication(s).

This field should be left empty until details of the completed review are available.

Give the link to the published review.

Supplementary file 2. Search Strategy OVID Medline: Dairy, CVD, Adults

1. Randomized controlled trial*.tw.
2. experimental design.tw.
3. intervention*.tw.
4. (RCT* or rct*).tw.
5. random* control* trial*.tw.
6. clinical trial*.tw.
7. field trial*.tw.
8. community trial*.tw.
9. controlled clinical trial*.tw.
10. pragmatic trial*.tw.
11. observational stud*.tw.
12. cohort stud*.tw.
13. prospective cohort*.tw.
14. retrospective cohort*.tw.
15. case control*.tw.
16. ecological stud*.tw.
17. time series analys?s*.tw.
18. before-after stud*.tw.
19. pre-post stud*.tw.
20. follow up stud*.tw.
21. comparative stud*.tw.
22. evaluation stud*.tw.
23. dairy.mp.
24. dairy intake*.mp.

- 1
2
3 25. dairy consumption.mp.
4
5 26. dairy food*.mp.
6
7 27. Dairy Products/ or dairy product*.mp.
8
9 28. dairy serv*.mp.
10
11 29. dairy type*.mp.
12
13 30. dairy source*.mp.
14
15
16 31. (calcium adj15 food sourc*).mp. [mp=title, abstract, original title, name of substance word,
17 subject heading word, keyword heading word, protocol supplementary concept word, rare
18 disease supplementary concept word, unique identifier]
19
20 32. (vitamin D adj15 food sourc*).mp. [mp=title, abstract, original title, name of substance word,
21 subject heading word, keyword heading word, protocol supplementary concept word, rare
22 disease supplementary concept word, unique identifier]
23
24 33. (milk and (cow or goat or sheep)).mp. [mp=title, abstract, original title, name of substance
25 word, subject heading word, keyword heading word, protocol supplementary concept word, rare
26 disease supplementary concept word, unique identifier]
27
28 34. yogurt.mp. or Yogurt/
29
30 35. cheese.mp. or Cheese/
31
32
33 36. custard.mp.
34
35
36 37. (milk and (skim or full fat or low fat)).mp. [mp=title, abstract, original title, name of
37 substance word, subject heading word, keyword heading word, protocol supplementary concept
38 word, rare disease supplementary concept word, unique identifier]
39
40 38. (yogurt and (skim or full fat or low fat)).mp. [mp=title, abstract, original title, name of
41 substance word, subject heading word, keyword heading word, protocol supplementary concept
42 word, rare disease supplementary concept word, unique identifier]
43
44 39. Milk/
45
46
47 40. 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or
48 39
49
50 41. cardiovascular disease.mp. or exp Cardiovascular Diseases/
51
52
53 42. coronary*.tw.
54
55
56
57
58
59
60

- 1
- 2
- 3 43. heart*.tw.
- 4
- 5 44. cardia*.tw.
- 6
- 7 45. cardio*.tw.
- 8
- 9 46. myocard*.tw.
- 10
- 11 47. isch?em*.tw.
- 12
- 13 48. angina*.tw.
- 14
- 15 49. ventric*.tw.
- 16
- 17 50. tachycardi*.tw.
- 18
- 19 51. pericard*.tw.
- 20
- 21 52. endocardi*.tw.
- 22
- 23 53. atrial fibrillat*.tw.
- 24
- 25 54. arrhythmi*.tw.
- 26
- 27 55. athero*.tw.
- 28
- 29 56. arterio*.tw.
- 30
- 31 57. exp Atherosclerosis/
- 32
- 33 58. exp Arteriosclerosis/
- 34
- 35 59. HDL.tw.
- 36
- 37 60. LDL.tw.
- 38
- 39 61. VLDL.tw.
- 40
- 41 62. lipid*.tw.
- 42
- 43 63. lipoprotein*.tw.
- 44
- 45 64. triacylglycerol*.tw.
- 46
- 47 65. exp Hyperlipidemias/
- 48
- 49 66. hyperlipid*.tw.
- 50
- 51 67. hypercholesterol*.tw.
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

- 1
- 2
- 3 68. hypercholester?emia*.tw.
- 4
- 5 69. hypertriglycerid?emia*.tw.
- 6
- 7 70. exp Cholesterol/
- 8
- 9 71. cholesterol*.tw.
- 10
- 11 72. exp Stroke/
- 12
- 13 73. stroke*.tw.
- 14
- 15 74. CVA.tw.
- 16
- 17 75. cerebrovasc*.tw.
- 18
- 19 76. "vascular accident".tw.
- 20
- 21 77. TIA.tw.
- 22
- 23 78. cerebral vascular.tw.
- 24
- 25 79. thrombo*.tw.
- 26
- 27 80. emboli*.tw.
- 28
- 29 81. apoplexy.tw.
- 30
- 31 82. (brain adj2 accident*).tw.
- 32
- 33 83. ((brain* or cerebral or lacunar) adj2 infarct*).tw.
- 34
- 35 84. Hypertension/
- 36
- 37 85. exp Blood Pressure/
- 38
- 39 86. hypertensi*.tw.
- 40
- 41 87. blood pressure*.tw.
- 42
- 43 88. systolic blood pressure.tw.
- 44
- 45 89. diastolic blood pressure.tw.
- 46
- 47 90. peripheral arter* disease*.tw.
- 48
- 49 91. (coronar\$ adj5 (bypas\$ or graft\$ or disease\$ or event\$)).tw.
- 50
- 51 92. (cerebrovasc\$ or cardiovasc\$ or mortal\$ or angina\$ or stroke or strokes).tw.
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

1
2
3 93. (myocardi\$ adj5 (infarct\$ or revascular\$ or ischaemi\$ or ischemi\$)).tw.
4

5 94. (morbid\$ adj5 (heart\$ or coronar\$ or ischaem\$ or ischem\$ or myocard\$)).tw.
6

7 95. (vascular\$ adj5 (peripheral\$ or disease\$ or complication\$)).tw.
8

9 96. (heart\$ adj5 (disease\$ or attack\$ or bypass\$)).tw.
10

11 97. 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or
12 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73
13 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or
14 90 or 91 or 92 or 93 or 94 or 95 or 96
15
16

17 98. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or
18 19 or 20 or 21 or 22
19
20

21 99. 40 and 97 and 98
22

23 100. limit 99 to yr="2000 - 2019"
24

25 101. limit 100 to humans
26

27 102. limit 101 to "all adult (19 plus years)"
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary File 3. List of confounders

Outcome	Confounders	Confounders (all outcomes)
1. CVD mortality	Fibre supplement (p) Red Meat (h) Sodium (Na+) (h)	Age Sex BMI
2. CVD events	Fibre supplement (p) Magnesium supplement (p)	Smoking Alcohol intake
3. CHD mortality (incident CVD)	Fibre supplement (p) Trans Fat (h) Polyunsaturated fat (n-6) (p) Sodium (+Na) (h)	History of co-morbidities Parenteral/Fhx MI < 60 yrs PA levels SES
4. CHD events (incident CHD)	Fibre supplement (p) Trans fat (h) Magnesium supplement (p) Polyunsaturated fat (n-6) (p)	Total energy intake Fruit & Vegetable intake <i>Specialised Confounders</i>
5. Total MI	Aspirin (p) Vitamin E supplement (p)	Hormone therapy
6. Fatal MI	Vitamin E supplement (p)	
7. Non-fatal MI	Aspirin (p)	
8. Total stroke	Potassium supplement (p) Red Meat (h) Sodium (+Na) (h)	
9. Ischemic stroke	Aspirin (p) Polyunsaturated fat (LC n-3) (p) Red meat (h)	
10. Haemorrhagic stroke	Aspirin (h)	
11. Systolic BP	Magnesium supplement (p) Sodium (-Na) (p) Polyunsaturated fat (supplement) (LC n-3) (p) Potassium supplement (p)	
12. Diastolic BP	Magnesium supplement (p) Sodium (-Na) (p) Polyunsaturated fat (supplement) (LC n-3) (p) Potassium supplement (p)	

p = protective, h = harmful

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

a) Not Confounders (inconclusive evidence)

Outcome	Not a confounder (inconclusive)
1. CVD mortality	Aspirin Dietary Saturated Fat Folate supplement Monounsaturated Fat Multivitamin Polyunsaturated Fat Total Dietary Fat Vitamin E supplement
2. CVD events	Folate supplement Monounsaturated Fat Multivitamin Polyunsaturated Fat Sodium Total Dietary Fat Vitamin E supplement
3. CHD mortality	Dietary Saturated Fat Magnesium supplement
4. CHD events	Dietary Saturated Fat Sodium Red Meat
5. Total MI	Dietary Saturated Fat Folate supplement Magnesium supplement Multivitamin Polyunsaturated Fat Total Dietary Fat
6. Fatal MI	Folate supplement Multivitamin
7. Non-fatal MI	Dietary Saturated Fat Folate supplement Multivitamin Polyunsaturated Fat Total Dietary Fat Vitamin E supplement

1		
2		
3		
4		
5		
6		
7		
8		
9		
10	8. Total stroke	Aspirin Dietary Saturated Fat Folate supplement Monounsaturated Fat Multivitamin Polyunsaturated Fat Total Dietary Fat Vitamin E supplement
11	9. Ischemic stroke	Dietary Saturated Fat Trans Fat
12		
13	10. Haemorrhagic stroke	Polyunsaturated Fat Red Meat
14		
15	11. Systolic BP	Polyunsaturated Fat (dietary)
16	12. Diastolic BP	Polyunsaturated Fat (dietary)
17		
18		
19		
20		
21		
22		
23		
24		
25		
26		
27		
28		
29		
30		
31		
32		
33		
34		
35		
36		
37		
38		
39		
40		
41		
42		
43		
44		
45		
46		

Supplementary file 4: List of excluded studies and reasons for exclusion

Author	Title	Reason for Exclusion
Akbaraly, T 2013 ¹	Does overall diet in midlife predict future aging phenotypes? A cohort study	Dietary patterns only were assessed, not dairy foods
Anderson, LA 2011 ²	Dietary Patterns and Survival of Older Adults	No relevant outcomes were measured
Baylin, A 2003 ³	High 18:2 trans-fatty acids in adipose tissue are associated with increased risk of nonfatal acute myocardial infarction in Costa Rican adults	Effects of dairy foods not measured
Beydoun, MA 2018 ⁴	Dairy product consumption and its association with metabolic disturbance in a prospective study of urban adults	Groups exposed to dairy not clearly defined
Biong, AS 2006 ⁵	Intake of milk fat, reflected in adipose tissue fatty acids and risk of myocardial infarction: a case-control study	Effects of dairy foods not measured
Chen, y 2013 ⁶	Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh	Dietary patterns only were assessed, not dairy foods
Ding, M 2017 ⁷	Dairy consumption, systolic blood pressure, and risk of hypertension: Mendelian randomization study	Not an observational design study
Eguchi, E 2012 ⁸	Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study	Dietary patterns only were assessed, not dairy foods
Geleijnse, JM 2017 ⁹	Dietary Patterns in Relation to Cardiovascular Disease Incidence and Risk Markers in a Middle-Aged British Male Population: Data from the Caerphilly Prospective Study	Dietary patterns only were assessed, not dairy foods
Goldbohm, RA 2011 ¹⁰	Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in the Netherlands	No combined outcome data
Julián-Almárcegui, C 2016 ¹¹	Association of heart rate and blood pressure among European adolescents with usual food consumption: The HELENA study	Participants were adolescents, not adults
Larsson, SC 2018 ¹²	Dietary patterns, food groups, and incidence of aortic valve stenosis: A prospective cohort study	Dietary patterns only were assessed, not dairy foods
Lupton, BS 2003 ¹³	The Finnmark Intervention Study: is it possible to change CVD risk factors by community-based intervention in an Arctic village in crisis?	No combined outcome data
Meyer, J 2011 ¹⁴	Dietary patterns, subclinical inflammation, incident coronary heart disease and mortality	Dietary patterns only were assessed, not dairy foods

	in middle-aged men from the MONICA/KORA Augsburg cohort study	
Michaelsson, K 2013 ¹⁵	Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study	Dietary calcium only was assessed, not dairy foods
Oomen, CM 2000 ¹⁶	Arginine intake and risk of coronary heart disease mortality in elderly men	Effects of dairy foods not measured
Paillard, F 2015 ¹⁷	Cardiovascular risk and lifestyle habits of consumers of a phytosterol-enriched yogurt in a real-life setting	Yogurt was enriched with phytosterols
Praagman, J 2016 ¹⁸	The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort	Effects of dairy foods not measured
Streppel, MT 2014 ¹⁹	Nutrient-rich foods, cardiovascular diseases and all-cause mortality: the Rotterdam study	Dietary patterns only were assessed, not dairy foods
Umesawa, M 2006 ²⁰	Dietary intake of calcium in relation to mortality from cardiovascular disease: the JACC Study	No combined outcome data
van der Pols, J C 2009 ²¹	Childhood dairy and calcium intake and cardiovascular mortality in adulthood: 65-year follow-up of the Boyd Orr cohort	Participants were children, not adults
Warensjo, E 2009 ²²	Stroke and plasma markers of milk fat intake – a prospective nested case-control study	Effects of dairy foods not measured
Warensjo, E 2009 ²³	Milk Fat Biomarkers and the Risk of a First Ever Acute Myocardial Infarction - A Prospective Nested Case-Control Study. <i>Journal of the American Dietetic Association</i> . 2009;1	Poster presentation only, full study not available
Warensjo, E 2010 ²⁴	Biomarkers of milk fat and the risk of myocardial infarction in men and women: a prospective, matched case-control study	No combined outcome data

1. Akbaraly T, Sabia S, Hagger-Johnson G, et al. Does overall diet in midlife predict future aging phenotypes? A cohort study. *The American journal of medicine*. 2013;126(5):411-419.e413.
2. Anderson AL, Harris TB, Tylavsky FA, et al. Dietary Patterns and Survival of Older Adults. *Journal of the American Dietetic Association*. 2011;111(1):84-91.
3. Baylin A, Kabagambe EK, Ascherio A, et al. 18:2 trans-fatty acids in adipose tissue are associated with increased risk of nonfatal acute myocardial infarction in costa rican adults. *Journal of Nutrition*. 2003;133(4):1186-1191.
4. Beydoun MA, Fanelli-Kuczmarski MT, Beydoun HA, et al. Dairy product consumption and its association with metabolic disturbance in a prospective study of urban adults. *British Journal of Nutrition*. 2018;119(6):706-719.

5. Biong AS, Veierod MB, Ringstad J, et al. Intake of milk fat, reflected in adipose tissue fatty acids and risk of myocardial infarction: a case-control study. *European Journal of Clinical Nutrition*. 2006;60(2):236-244.
6. Chen Y, McClintock TR, Segers S, et al. Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh. *International Journal of Cardiology*. 2013;167(4):1495-1501.
7. Ding M, Huang T, Bergholdt HK, et al. Dairy consumption, systolic blood pressure, and risk of hypertension: Mendelian randomization study. *Bmj*. 2017;356:j1000.
8. Eguchi E, Iso H, Tanabe N, et al. Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study. *European heart journal*. 2012;33(4):467-477.
9. Geleijnse JM, Mertens E, Markey O, et al. Dietary Patterns in Relation to Cardiovascular Disease Incidence and Risk Markers in a Middle-Aged British Male Population: Data from the Caerphilly Prospective Study. *Nutrients*. 2017;9(1):75.
10. Goldbohm RA, Chorus AMJ, Galindo Garre F, et al. Dairy consumption and 10-y total and cardiovascular mortality: a prospective cohort study in the Netherlands. *American Journal of Clinical Nutrition*. 2011;93(3):615-627 613p.
11. Julián-Almárcegui C, Vandevijvere S, Gottrand F, et al. Association of heart rate and blood pressure among European adolescents with usual food consumption: The HELENA study. *Nutrition, Metabolism & Cardiovascular Diseases*. 2016;26(6):541-548.
12. Larsson SC, Wolk A, Bäck M. Dietary patterns, food groups, and incidence of aortic valve stenosis: A prospective cohort study. *International Journal of Cardiology*. 2018.
13. Lupton BS, Fonnebo V, Sogaard AJ, et al. The Finnmark Intervention Study: is it possible to change CVD risk factors by community-based intervention in an Arctic village in crisis? *Scandinavian Journal of Public Health*. 2003;31(3):178-186.
14. Meyer J, Doring A, Herder C, et al. Dietary patterns, subclinical inflammation, incident coronary heart disease and mortality in middle-aged men from the MONICA/KORA Augsburg cohort study. *European journal of clinical nutrition*. 2011;65(7):800-807.
15. Michaelsson K, Melhus H, Warensjo E, et al. Long term calcium intake and rates of all cause and cardiovascular mortality: community based prospective longitudinal cohort study. *Bmj*. 2013;346:f228.
16. Oomen CM, van Erk MJ, Feskens EJ, et al. Arginine intake and risk of coronary heart disease mortality in elderly men. *Arteriosclerosis, thrombosis, and vascular biology*. 2000;20(9):2134-2139.
17. Paillard F, Bruckert E, Naelten G, et al. Cardiovascular risk and lifestyle habits of consumers of a phytosterol-enriched yogurt in a real-life setting. *Journal of Human Nutrition & Dietetics*. 2015;28(3):226-235 210p.
18. Praagman J, Beulens JW, Alsema M, et al. The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort. *American Journal of Clinical Nutrition*. 2016;103(2):356-365.
19. Streppel MT, Sluik D, van Yperen JF, et al. Nutrient-rich foods, cardiovascular diseases and all-cause mortality: the Rotterdam study. *European journal of clinical nutrition*. 2014;68(6):741-747.
20. Umesawa M, Iso H, Date C, et al. Dietary intake of calcium in relation to mortality from cardiovascular disease: the JACC Study. *Stroke*. 2006;37(1):20-26.
21. van der Pols JC, Gunnell D, Williams GM, et al. Childhood dairy and calcium intake and cardiovascular mortality in adulthood: 65-year follow-up of the Boyd Orr cohort. *Heart*. 2009;95(19):1600-1606.
22. Warensjo E, Smedman A, Stegmayr B, et al. Stroke and plasma markers of milk fat intake--a prospective nested case-control study. *Nutrition Journal*. 2009;8:21.

- 1
2
3 23. Warensjo E, Sjogren P, Cederholm T, et al. Milk Fat Biomarkers and the Risk of a First Ever
4 Acute Myocardial Infarction - A Prospective Nested Case-Control Study. *Journal of the*
5 *American Dietetic Association*. 2009;109(9, Supplement):A51.
6 24. Warensjö E, Jansson JH, Cederholm T, et al. Biomarkers of milk fat and the risk of myocardial
7 infarction in men and women: a prospective, matched case-control study. *American Journal of*
8 *Clinical Nutrition*. 2010;92(1):194-202 199p.
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary file 5: Characteristics of included studies

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Verbatim)	Funding Source	Disclosed author conflicts of interest
Aerde, M 2013 ⁽¹⁾	Cohort	12.4 years	1,956 men & women	61.6 years	Total Dairy, 271 g/day per SD of the mean intake for Total dairy (all dairy products except butter)		Total CVD	Non-Industry ¹	Yes ^a
Al-Delaimy, WK 2003 ⁽²⁾	Cohort	12 years	39,800 men	40-75 years	Dairy Calcium Q5, 819 mg/day (median) (dairy calcium intake summed the calcium intake from whole milk, skim or low-fat milk, yogurt, ice cream, cottage cheese, and other cheese was summed)	Q1, 106 mg/day	Total Ischemic Heart Disease	Non Industry ²	No ^b
Alonso A, 2005 ⁽³⁾	Cohort	27 months	5,880 men & women	37 years	Dairy Q 5, 798.8 g/day (whole-fat milk, partially skim milk, skim milk, condensed milk, whipped cream, yogurt, skim yogurt, milk-shake, cottage cheese or junket, petit Suisse cheese, spreadable cheese wedges, soft unripened cheese, other cheese, custard, and ice cream)	Q 1, 155.6 g/day	Hypertension	Non-industry ³	No ^c

36/bmjopen-2020-039033 Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Altorf-van der Kuil, W2012 ⁽⁴⁾	Cohort	Mean follow up 7.5 years	3,588 men & women	44 years	Dairy Protein T3, ≥ 27 g/day (dairy protein was calculated as protein from milk, yogurt, coffee creamer, curd, pudding, porridge, custard, whipped cream and cheese)	T1, ≤ 19 g/day	Hypertension	Industry ⁴	Yes ^d
Avalos, EE 2013 ⁽⁵⁾	Cohort	Mean follow up 16.2 years	1,759 men & women	70.6 years men, 70.1 women	Whole Milk, Non-Fat Milk, Yogurt & Cheese, Sometimes/often (included daily, 4–6 times/week, 1–3 times/week and 1–3 times/months)	Rarely/never (included never & 1–11 times/year)	Incident CHD	Non-industry ⁵	No ^e
Bernstein, AM 2012 ⁽⁶⁾	2 Cohorts	26 and 22 years of follow-up in women and men, respectively	127,160 (43 150 men 84 010 women)	Men 40 to 75 years, Woman 30 to 55 years	Whole Fat Q 5, Men 2.55 servings/day, Woman 2.81 servings/day (whole milk, ice cream, hard cheese, full fat cheese, cream, sour cream, cream cheese, butter) Low Fat Q5, Men 2.64 servings/day, Women 2.20 servings/day (skim/low-fat milk, 1% and 2% milk, yogurt, cottage and ricotta cheeses, low-fat cheese, sherbet)	Q 1, Men 0.21 servings/day, Woman 0.34 servings/day. Low Fat Q1, Men 0.11 servings/day, Women 0.07 servings/day	Total Stroke	Non-industry ⁶	Yes ^f
Biong, A 2008 ⁽⁷⁾	Case Control		218 men & women	62.4 years	Dairy Fat, > 34.1 g/day	<14.6 g/day	First Myocardial Infarction	Industry ⁷	Yes ^g

36/bmjopen-2020-039132 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Bonthuis, M 2010 ⁽⁸⁾	Cohort	Mean 14.4 years	1,529 men & women	25–78 years	Total Dairy T3, 599 g/day (median) ('low-fat dairy products was computed by adding daily servings (in grams) of skim milk, low-fat milk, low-fat yoghurt, cottage or ricotta cheese, whereas the food group 'high-fat/unmodified dairy' included whole milk, cream, ice cream, yoghurt, full-fat cheese and custard. Total dairy intake was the sum of intake of all these dairy foods)	T1, 174 g/day	Cardiovascular Disease Mortality	Non-Industry ⁸	No ^h
Buendia, JR 2018 ⁽⁹⁾	3 Cohorts	30 years of follow-up in NHS, 20 years in NHS II, 24 years in the HPFS	NHS (N=69298), NHS II (N=84368), HPFS (N=30512)	Mean baseline ages in the 3 cohorts were 44.6, 35.8, and 50.7 years, respectively	Total Dairy Q4, 3 - <6 servings/day (total dairy intake included: milk (skim, low-fat, whole), ice cream, sherbet/ frozen yogurt, cheese (cottage, ricotta, hard, sliced), and yogurt (all types)	Q1, <0.5 servings/day	High Blood Pressure	Industry ⁹	No ⁱ
Chen, M 2016 ⁽¹⁰⁾	3 Cohorts	24 years in the HPFS, 32 years NHS, 20 years in NHS II	222,234 - 43,652 men HPFS, 87,907 women NHS, 90,675 women NHS II	40–75 years HPFS, 30–55 years NHS, 25–42 y NHS II	Dairy Fat, Q5	Q1	CHD	Non-Industry ¹⁰	No ^j

36/bmjopen-2020-039136 on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Dalmeijer,G 2013 ⁽¹¹⁾	Cohort	13 years	33,625 men & women	49.0 years	Total dairy and its subtypes were evaluated as continuous variables per standard deviation of the mean intake which is 265 g/d for total dairy (total dairy included all dairy food products except for butter and ice cream. Milk and milk products included all kinds of milk, yogurt, coffee creamers, curd, pudding, porridge, custard, and whipping cream)		Incident of Coronary Heart Disease & Incident Stroke	Non-Industry ¹¹	Yes ^k
Dauchet, L 2007 ⁽¹²⁾	Cohort	5.4 years	2,341 men & women	Men 52.7 years, Women 46.9 years	Dairy Q4, 456 g/day (dairy products including milk, cheese, yogurt, and other dairy products)	Q1, 84 g/day	Systolic & Diastolic Blood Pressure	Non-Industry ¹²	No ^l

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

36/bmjopen-2020-039136 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Study ID	Study Deign	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Dehghan, M 2018 ⁽¹³⁾	Cohort	9.1 yrs	136,384 men & women	50-1 years	Dairy Q4, >2 servings/day (median) (dairy comprised milk, yoghurt, various types of cheese, yoghurt drink, and mixed dishes prepared with dairy. Mixed dishes prepared with dairy were dis- aggregated into their constituents and a proportional weight was assigned to each component. Then each component was included in the related dairy group.	Q1, 0 servings/day	Cardiovascular Mortality or Major Events	Industry ¹³	No ^m
Elwood, PC 2004 ⁽¹⁴⁾	Cohort	20-24 years	2,403 men	45-59 years	Milk Q4, >1 pint per day	Q1, None	ascular Event	Non-Industry ¹⁴	No disclosure

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (verbatim)	Funding Source	Disclosed author conflicts of interest
Engberink, MF 2009 ⁽¹⁵⁾	Cohort	6 years	2,245 men & women	>55 years	Dairy Q4, 691 g/day (i.e. 4.5 servings/day) (median intake) (calculated total dairy intake by summing the intake of individual dairy items, except butter and ice cream. The category "milk and milk products" included all kinds of milk, yogurt, coffee creamer, curd, pudding, porridge, custard, and whipped cream. The category "cheese" included all kinds of cheese products, ie, soft cheese, hard cheese, and cheese spreads)	Q1, 164 g/day (i.e. 1 serving/day) (median intake)	Hypertension	No disclosure	No ^a
Farvid, MS 2017 ⁽¹⁶⁾	Cohort	8 years	42,403 men & women	51.6 years	Total Dairy Q5, 2.4 servings/day (median) (total dairy product items listed in the food frequency questionnaire included milk, cheese, yogurt, liquid yogurt (doogh), dried yogurt paste (kashk), and cream)	Q1, 0.4 servings/day (median)	Cardiovascular Disease Mortality	Non-Industry ¹⁵	No ^o
Haring, B 2014 ⁽¹⁷⁾	Cohort	22 years (median)	12,066 men & women	45-64 years	Dairy Protein Q5, 2.9 servings/day	Q1, 0.1 median servings/day	Coronary Heart Disease	Non-Industry ¹⁶	No ^p
He, K 2003 ⁽¹⁸⁾	Cohort	14 years	43,732 men	40-75 years	High Fat Dairy Q5, ≥1/day	Q1, <1/week	Ischaemic & Haemorrhagic Stroke	Non-Industry ¹⁷	No ^q

36/bmjopen-2020-039136 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> by guest. Protected by copyright.

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Heraclides, A 2012 ⁽¹⁹⁾	Cohort	10 years	1,750 men & women	Men 43 years, Women 53 years	Total Dairy T3, 309.0 g/day (median) (full-fat milk; semi-skimmed milk; skimmed milk; milk-containing beverages (full fat, semi-skimmed and skimmed); full-fat cheese; low-fat cheese; full-fat yoghurt; low-fat yoghurt; fruit-flavoured yoghurt (full fat and low fat); and milk-based puddings)	T1, 224.1 g/day	Incident Hypertension	Non-Industry ¹⁸	Yes ^r
Johansson, I 2018 ⁽²⁰⁾	Cohort	8-12 years	27,682 men & women	29-65 years	Dairy Q 5, 7.1 servings/day (median)	Q1, 1.6 servings/day (median)	Blood Pressure	Non-Industry ¹⁹	No ^s
Johansson, I 2019 ⁽²¹⁾	Cohort	14.2 years	108,065 men & women	calculated mean = 52.5 years *	High Fat & Low Fat Non-Fermented Milk & Cheese Q 4, high dose	Q1, low dose	Myocardial Infarction & Stroke	Non-Industry ²⁰	No ^t
Kim, D 2017 ⁽²²⁾	Cohort	67-4 months	4,335 men & women	40-69 years	Total Dairy Q 5, >7 servings/week	Q 1, <1 servings/week	Blood Pressure	Non-Industry ²¹	No ^u
Larsson,S 2009 ⁽²³⁾	Cohort	13.6 years	26,556 men	50-69 years	Dairy Q5, 1295.6 g/day (median) (including low-fat milk, whole milk, sour milk, yogurt, cheese, cream, ice cream, and butter)	Q1 286.5 g/day	Cerebral Infarction, Intracerebral Haemorrhage, Subarachnoid Haemorrhage	Non-Industry ²²	No disclosure

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (verbatim)	Funding Source	Disclosed author conflicts of interest
Larsson, SC 2012 ⁽²⁴⁾	Cohort	10.2 years	74,961 men & women	45-83 years	Dairy Q5, 9.3 servings/day (median) (dairy foods included low-fat milk (0.5% fat), medium-fat milk (1.5% fat), full-fat milk (3% fat), milk in pancakes, low-fat sour milk/yogurt (0.5% fat), full-fat sour milk/yogurt (3% fat), cottage cheese (4% fat), low-fat cheese (10%-17% fat), full-fat cheese (approximately 28% fat), ice cream, cream, and creme fraiche)	Q1, 2.3 servings/day	Total Stroke	Non-Industry ²³	No ^v
Li, K 2012 ⁽²⁵⁾	Cohort	11 years	23,980 men & women	35-64 years	Dairy Calcium Q4, 780 mg/day	Q1, 188 mg/day	CVD Mortality	Non-Industry ²⁴	No ^w
Lin, PH 2013 ⁽²⁶⁾	Cohort	12 years	2,061 men & women	45.8 years (no information for stroke group)	Dairy T3, (dairy milk of any kind, cheese, yogurt).	T1	Total Stroke	Non-Industry ²⁵	No ^x
Lockheart, MSK 2007 ⁽²⁷⁾	Case Control		211 men & women	62.5 years cases and 62.2 years controls	Low Fat Dairy T3, 618 g/day (Low-fat milk, skimmed milk, light sour cream)	T 1, 48 g/day	First Myocardial Infarction	Industry ²⁶	No disclosure
Louie, JCY 2013 ⁽²⁸⁾	Cohort	15 years	2,625 men & women	49-97 years	Total Dairy T3, 2.9 servings/day (median) (included all dairy foods)	T1, 0.6 servings/day	Total CVD	Industry ²⁷	No disclosure
Mazidi, M, 2018 ⁽²⁹⁾	Cohort	76.4 months	24,474 men & women	47.6 years	Total Dairy Q4, 3.08 cup equivalent servings/day (total dairy, milk, cheese, and yogurt)	Q1, 0.25 cup equivalent servings/day	CHD Mortality Cerebrovascular Disease mortality	Non-Industry ²⁸	No ^y

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Ness, AR 2001 ⁽³⁰⁾	Cohort	25 years	5,765 men	35-64 years	Milk T3, > 1 pint (= 0.568 liters)	T1, None	Cardiovascular Disease Deaths	Non-Industry ²⁹	No ^z
Nettleton, J 2008 ⁽³¹⁾	Cohort	13.3 years	14,153 men & women	45 to 64 years	High Fat Dairy, per 1 daily serving difference in food group intake		Ischemic Heart Failure	Non Industry ³⁰	No ^{aa}
Panagiotakos, D 2009 ⁽³²⁾	Cohort	5 years	3,042 men & women	18-89 years	Low Fat Dairy, 1-unit increase in components' scores (0%, 2% or total fat), like cheese, yogurt, milk)		CVD Events	Non-Industry ³¹	No disclosure
Patterson, E 2013 ⁽³³⁾	Cohort	11.6 years	33,636 women	48-83 years	Total Dairy, Q5 8.4 servings/day (median) (total dairy intake was the sum of milk [full-fat ($\geq 3.0\%$ fat), semi-skimmed ($\leq 1.5\%$ fat), skimmed (0.5% fat), and pancakes], cultured milk/yogurt [full-fat ($\geq 3.0\%$ fat) and low-fat ($\leq 1.5\%$ fat)], cheese [full-fat ($> 17\%$ fat), low-fat ($\leq 17\%$ fat), and cottage cheese/ quark], cream and creme fariche (full fat and low fat) intakes)	Q1, 2.2 servings/day	Myocardial Infarction	Non Industry ³²	No ^{bb}
Praagman, J 2015 (a) ⁽³⁴⁾	Cohort	13.3 years (median)	4,235 men & women	66.9 years	Total Dairy, T3 >400g/day (total dairy included milk, buttermilk, yogurt, coffee creamer, curd, pudding, porridge, custard, whipped cream, ice cream, and cheese, but not butter)	Total Dairy, T 1 <200 g/day	Fatal Stroke & Fatal CHD	Industry ³³	Yes ^{cc}

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Praagman, J 2015 (b) ⁽³⁵⁾	Cohort	15 years	34,409 men & women	Men 51 years & women 43 years	Total Yogurt & Cheese Q4, (fermented dairy foods)	Q1	CVD Mortality	Non-Industry ³⁴	Yes ^{dd}
Sauvaget, C 2003 ⁽³⁶⁾	Cohort	16 years	37,130 men & women	56 years	Dairy Q4, Almost Daily (dairy products (butter and cheese, excluding margarine))	Q1, Never	Total Stroke	Non-Industry ³⁵	No disclosure
Snijder, MB 2008 ⁽³⁷⁾	Cohort	6.4 years	1,124 men & women	50-75 years	Dairy Q4, 5.75-17.24 servings/day (range) (total dairy consumption was categorized as low-fat dairy ($\leq 2\%$ fat) or high-fat dairy ($> 2\%$ fat). The variable dairy desserts included yoghurt, curds, and custard. The variable milk included low-fat, skim, and, whole milk. The variable yoghurt included all low-fat, skim, and whole yoghurts)	Q1 0-2.97 servings/day (range)	Systolic & Diastolic Blood Pressure	Industry ³⁶	Yes ^{ee}
Soedamah-Muthu, SS 2013 ⁽³⁸⁾	Cohort	10.8 years	4,255 men & women	56 years	Dairy, T3 575 g/day (median) (all dairy products, except butter and ice cream)	T1, 246 g/day (median)	Fatal & Non-Fatal CHD	Non-Industry ³⁷	Yes ^{ff}
Steffen, LM 2005 ⁽³⁹⁾	Cohort	15 years	4,304 men & women	18-30 years	Dairy Foods Q5, > 3.4 times/day (dairy foods, including milk, cheese, yogurt, and dairy desserts)	Q1, < 1.1 times/day	Blood Pressure	Non-Industry ³⁸	No ^{gg}

Study ID	Study Design	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or 'yes' to dairy foods)	Comparison (lowest tertile/quartile/quintile or 'no' to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Tavani, A 2002 ⁽⁴⁰⁾	Case Control		985 men & women	61 years (median)	Total milk >7 cups/week, Yogurt >= 7 portions/week, Cheese >=350g/week	Total milk 0 cups/week, Yogurt 0 portions/week, Cheese <200g/week	Acute Myocardial Infarction	Non-Industry ³⁹	No ^{hh}
Um, C 2017 ⁽⁴¹⁾	Cohort	5.7 years of follow-up	21,427 men & women	calculated mean = 64.8 years**	Total Dairy Q5, 17.8 servings/day (dairy products (milk, cream, fermented dairy products, ice cream, butter, cheeses))	Q1, 0.9 servings/day	CVD Mortality	Non-Industry ⁴⁰	No ⁱⁱ
Umesawa, M, 2008 ⁽⁴²⁾	Cohort	12.9-year follow-up	41,526 men & women	40-59 years	Dairy Calcium, Q5, 116 mg/day (median) (to calculate dairy calcium intake, we specified 2 kinds of dairy products, ie, cheese and dairy products except cheese, for the baseline questionnaire, and 4 kinds, ie, whole milk, low fat milk, cheese, and yogurt, for the 5-year follow-up questionnaire)	Q1, 0 mg/day	Total Stroke & CHD	Non-Industry ⁴¹	No ^{jj}

Study ID	Study Deign	Length of Intervention /Follow up	Number of Participants	Age (mean years)	Exposure (highest tertile/quartile/quintile or ‘yes’ to dairy foods)	Comparison (lowest tertile/quartile/quintile or ‘no’ to dairy foods)	Outcomes Measured (Perbatim)	Funding Source	Disclosed author conflicts of interest
Wang,L 2008 ⁽⁴³⁾	Cohort	10 years	28,886 women	53.8 years	Total Dairy Q5, 3.69 servings/day (median) (total dairy product intake was calculated by summing the intake of individual dairy items: low-fat dairy items include skim or low-fat milk, sherbet, yogurt, and cottage/ricotta cheese, high-fat dairy items include whole milk, cream, sour cream, ice cream, cream cheese, and other cheese)	Q1, 0.56 servings/day (median)	Hypertension	Non-Industry ⁴²	No ^{kk}

* We calculated the mean age score of participants by summing Non-cases, T2D, MI and stroke cases at baseline and dividing them by 4

**We calculated the mean age score of participants by summing all quintiles 1, 3, & 5 (they were the only ones available) at baseline and dividing them by 5

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Description of Funding Source (Verbatim)

1. The Hoorn Study has been made possible by the Vrije Universiteit Amsterdam and the VU University Medical Center, and by grants from the Dutch Diabetes Research Foundation, the Dutch Organization for Scientific Research, the Netherlands Heart Foundation, and the Health Research and Development Council of the Netherlands.
2. Supported by research grants HL24074, HL34594, DK36798, and CA87969 from the National Institutes of Health.
3. Supported by the Spanish Ministry of Health (grants PI040233 and G03-140), the Navarra Regional Government (141-2005), and the University of Navarra (línea especial Nutricio LE-97). AA was supported partially by a Fulbright fellowship and an MMA Foundation grant.
4. The Doetinchem Cohort Study was financially supported by the Ministry of Health, Welfare and Sport of the Netherlands and the National Institute for Public Health and the Environment. For the present analysis, Wageningen University was supported by the Top Institute Food and Nutrition, which is a public/private partnership that generates vision on scientific breakthroughs in food and nutrition, resulting in the development of innovative products and technologies. Partners are major Dutch Food companies and research organisations.
5. The study was supported by grants AG007181 and AG028507 from the National Institutes of Health/National Institute on Aging, and by grant DK31801 from the National Institute of Diabetes and Digestive and Kidney Diseases.
6. This study was supported by grant P01CA087969 from the National Institutes of Health, Department of Health and Human Services. A.M.B. was supported through the Harvard Human Nutrition Program.
7. The study was supported financially by the Research Council of Norway, Throne Holst's Foundation for Nutrition Research, The Norwegian Association of Margarine Producers, DeNoFa Fabrikker A/S and Tine BA. Tine BA is a dairy company.
8. This study was supported by the National Health and Medical Research Council of Australia.
9. Funding sources: The Nurses' Health Study and Health Professionals Follow-up Study cohorts are supported by grants UM1 CA186107, UM1 CA176726, and UM1 CA167552 from the National Institutes of Health. The current analyses were supported by small grants from the National Dairy Council, the General Mills Bell Institute for Health and Nutrition, and the Boston Nutrition and Obesity Research Center.
10. Supported by the NIH (grants R01 HL034594, UM1 CA176726, UM1 CA186107, R01 HL35464, R01 HL088521, R01 CA67262, HL60712, and UM1 CA167552).
11. This research was supported by a personal Dr. Dekker postdoctoral grant (2008T062) from The Netherlands Heart Foundation (JWJ Beulens).
12. The SU.VI.MAX study is supported by the Direction Générale de la Santé, the Ministère de la Santé, and the Institut Virtuel de Recherche en Santé Publique (groupe cohorte) INSERM.
13. The PURE Study is an investigator-initiated study that is funded by the Population Health Research Institute, the Canadian Institutes of Health Research (CIHR), Heart and Stroke Foundation of Ontario, support from CIHR's Strategy for Patient Oriented Research (SPOR) through the Ontario SPOR Support Unit, as well as the Ontario Ministry of Health and Long-Term Care and through unrestricted grants from several pharmaceutical companies, with major contributions from AstraZeneca (Canada), Sanofi-Aventis (France and Canada), Boehringer Ingelheim (Germany and Canada), Servier, and GlaxoSmithKline, and additional contributions from Novartis and King Pharma and from various

- national or local organisations in participating countries. These include Brazil: Unilever Health Institute, Brazil; South Africa: The SA Sugar Association (SASA).
14. The Medical Research Council, the University of Wales College of Medicine and Bristol University, Food Standards Agency.
 15. This work was supported by Tehran University of Medical Sciences (grant 82-603); Cancer Research UK (grant C20/A5860); the Intramural Research Program of the National Cancer Institute, US National Institutes of Health (grant Z01 CP000185-03); and various collaborative research agreements with the International Agency for Research on Cancer. M.F. was supported by a Takemi Fellowship from the Japan Pharmaceutical Manufacturers Association.
 16. The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C).
 17. This work was supported by the research grant HL35464 and CA55075 from the National Institutes of Health.
 18. The study was funded by the Medical Research Council, and some aspects of the analysis were funded by The European Commission, Quality of Life and Management of Living Resources Programme, contract number QLGI-CT-2000-01643.
 19. The present study was supported by the Swedish Research Council for Health, Working Life and Welfare (FORTE).
 20. This research was funded by The Swedish Research Council for Health, Working Life and Welfare (FORTE), grant number 2016-00960. The Northern Sweden Diet Database has been supported by the Swedish Research Council for Health, Working Life and Welfare (FORTES) and The Swedish Research Council.
 21. This research was supported by the Basic Science Research Program of the National Research Foundation of Korea (NRF), funded by the Ministry of Education, Science, and Technology (NRF2016R1D1A1B03931307).
 22. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study was supported by Public Health Service contracts N01-CN-45165, N01-RC-45035 and N01-RC-37004 from the US National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Md. Dr. Larsson's research at the National Public Health Institute in Helsinki, Finland, was supported by a grant from the Swedish Council for Working Life and Social Research.
 23. This study was supported by a research grant from the Swedish Council for Working Life and Social Research (FA), the Swedish Research Council, and by a Research Fellow grant from Karolinska Institutet (to Dr Larsson).
 24. This work was supported by supported by the Deutsche Krebshilfe (grant-No70-488-Ha I) and the Graduiertenkolleg 793: Epidemiology of communicable and chronic non-communicable disease and their inter-relationships.
 25. Data collection was supported by the Department of Health in Taiwan.
 26. The present study was supported by NIH NRSA T32HL007779, CVD Epidemiology and Prevention, American Heart Association – Greater Midwest Affiliate, Throne Holst's Foundation for Nutrition Research, The Norwegian Association of Margarine Producers, DeNoFa Fabriker A/S and Tine Norwegian Dairies.
 27. This study was funded by Dairy Australia.

28. This manuscript was written independently; no company or institution supported it financially.
29. Funding: this study was provided with funding by a grant from the NHS Management Executive Cardiovascular Disease and Stroke Research and Development Initiative.
30. This research was supported by the National Institutes of Health grant HL73366, training grant T32 HL07779, and contracts N01-HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, and N01-HC-55022 from the National Heart, Lung, and Blood Institute.
31. The ATTICA study was supported by research grants from the Hellenic Cardiological Society (HCS2002).
32. Supported by research grants from the Swedish Council for Working Life and Social Research and from the Swedish Research Council/Infrastructure Medicine.
33. This study was supported by an unrestricted grant from the Dutch Dairy Organization (NZO) for epidemiological analyses on dairy intake and cardiovascular diseases.
34. The present study was supported by a personal Dr Dekker postdoctoral grant (2008T062) from the Netherlands Heart Foundation (J. W. J. B.).
35. This publication is based on research performed at the Radiation Effects Research Foundation (RERF), Hiroshima and Nagasaki, Japan. RERF is a private nonprofit foundation funded equally by the Japanese Ministry of Health, Labor and Welfare and the US Department of Energy through the National Academy of Sciences.
36. This particular study has been supported by a grant from the Dutch Dairy Association (NZO).
37. The Whitehall II study was supported by grants from the Medical Research Council (G0902037), the British Heart Foundation (RG/07/008/23674), the Stroke Association, the National Heart Lung and Blood Institute (5RO1 HL036310), the National Institute on Aging (5RO1AG13196) and the Agency for Health Care Policy Research (5RO1AG034454).
38. The CARDIA Study is supported by National Heart, Lung, and Blood Institute contracts N01-HC-48047, N01-HC-48048, N01-HC-48049, N01-HC-48050, and N01-HC-95095.
39. Funding: partly supported by the Italian Ministry of Health (Programmi Speciali).
40. The REGARDS research project is supported by a cooperative agreement U01 NS041588 from the National Institute of Neurological Disorders and Stroke, National Institutes of Health, Department of Health and Human Service. Additional support provided by the Franklin Foundation.
41. This study was supported by grants-in-aid for cancer research and by the Third Term Comprehensive Ten-Year Strategy for Cancer Control from the Ministry of Health, Labor and Welfare of Japan.
42. This work was supported by research grants CA-047988 and HL-080467 from the National Institutes of Health, Bethesda, Md.

Description of Author Disclosure Statement (Verbatim)

- 1
2
3 a) Sabita S. Soedamah-Muthu and Johanna M. Geleijnse obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out
4 meta-analyses on the association between dairy products and CVD.
5
6 b) None of the authors had any conflict of interest from a financial, personal, or professional aspect in relation to the findings of this study.
7
8 c) None of the authors had any conflicts of interest.
9
10 d) Altorf-van der Kuil W, Engberink MF, Geleijnse JM - Top Institute Food and Nutrition, PO Box 557, 6700 AN, Wageningen, The
11 Netherlands.
12
13 e) The authors have no conflicts of interest.
14
15 f) D.M. received research grants for studying the effects of diet on cardiometabolic diseases from the National Institutes of Health; the Searle
16 Scholar Award from the Searle Funds at The Chicago Community Trust; the Genes and Environment Initiative at the Harvard School of
17 Public Health; and the Gates Foundation/World Health Organization Global Burden of Diseases, Injuries, and Risk Factors Study; and from
18 GlaxoSmithKline, Sigma Tau, Pronova, and the National Institutes of Health for an investigator-initiated, not-for-profit clinical trial of fish oil
19 and postsurgical complications. He also received ad hoc travel reimbursement and/or honoraria for research presentations from the Chicago
20 Council, International Life Sciences Institute, Aramark, Unilever, PRIM, Nutrition Impact, Norwegian Seafood Export Council, United
21 Nations Food and Agricultural Organization, World Health Organization, US Food and Drug Administration, and several universities. He
22 received ad hoc consulting fees from Foodminds and royalties from UpToDate for an online chapter on fish oil.
23
24 g) A. S. Biong is employed as a Ph.D. student in a research project funded jointly by TINE BA, a Norwegian dairy company, and the Norwegian
25 Research Council.
26
27 h) The authors declare no conflict of interest.
28
29 i) There are no conflicts of interest.
30
31 j) None of the authors reported a conflict of interest related to the study.
32
33 k) SS-Mand MG obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out meta-analyses on the association between
34 dairy products and cardiovascular diseases.
35
36 l) None of the authors had any personal or financial conflicts of interest.
37
38 m) We declare no competing interests.
39
40 n) There were no conflicts of interest.
41
42 o) Conflict of interest: none declared
43
44 p) The authors have declared that no competing interests exist.
45
46 q) Competing interests: None declared.
47
48 r) SSM, JMG and AH and were supported by an unrestricted grant from the Dutch dairy industry (NZO).
49
50 s) The authors declare that they have no competing interests.
51
52 t) The authors declare no conflict of interest
53
54 u) The authors have no conflicts of interest to declare.

- 1
2
3 v) Disclosures: None.
4 w) Competing interests None.
5 x) AUTHOR DISCLOSURES None.
6 y) All authors have nothing to declare in relation to the subject of this paper.
7 z) Conflicts of interest: none.
8 aa) The authors have no conflicts of interest to report.
9 bb) Author disclosures: E. Patterson, S. C. Larsson, A. Wolk, and A. A kesson, no conflicts of interest.
10 cc) J.M.G and S.S.S.M received an unrestricted grant from the Dutch Dairy Organization (NZO) for epidemiological analyses on dairy intake and
11 cardiovascular diseases.
12 dd) S. S. S. M. received an unrestricted research grant from the Global Dairy Platform, Dairy Research Institute and Dairy Australia for a meta-
13 analysis project on the effect of cheese on lipids.
14 ee) Gerrit J. Hiddink - Dutch Dairy Association (NZO), Zoetermeer, The Netherlands.
15 ff) S. S. S.-M., L. V. and J. M. G. obtained an unrestricted grant from the Dutch Dairy Association (NZO) to carry out meta-analyses on the
16 association between dairy products.
17 gg) None of the authors had any conflicts of interest.
18 hh) Conflicts of interest: none.
19 ii) Conflict of Interests: None.
20 jj) Disclosures: None.
21 kk) Disclosures: None.
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

References

1. Aerde M, Soedamah-Muthu S, Geleijnse J, et al. Dairy intake in relation to cardiovascular disease mortality and all-cause mortality: the Hoorn Study. *European Journal of Nutrition*. 2013;52(2):609-16 8p.
2. Al-Delaimy WK, Rimm E, Willett WC, et al. A prospective study of calcium intake from diet and supplements and risk of ischemic heart disease among men. *American Journal of Clinical Nutrition*. 2003;77(4):814-8 5p.
3. Alonso A, Beunza JJ, Delgado-Rodriguez M, et al. Low-fat dairy consumption and reduced risk of hypertension in the Seguimiento Universidad de Navarra (SUN) cohort. *American Journal of Clinical Nutrition*. 2005;82(5):972-9.
4. Altorf-van der Kuil W, Engberink MF, Geleijnse JM, et al. Sources of dietary protein and risk of hypertension in a general Dutch population. *British Journal of Nutrition*. 2012;108(10):1897-903 7p.
5. Avalos EE, Barrett-Connor E, Kritz-Silverstein D, et al. Is dairy product consumption associated with the incidence of CHD? *Public health nutrition*. 2013;16(11):2055-63.
6. Bernstein AM, Pan A, Rexrode KM, et al. Dietary protein sources and the risk of stroke in men and women. *Stroke*. 2012;43(3):637-44.
7. Biong AS, Rebord HM, Fimreite RL, et al. Intake of dairy fat and dairy products, and risk of myocardial infarction: A case-control study. *International Journal of Food Sciences and Nutrition*. 2008;59(2):155-65.
8. Bonthuis M, Hughes MCB, Ibiebele TI, et al. Dairy consumption and patterns of mortality of Australian adults. *European journal of clinical nutrition*. 2010;64(6):569-77.
9. Buendia JR, Yanping L, Hu FB, et al. Long-term yogurt consumption and risk of incident hypertension in adults. *Journal of Hypertension*. 2018;36(8):1671-9.
10. Chen M, Li Y, Sun Q, et al. Dairy fat and risk of cardiovascular disease in 3 cohorts of US adults. *American Journal of Clinical Nutrition*. 2016;104(5):1209-17.
11. Dalmeijer GW, Struijk EA, van der Schouw YT, et al. Dairy intake and coronary heart disease or stroke—A population-based cohort study. *International Journal of Cardiology*. 2013;167(3):925-9.
12. Dauchet L, Kesse-Guyot E, Czernichow S, et al. Dietary patterns and blood pressure change over 5-y follow-up in the SU.VI.MAX cohort. *The American journal of clinical nutrition*. 2007;85(6):1650-6.
13. Dehghan M, Mente A, Rangarajan S, et al. Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. *Lancet*. 2018;392 North American Edition(10161):2288-97.
14. Elwood PC, Pickering JE, Fehily AM, et al. Milk drinking, ischaemic heart disease and ischaemic stroke I. Evidence from the Caerphilly cohort. *European Journal of Clinical Nutrition*. 2004;58(5):711-7.
15. Engberink MF, Hendriksen MA, Schouten EG, et al. Inverse association between dairy intake and hypertension: the Rotterdam Study. *The American journal of clinical nutrition*. 2009;89(6):1877-83.
16. Farvid MS, Malekshah AF, Pourshams A, et al. Dairy Food Intake and All-Cause, Cardiovascular Disease, and Cancer Mortality. *American Journal of Epidemiology*. 2017;185(8):697-711.

17. Haring B, Gronroos N, Nettleton JA, et al. Dietary Protein Intake and Coronary Heart Disease in a Large Community Based Cohort: Results from the Atherosclerosis Risk in Communities (ARIC) Study. *PLoS one*. 2014;9(10):e109552.
18. He K, Merchant A, Rimm EB, Rosner BA, et al. Dietary fat intake and risk of stroke in male US healthcare professionals: 14 year prospective cohort study. *BMJ*. 2003;327(7418):777-82.
19. Heraclides A, Mishra GD, Hardy RJ, et al. Dairy intake, blood pressure and incident hypertension in a general British population: the 1946 birth cohort. *European journal of nutrition*. 2012;51(5):583-91.
20. Johansson I, Nilsson LM, Esberg A, et al. Dairy intake revisited - associations between dairy intake and lifestyle related cardio-metabolic risk factors in a high milk consuming population. *Nutrition Journal*. 2018;17(1):N.PAG-N.PAG.
21. Johansson I, Esberg A, Nilsson LM, et al. Dairy Product Intake and Cardiometabolic Diseases in Northern Sweden: A 33-Year Prospective Cohort Study. *Nutrients*. 2019;11(2):284.
22. Kim D, Kim J. Dairy consumption is associated with a lower incidence of the metabolic syndrome in middle-aged and older Korean adults: the Korean Genome and Epidemiology Study (KoGES). *British Journal of Nutrition*. 2017;117(1):148-60.
23. Larsson SC, Männistö S, Virtanen MJ, et al. Dairy foods and risk of stroke. *Epidemiology (Cambridge, Mass)* [Internet]. 2009; 20(3):[355-60 pp.]. Available from: <http://onlinelibrary.wiley.com/doi/10.1111/j.1469-7610.2009.02031.x>
24. Larsson SC, Virtamo J, Wolk A. Dairy consumption and risk of stroke in Swedish women and men. *Stroke*. 2012;43(7):1775-80.
25. Li K, Kaaks R, Linseisen J, et al. Associations of dietary calcium intake and calcium supplementation with myocardial infarction and stroke risk and overall cardiovascular mortality in the Heidelberg cohort of the European Prospective Investigation into Cancer and Nutrition study (EPIC-Heidelberg). *Heart*. 2012;98(12):920-5.
26. Lin PH, Yeh WT, Svetkey LP, et al. Dietary intakes consistent with the DASH dietary pattern reduce blood pressure increase with age and risk for stroke in a Chinese population. *Asia Pacific journal of clinical nutrition*. 2013;22(3):482-91.
27. Lockheart MSK, Steffen LM, Rebnord HM, et al. Dietary patterns, food groups and myocardial infarction: a case-control study. *British Journal of Nutrition*. 2007;98(2):380-7.
28. Louie JCY, Flood VM, Burlutsky G, et al. Dairy consumption and the risk of 15-year cardiovascular disease mortality in a cohort of older Australians. *Nutrients*. 2013;5(2):441-54.
29. Mazidi M, Mikhailidis DP, Sattar N, et al. Consumption of dairy product and its association with total and cause specific mortality - A population-based cohort study and meta-analysis. *Clin Nutr*. 2018.
30. Ness AR, Smith GD, Hart C. Milk, coronary heart disease and mortality. *Journal of Epidemiology & Community Health*. 2001;55(6):379-82.
31. Nettleton JA, Steffen LM, et al. Incident heart failure is associated with lower whole-grain intake and greater high-fat dairy and egg intake in the Atherosclerosis Risk in Communities (ARIC) study. *Journal of the American Dietetic Association*. 2008;108(11):1881-7.
32. Panagiotakos D, Pitsavos C, Chrysohoou C, et al. Dietary patterns and 5-year incidence of cardiovascular disease: A multivariate analysis of the ATTICA study. *Nutrition, Metabolism and Cardiovascular Diseases*. 2009;19(4):253-63.
33. Patterson E, Larsson SC, Wolk A, et al. Association between dairy food consumption and risk of myocardial infarction in women differs by type of dairy food. *The Journal of nutrition*. 2013;143(1):74-9.

- 1
2
3 34. Praagman J, Franco OH, Ikram MA, et al. Dairy products and the risk of stroke and coronary heart disease: the Rotterdam Study. *European journal of nutrition*. 2015;54(6):981-90.
- 4
5 35. Praagman J, Dalmeijer GW, van der Schouw YT, et al. The relationship between fermented food intake and mortality risk in the European
6 Prospective Investigation into Cancer and Nutrition-Netherlands cohort. *British Journal of Nutrition*. 2015;113(3):498-506.
- 7
8 36. Sauvaget C, Nagano J, Allen N, et al. Intake of animal products and stroke mortality in the Hiroshima/Nagasaki Life Span Study.
9 *International journal of epidemiology*. 2003;32(4):536-43.
- 10 37. Snijder MB, van Dam RM, Stehouwer CD, et al. A prospective study of dairy consumption in relation to changes in metabolic risk factors:
11 the Hoorn Study. *Obesity (Silver Spring, Md)*. 2008;16(3):706-9.
- 12 38. Soedamah-Muthu SS, Masset G, Verberne L, Geleijnse JM, et al. Consumption of dairy products and associations with incident diabetes,
13 CHD and mortality in the Whitehall II study. *The British journal of nutrition*. 2013;109(4):718-26.
- 14 39. Steffen LM, Kroenke CH, Yu X, et al. Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood
15 pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *American Journal of Clinical*
16 *Nutrition*. 2005;82(6):1169-77; quiz 363-4.
- 17 40. Tavani A, Gallus S, Negri E, et al. Milk, dairy products, and coronary heart disease. *Journal of Epidemiology & Community Health*.
18 2002;56(6):471-2.
- 19 41. Um CY, Judd SE, Flanders WD, et al. Associations of Calcium and Dairy Products with All-Cause and Cause-Specific Mortality in the
20 REasons for Geographic and Racial Differences in Stroke (REGARDS) Prospective Cohort Study. *Nutrition & Cancer*. 2007;69(8):1185-95.
- 21 42. Umesawa M, Iso H, Ishihara J, et al. Dietary calcium intake and risks of stroke, its subtypes, and coronary heart disease in Japanese: the
22 JPHC Study Cohort I. *Stroke*. 2008;39(9):2449-56.
- 23 43. Wang L, Manson JE, Buring JE, et al. Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged
24 and older women. *Hypertension*. 2008;51(4):1073-9.
- 25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Supplementary File 6. Risk of bias in included studies

Funding Source, n (%^a)

Characteristic	Category	Total N = 43	Sponsorship		COI		Industry Ties	
			Industr y N= 8	Non- Industry N=35	COI N =10	No COI N=33	Industry /COI N = 14	Non- Industry/ No COI N = 29
Risk of Bias Assessment								
	Serious/Critical Bias due to confounding	43 (100)	8 (100)	35 (100)	10 (100)	33 (100)	14 (100)	29 (100)
	Serious/Critical Bias in selection of participants into the study	6 (14)	1 (13)	5 (14)	1 (10)	5 (15)	2 (14)	4 (14)
	Serious/Critical Bias in classification of exposures	16 (37)	3 (38)	13 (37)	2 (20)	14 (42)	3 (21)	13 (44)
	Serious/Critical Bias due to deviations from exposures	21 (49)	3 (38)	18 (51)	6 (60)	15 (45)	7 (50)	14 (48)
	Serious/Critical Bias due to missing data	10 (23)	2 (25)	8 (23)	3 (30)	7 (21)	3 (21)	7 (24)

	Serious/Critical Bias in measurement of outcomes	6 (14)	2 (25)	4 (11)	1 (10)	5 (15)	2 (14)	4 (14)
	Serious/Critical Bias in selection of reported results	4 (9)	1 (13)	3 (9)	2 (20)	2 (6)	2 (14)	2 (7)
	Serious/Critical overall risk of bias	43 (100)	8 (100)	35 (100)	10 (100)	33 (100)	14 (100)	29 (100)

^a Percentages may not add to 100 due to rounding

Supplementary File 7: Favorable Outcomes by Industry Ties v No Industry Ties, Industry Sponsorship v No Industry Sponsorship and Conflicts of Interest v No Conflicts of Interest

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
Aerde, M 2013	Non-Industry	Yes	U	U	Al-Delaiimy, WK 2003	Non Industry	No	U	U
Altorf-van der Kuil, W2012	Industry	Yes	U	U	Alonso A, 2005	Non-industry	No	U	U
Bernstein, AM 2012	Non-industry	Yes	U	U	Avalos, EE 2013	Non-industry	No	U	U
Biong, A 2008	Industry	Yes	U	F	Bonthuis, M 2010	Non-Industry	No	U	U
Buendia, JR 2018	Industry	No	F	F	Chen, M 2016	Non-Industry	No	U	F
Dalmeijer, G 2013	Non-Industry	Yes	U	F	Dauchet, L 2007	Non-Industry	No	U	U
Dehghan, M 2018	Industry	No	U	F	Elwood, PC 2004	Non-Industry	No disclosure	U	U
Heraclides, A 2012	Non-Industry	Yes	U	U	Engberink, MF 2009	No disclosure	No	U	F
Lockheart, MSK 2007	Industry	No disclosure	U	U	Farvid, MS 2017	Non-Industry	No	F	F
Louie, JCY 2013	Industry	No disclosure	U	U	Haring, B 2014	Non-Industry	No	U	U
Praagman, J 2015	Industry	Yes	U	U	He, K 2003	Non-Industry	No	U	U

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
Praagman J, 2015	Non-Industry	Yes	U	U	Johansson, I 2018	Non-Industry	No	U	U
Snijder, MB 2008	Industry	Yes	U	U	Johansson, I 2019	Non-Industry	No	U	U
Soedamah-Muthu, SS 2013	Non-Industry	Yes	U	U	Kim, D 2017	Non-Industry	No	F	F
					Larsson,S 2009	Non-Industry	No disclosure	U	U
					Larsson, SC 2012	Non-Industry	No	U	U
					Li, K 2012	Non-Industry	No	U	U
					Lin, PH 2013	Non-Industry	No	U	U
					Mazidi, M, 2018	Non-Industry	No	F	F
					Ness, AR 2001	Non-Industry	No	U	U
					Nettleton, J 2008	Non-Industry	No	U	U
					Panagiotakos, D 2009	Non-Industry	No disclosure	U	U
					Patterson, E 2013	Non-Industry	No	F	F
					Sauvaget, C 2003	Non-Industry	No disclosure	F	F
					Steffen, LM 2005	Non-Industry	No	U	U

36/bmjopen-2020-019036 on 14 September 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Industry Ties: Industry Sponsorship and/or Author Conflicts of Interest					No Industry Ties: No Industry Sponsorship and No Author Conflicts of Interest				
Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable	Study ID	Funding Source	Disclosed author conflicts of interest	Results Favourable/ Unfavourable	Conclusions Favourable/ Unfavourable
					Tavani, A 2002	Non-Industry	No	F	F
					Um, C 2017	Non-Industry	No	U	F
					Umesawa, M, 2008	Non-Industry	No	F	F
					Wang,L 2008	Non-Industry	No	F	F

Favourable results - Statistical significance: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no COI

Industry Ties

	Industry/COI	Non-Industry/No COI
Favourable	1	8
Unfavourable	13	21

RR= 0.26 (95% CI 0.04, 1.87)

Industry Sponsorship

	Industry	Non-Industry
Favourable	1	8
Unfavourable	7	27

RR = 0.55 (95% CI 0.08, 3.77)

Conflicts of Interest

	COI	No/COI
Favourable	0	9
Unfavourable	10	24

RR= 0.16 (95% CI 0.01, 2.57)

Favourable conclusions: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no COI

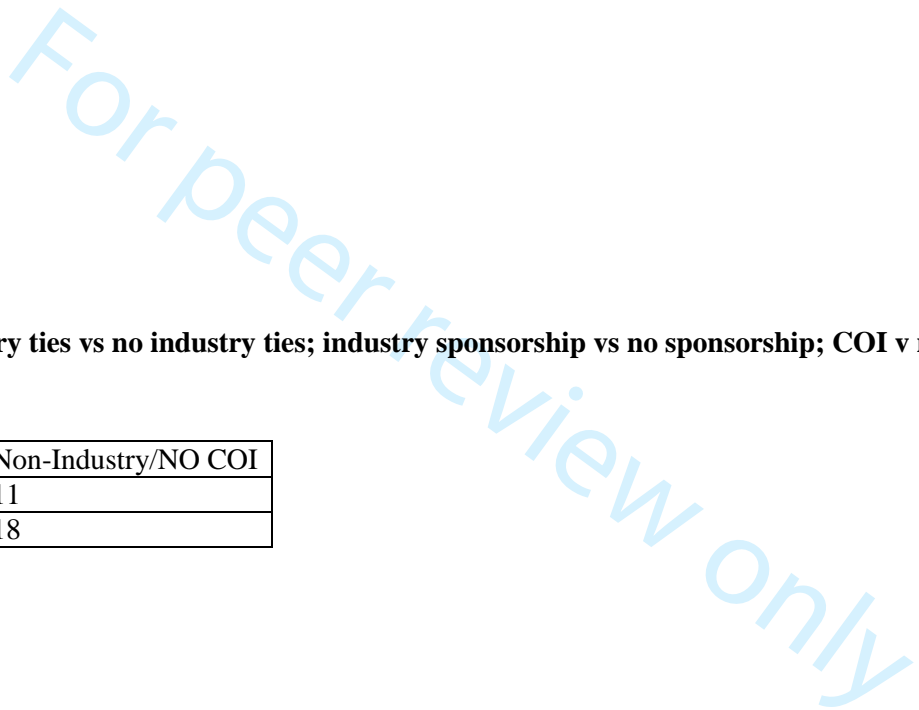
Industry Ties

	Industry/COI	Non-Industry/NO COI
Favourable	4	11
Unfavourable	10	18

RR = 0.75 (95% CI 0.29, 1.95)

Industry Sponsorship

	Industry	Non-Industry
Favourable	3	12
Unfavourable	5	23



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

RR= 1.09 (95% CI 0.40, 2.99)

Conflicts of Interest

	COI	No COI
Favourable	2	13
Unfavourable	8	20

RR =0.51 (95% 0.14, 1.88)

Concordance between study results and conclusions: Industry ties vs no industry ties; industry sponsorship vs no sponsorship; COI v no

COI Industry Ties

Industry Ties

	Industry/COI	Non-Industry/NO COI
Discord	3	3
Concord	11	26

RR = 2.07 (95% CI 0.48, 8.99)

Industry Sponsorship

	Industry	Non-Industry
Discord	2	4
Concord	6	31

RR = 2.19 (95% CI 0.48, 9.94)

Conflicts of Interest

	COI	No/COI
Favourable	2	4
Unfavourable	8	29

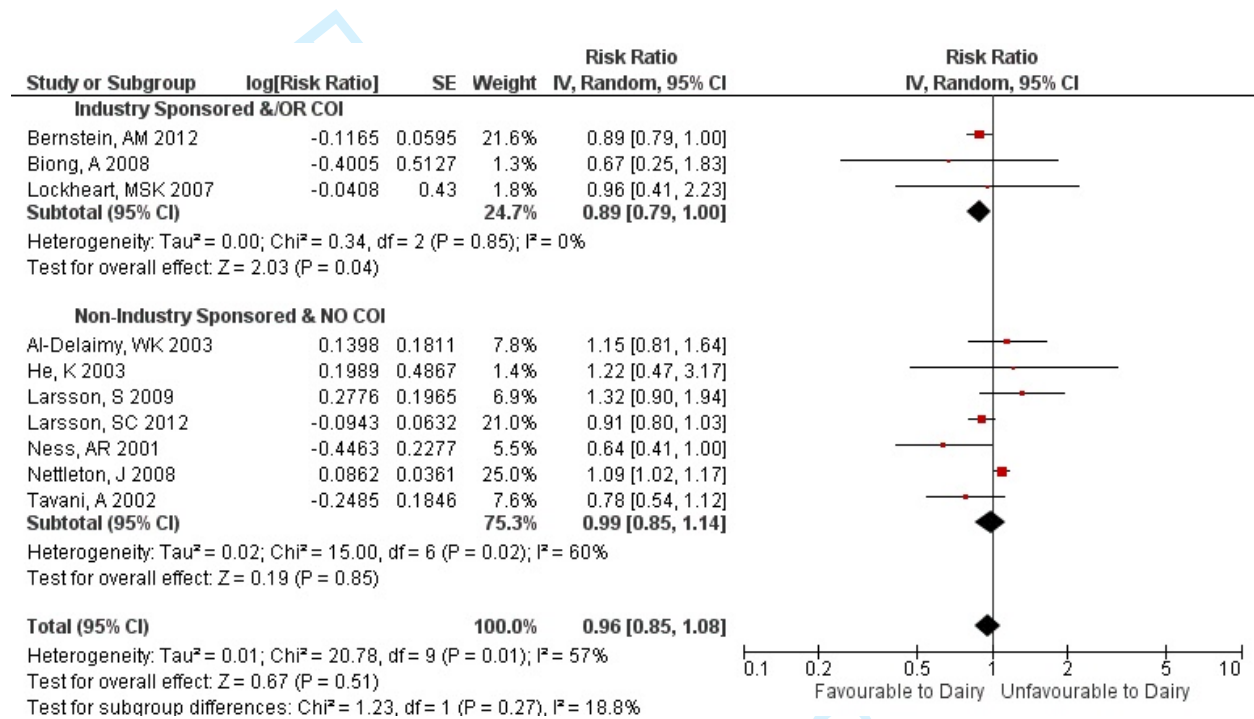
RR = 1.65 (95% CI 0.35, 7.72)

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

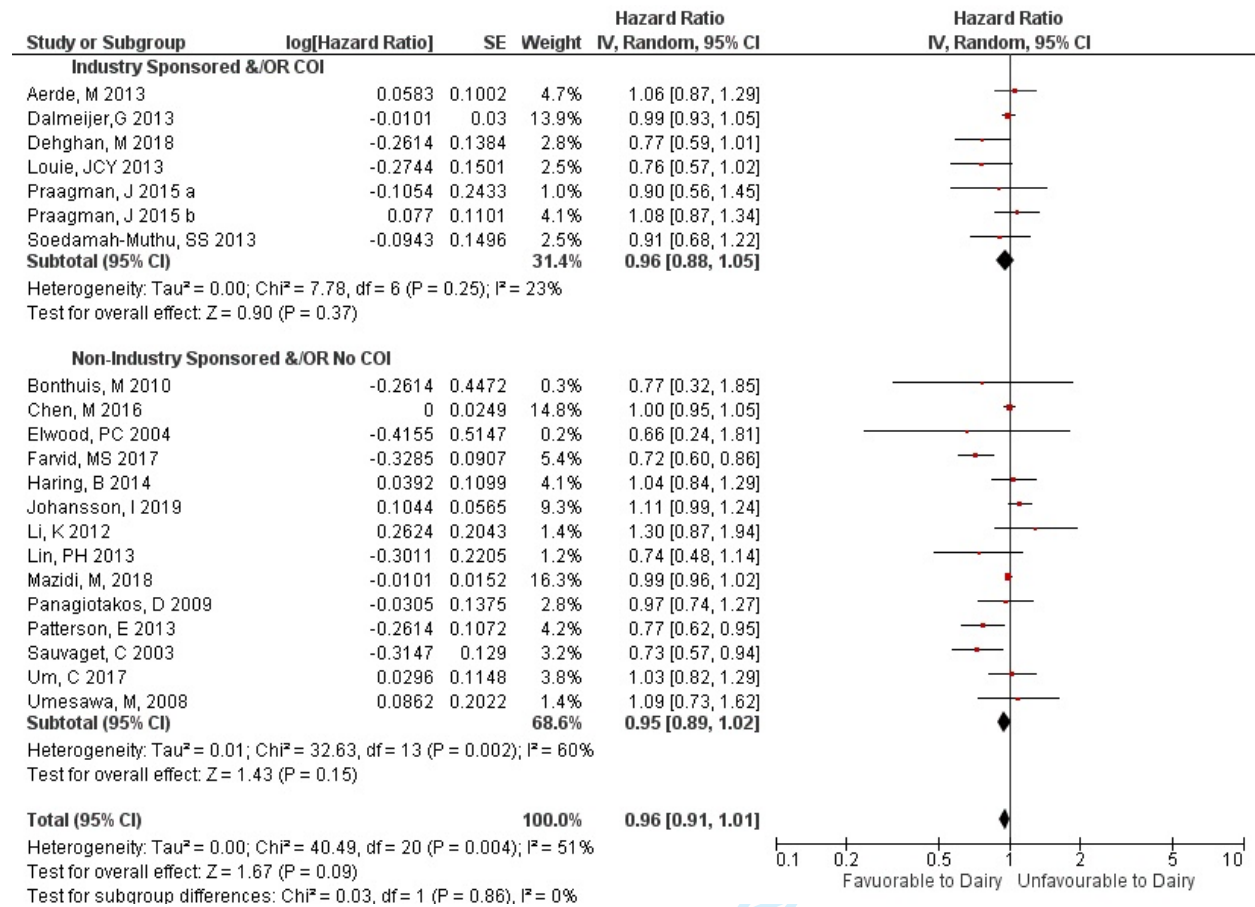
Supplementary File 8. Results for each of the meta-analyses conducted

Effect Size, Cardiovascular Disease: Industry ties v no industry ties, Risk Ratio

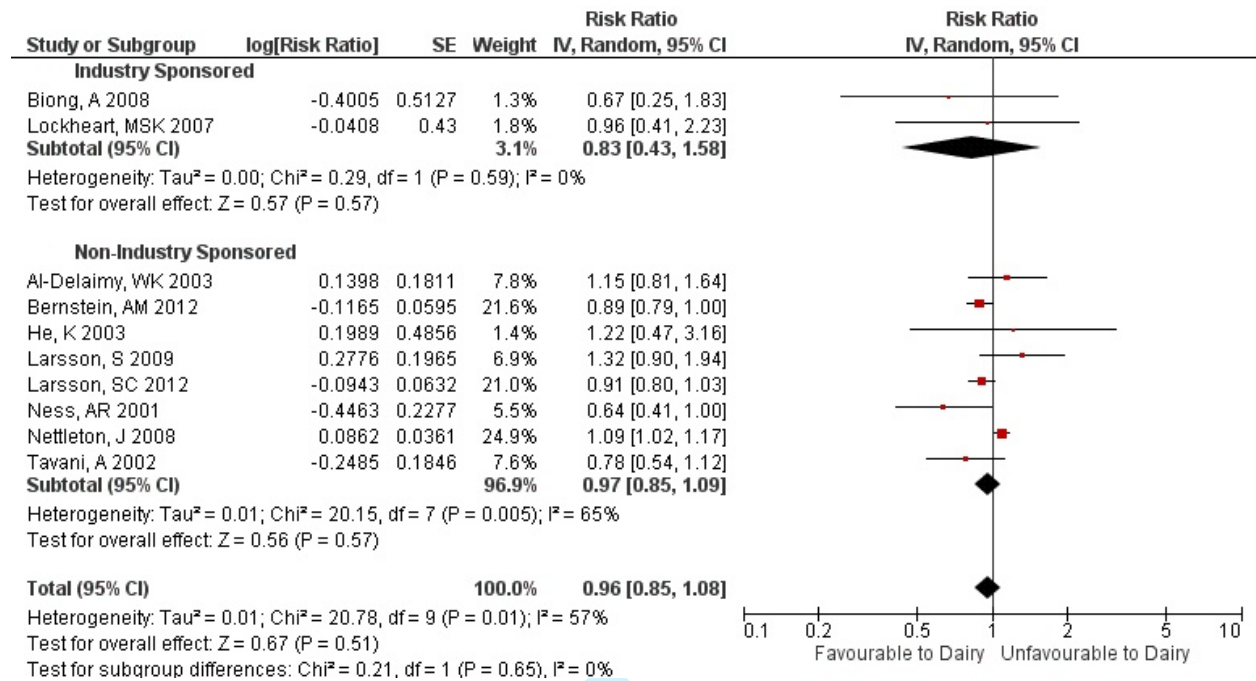


BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Effect Size, Cardiovascular Disease: Industry ties v no industry ties, Hazard Ratio

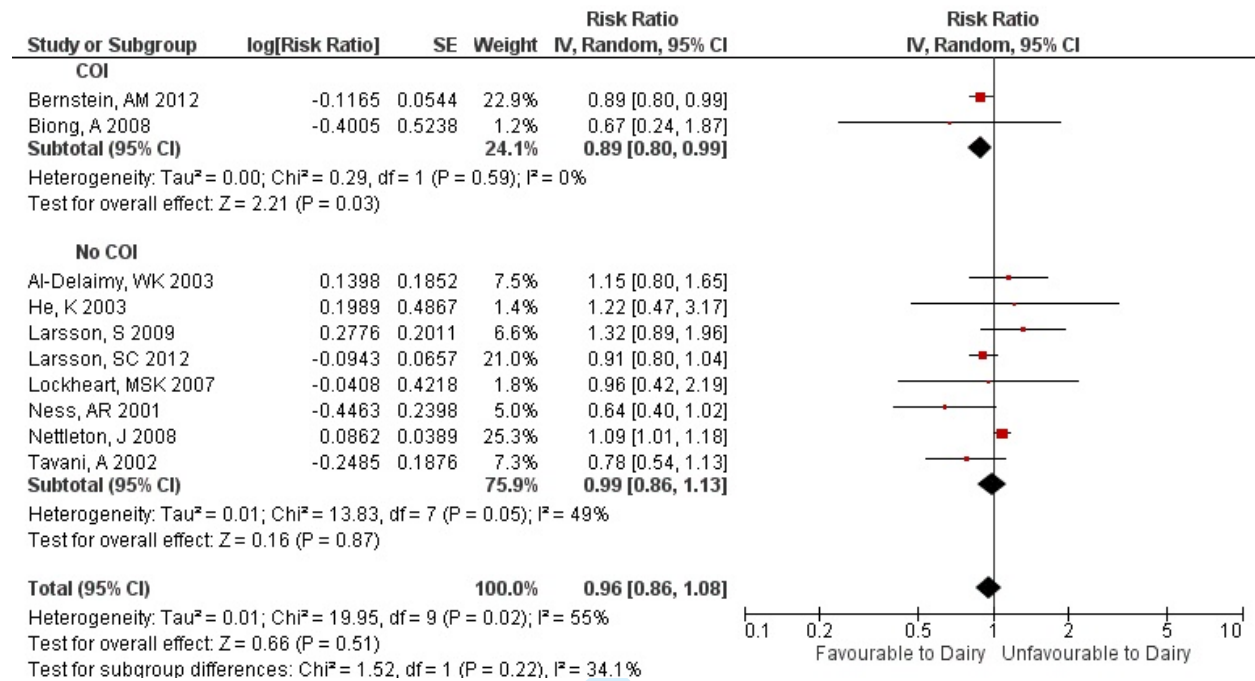


Effect Size, Cardiovascular Disease: Industry sponsorship vs no industry sponsorship, Risk Ratio

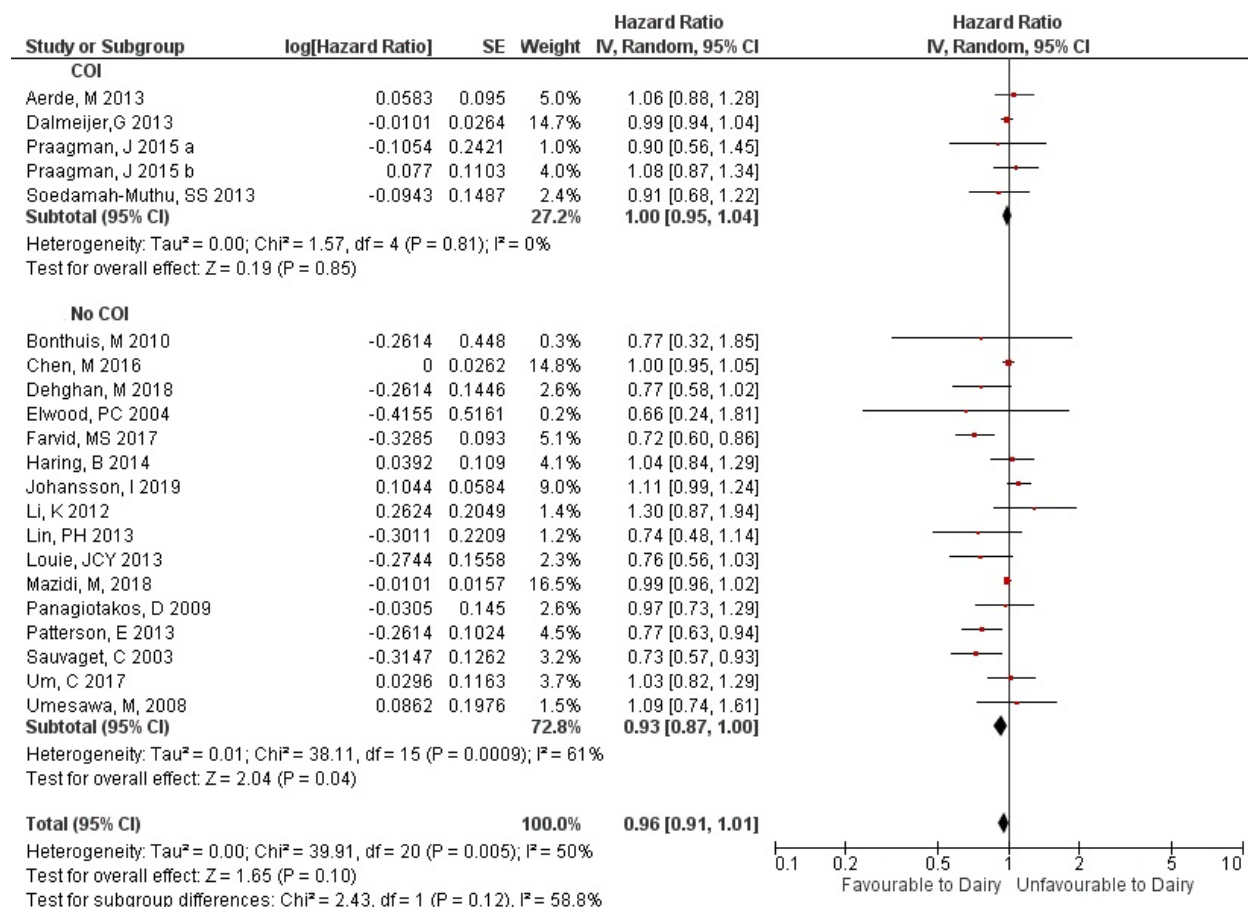


BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Effect Size, Cardiovascular Disease: COI vs No COI, Risk Ratio

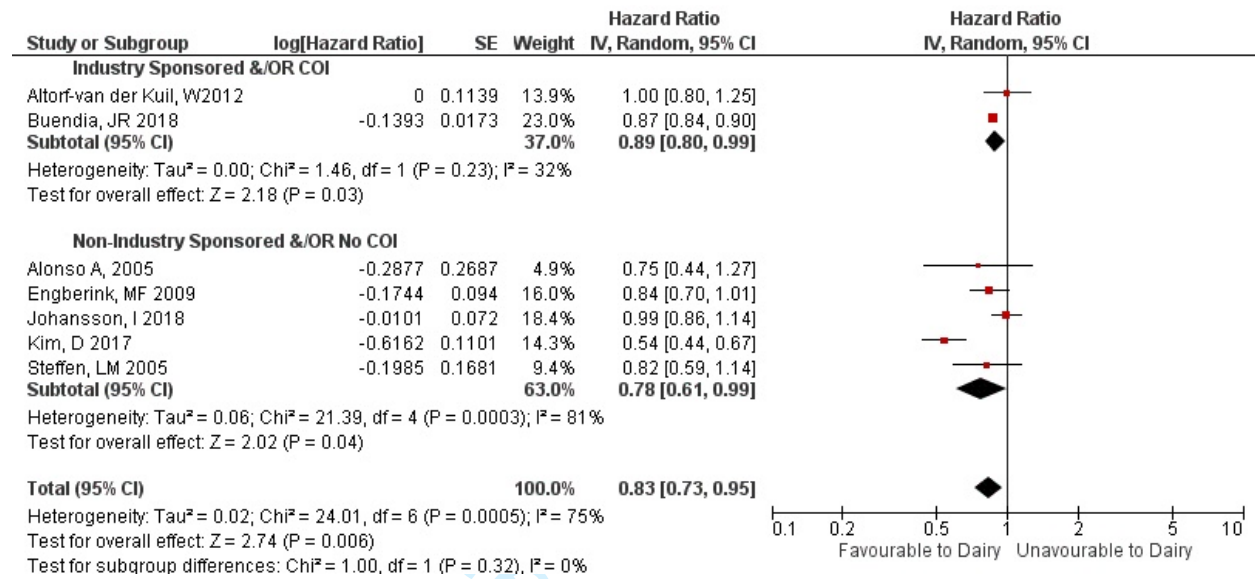


Effect Size, Cardiovascular Disease: COI vs no COI, Hazard Ratio



BMJ Open: first published as 10.1136/bmjopen-2020-039036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

Effect Size, Elevated Blood Pressure / Hypertension: Industry ties v no industry ties





PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3&5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5, Supp file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7 & 11
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6 & 10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2 for each meta-analysis).	10 -11



PRISMA 2009 Checklist

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10-11
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	11, Figure 1, Supp file 4
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICO(S), follow-up period) and provide the citations.	Supp file 5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	13, Supp File 6, Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13-15
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	13-15, Supp file 7 & 8, Figure 3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	13, Supp file 6, Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16



PRISMA 2009 Checklist

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	3&20

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Page 2 of 2

For peer review only

36/bmjopen-2020-033036 on 4 December 2020. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.