

How should we judge edible oils and fats? An umbrella review of the health effects of nutrient and bioactive components found in edible oils and fats

Teasdale, Scott B; Marshall, Skye; Abbott, Kylie; Cassettari, Tim; Duve, Emily; Fayet-Moore, Flavia

Published in:
Critical Reviews in Food Science and Nutrition

DOI:
[10.1080/10408398.2021.1882382](https://doi.org/10.1080/10408398.2021.1882382)

Licence:
Other

[Link to output in Bond University research repository.](#)

Recommended citation(APA):
Teasdale, S. B., Marshall, S., Abbott, K., Cassettari, T., Duve, E., & Fayet-Moore, F. (2022). How should we judge edible oils and fats? An umbrella review of the health effects of nutrient and bioactive components found in edible oils and fats. *Critical Reviews in Food Science and Nutrition*, 62(19), 5167-5182.
<https://doi.org/10.1080/10408398.2021.1882382>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

For more information, or if you believe that this document breaches copyright, please contact the Bond University research repository coordinator.

How should we judge edible oils and fats? An umbrella review of the health effects of nutrient and bioactive components found in edible oils and fats

Running title: Health effects of edible oils

Authors:

Scott B. Teasdale, PhD^{1,2} ORCID 0000-0001-6769-8421, T: @scottbteasdale

Skye Marshall, PhD^{1,3} ORCID 0000-0001-8953-5068, T: @drskyemarshall

Kylie Abbott, PhD¹ ORCID 0000-0002-7378-1552, T: @kylie_a_abbott

Tim Cassettari, BSc (Nutr) (Hons)¹ ORCID 0000-0002-8800-2005

Emily Duve, MPH¹ ORCID 0000-0002-2608-1916

Flavia Fayet-Moore, PhD^{1*} ORCID 0000-0002-2544-7154 T: @drflavs

1. Nutrition Research Australia, Sydney, Australia.
2. School of Psychiatry, University of New South Wales, Sydney, Australia.
3. Bond University Nutrition & Dietetics Research Group, Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia.

* Corresponding author

Flavia Fayet-Moore, CEO Nutrition Research Australia, Level 10, 20 Martin Place, Sydney, Australia, 2000. E: flavia@nraus.com; T: 0415 990 050

Word count: 5746

Authorship: FFM, SM, and TC developed the study concept. KA, ED, and ST contributed to study selection and data extraction. ST drafted the manuscript with contributions from KA.

All co-authors revised the manuscript for accuracy and clarity; and approved the final version.

Funding: This project has been funded by a research grant from Boundary Bend Pty Ltd.

1 **Abstract**

2 Dietary guidelines for many Western countries base their edible oil and fat recommendations
3 solely on saturated fatty acid content. This study aims to demonstrate which nutritional and
4 bioactive components make up commonly consumed edible oils and fats; and explore the
5 health effects and strength of evidence for key nutritional and bioactive components of edible
6 oils. An umbrella review was conducted in several stages. Australian and American food
7 composition databases and studies were examined to profile nutrient and bioactive content of
8 edible oils and fats. PUBMED and Cochrane databases were searched for umbrella reviews,
9 systematic literature reviews of randomized controlled trials or cohort studies, individual
10 randomized controlled trials, and individual cohort studies to examine the effect of the
11 nutrient or bioactive on high-burden chronic diseases (cardiovascular disease, type 2 diabetes
12 mellitus, obesity, cancer, mental health, cognitive). Substantial systematic literature review
13 evidence was identified for fatty acid categories, tocopherols, biophenols, and phytosterols.
14 Insufficient evidence was identified for squalene. The evidence supports high mono- and
15 polyunsaturated fatty acid compositions, total biophenol content, phytosterols, and possibly
16 high α -tocopherol content as having beneficial effects on high burden health comes. Future
17 dietary guidelines should use a more sophisticated approach to judge edible oils beyond
18 saturated fatty acids.

19

20 **Keywords:** Guideline; Nutrition Policy; Fatty Acids; Tocopherols, Polyphenols,
21 Phytosterols, Squalene; Plant Oils; Fats.

22 **Introduction**

23 Although edible fats and oils have complex properties, dietary guidelines in Western
24 countries such as the United States of America (US), United Kingdom (UK), and Australia
25 recommend edible oil or fat to be consumed as part of a healthy diet based solely on its
26 saturated fatty acid content (SFA) ((NHMRC), 2013; Agriculture., 2015; England, 2018).
27 Those low in SFA (predominantly of plant origin) are recommended by dietary guidelines
28 and those high in SFA (predominantly of animal origin with the addition of palm and coconut
29 oil) are discouraged. The basis for this recommendation has been that SFA increases total and
30 non-HDL cholesterol, a risk factor for cardiovascular disease (CVD); whereas replacing SFA
31 with monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs) is
32 cardioprotective (Committee, 2020). Further, the recommendation for oil is described as an
33 allowance rather than as part of the core food groups, suggesting that there are no health
34 benefits associated with regular consumption of edible oils and fats as part of a healthy diet
35 ((NHMRC), 2013; Agriculture., 2015; England, 2018).

36 The first print of the US Scientific Report of the 2020 Dietary Guidelines Advisory
37 Committee was released in July 2020 (Committee, 2020). In line with current US dietary
38 guidelines (Agriculture., 2015), the 2020 Dietary Guidelines Advisory Committee report
39 recommends replacing fats which are solid at normal room temperature with liquid oils,
40 citing the SFA–CVD relationship (Committee, 2020). More specifically, the 2020 Dietary
41 Guidelines Advisory Committee report specifies that SFA should be replaced with PUFA
42 (INRA, 2015). In July 2020, the Australian Government announced funding for the
43 Australian National Health and Medical Research Council to review and update the
44 Australian dietary guidelines (Government, 2020).

45 It is an opportune time for a more sophisticated approach to dietary recommendations for
46 edible oils and fats as the importance of fatty acid intake extends past CVD to a number of

47 other high burden diseases and conditions including diabetes, cancer, dementia and mental
48 health (Afshin et al., 2019; Kyu et al., 2018). Further, in recent decades, potential health
49 implications of edible oils at a biochemical level have emerged with compounds such as
50 tocopherols, biophenols, phytosterols, stigmastadienes, terpenes, and squalene (Kris-Etherton
51 et al., 2002). To progress to a more sophisticated approach to judging edible oils and fats in
52 national dietary guidelines, there is a need to compare the nutrient and bioactive content
53 between edible oils and fats to determine which components have the strongest evidence-base
54 for preventing and improving high-burden diseases.

55 This study aims to: i) demonstrate which nutritional and bioactive components make up
56 commonly consumed edible oils and fats, and ii) explore the potential health effects and
57 strength of evidence for key nutritional and bioactive components of edible oils.

58 **Materials and Methods**

59 An umbrella review was undertaken. An umbrella review allows the examination of a broad
60 scope of issues related to a topic of interest, with the predominant included study type being
61 existing systematic reviews (*JBI Manual for Evidence Synthesis.*, 2020).

62 This umbrella review drew upon food composition databases and studies, umbrella reviews,
63 systematic literature reviews (SLRs), randomized controlled trials (RCTs), and cohort
64 studies. This study was not prospectively registered; and was reported according to the
65 Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping
66 Reviews (PRISMA-ScR) (de Oliveira).

67 ***Characterization of common edible oils and fats***

68 In order to select which edible oils and fats are included in this review, two rounds of
69 stakeholder consultation with edible oils and fats experts were undertaken. Edible oils and
70 fats which were considered for their importance for culinary use in Western society and were
71 grouped as “high”, “medium”, and “low” priority. High priority edible oils and fats were
72 olive oil (separated by grade where possible), canola oil, palm oil, soybean oil, sunflower oil,
73 rice bran oil, peanut oil, coconut oil (separated by grade where possible), cottonseed oil and
74 grapeseed oil. Medium priority was assigned to butter, avocado oil, corn oil and tallow/lard.
75 Low priority was assigned to sesame oil, safflower oil, mustard seed oil, almond oil, walnut
76 oil, flaxseed oil, macadamia nut oil, hempseed oil, pumpkin seed oil, and apricot seed oil.

77 Target nutrients and bioactive components included in the review were identified through a
78 brief review of the literature as well as through stakeholder engagement. The chosen target
79 nutrients and bioactives were: fatty acid categories (monounsaturated fatty acids [MUFA],
80 PUFA, SFA, and trans-unsaturated fatty acids [TFA]) and the bioactives: tocopherols,
81 biophenols (also commonly referred to as polyphenols), phytosterols, squalene,
82 stigmastadienes, and terpenes. However, the review identified that data on stigmastadienes

83 and terpenes content in edible oils and fats were extremely limited and were subsequently
84 removed from the review, leaving five target nutrients/bioactives.

85 ***Edible oil and fat nutrient and bioactive matrix***

86 To demonstrate which nutritional and bioactive components make up commonly consumed
87 edible oils and fats, food composition databases and studies were drawn upon using the
88 following method, executed by a single reviewer (ST or KA):

- 89 1. Food Standards Australia and New Zealand (FSANZ) Food Composition Database
90 ((FSANZ), 2019) and the U.S. Department of Agriculture FoodData Central ((USDA),
91 2019) for vitamin, mineral, fatty acid, tocopherol and phytosterol composition on the 6th
92 May 2020.
- 93 2. Industry websites: Olive Wellness Institute (Glanz & Scharf, 1985) and Australian
94 Oilseeds Industry (Bedell & Shackleton, 1989) were reviewed for reports or links to
95 studies on 6th May 2020.
- 96 3. Phenol explorer (version 3.0) was searched for biophenol composition data for edible oils
97 and fats on 6th May 2020 (INRA, 2015).
- 98 4. PUBMED and Google Scholar databases were searched on 7th-11th May 2020, using
99 targeted and rapid searching techniques based on keywords.

100 The nutrient and bioactive composition of the high, medium, and low priority edible oils and
101 fats were extracted by a single reviewer (ST, KA, or ED) and reported as mean (and range
102 when available) in mg per 100g/100mL in a matrix. For the fatty acid composition, data were
103 reported as a percentage of the oil, rather than in mg. Where a study reported multiple
104 analyses of the same edible oil or fat, the mean of these analyses was included in the report.

105 ***Eligibility criteria***

106 The eligibility criteria according to the PICO(S) (Participant, Intervention, Comparator,
107 Outcome, Source) format is described in Table 1. Edible oils which were considered high

108 priority were included for their association with the health outcomes. Health outcomes
109 selected for inclusion were those relevant to population health and currently used as evidence
110 in dietary guidelines (*Australian Dietary Guidelines*, 2013): CVD, type 2 diabetes mellitus
111 (T2DM), obesity, cancer, mental health disorders, cognitive impairment, and inflammation
112 and immune function.

113

114 *Insert Table 1 about here*

115

116 To fully understand the impact of the nutrient or bioactive components on health; studies
117 were included when the nutrient or bioactive was consumed from any source rather than only
118 edible oils and fats. Fatty acids which were marine derived (i.e. EPA/DHA) were excluded
119 due to the minimal content in the majority of edible oils and fats used for culinary purposes,
120 and the saturation of marine derived omega-3 in the peer-reviewed published literature. As it
121 was anticipated that the systematic review evidence on fatty acids relation to the health
122 outcomes would be exhaustive; search results were sorted by relevance to the search strategy
123 and a maximum of 50 of the most relevant SLRs were included. Studies were included which
124 reported on major classes and categories of fatty acids and major classes, categories and
125 individual bioactives.

126 ***Search strategy***

127 PUBMED and Cochrane Database of Systematic Reviews were searched on 3rd June 2020 to
128 identify umbrella reviews, SLRs, RCTs, and cohort studies that investigated the effect of the
129 five nutritional and bioactive components present in edible oils and fats on the health
130 outcomes. The literature search was completed in two steps. In step 1, umbrella reviews,
131 SLRs of RCTs, and SLRs of cohort studies for each nutritional component on the health
132 outcomes. If no umbrella review or SLR evidence was found, we progressed to step 2. In step

133 2, RCTs and cohort studies for each nutritional and bioactive component on the health
134 outcomes. The full search strategy is listed in Table S1. Reference lists of relevant narrative
135 reviews were searched for additional eligible studies.

136 ***Data extraction***

137 One reviewer (ST or KA) screened titles and abstracts for relevant studies against the
138 inclusion/exclusion criteria. The full texts of potentially eligible studies were then screened to
139 confirm eligibility by one reviewer (ST or KA). If insufficient umbrella or SLRs were included
140 after full text screening, full text screening of RCTs and cohort studies followed. Data were
141 extracted into summary tables according to study design. Data extracted were:

- 142 1. SLR: author, publication year, design, date of search, number of studies included,
143 study sample, details of the intervention/cohort studies, control condition, health
144 outcomes and their measurements, top line results, strengths/limitations.
- 145 2. RCTs and cohort: author, publication year, country, design, sample size, subject
146 characteristics, bioactive details, control condition, health outcomes and
147 measurements, top line results, strengths/limitations.

148 Studies that investigated health outcomes not eligible in this review were noted. One
149 reviewer (ST) identified the key strengths and limitations for each included study, presented
150 these in tables, and they were discussed.

151 **Results**

152

153 ***Edible oils and fats matrix***

154 A summary of the nutrient and bioactive content of edible oils and fats are demonstrated as a
155 summary in Table 2 (raw data are presented in the Supplementary Tables S2 to S10). Data on
156 pumpkin seed oil and virgin avocado oil were not identified in the literature, and hence not
157 included in the matrix. Data on different qualities of coconut oil were limited and included
158 when available.

159

160 *Insert Table 2 about here.*

161

162 ***Health effects of nutrients and bioactives found in edible oils and fats***

163 The number of studies identified according to the components are summarized in Table 3.

164 Sufficient SLR literature was identified for fatty acids, tocopherols, biophenols, and
165 phytosterols in step 1. The most frequent outcomes explored in fatty acid reviews was
166 cardiovascular outcomes; however, research is building for other high-burden diseases and
167 illnesses including mortality, cancer, and diabetes. Tocopherol outcomes were most
168 frequently all-cause mortality, cardiovascular, and cancer. The phytosterol literature most
169 frequently explored cardiovascular and cancer outcomes. Biophenol outcomes were broad
170 and included all-cause mortality, cardiovascular, diabetes, cancer, neurodegenerative, and
171 body composition outcomes. The squalene literature was limited to blood lipid outcomes.

172

173 *Insert Table 3 about here*

174

175 ***Health effects of fatty acids***

176 The SLR and meta-analysis (MA) evidence for fatty acid categories and health outcomes was
177 exhaustive and as such the first 50 relevant umbrella reviews and SLRs were included.

178 Snowball searching found three additional SLRs of high interest, leading to a total of 53
179 studies (Table S11). Twenty-four were SLRs and MA of RCTs, 13 SLRs and MA of cohort
180 studies, 4 SLRs and MA of cohort studies and case-control studies, 4 SLRs of RCTs, 3 SLRs
181 and MA of RCTs and cohort studies, 2 umbrella reviews of SLRs with MA, 2 SLRs of RCTs
182 and cohort studies and 1 SLRs of RCTs, cohort studies and case-control studies.

183 *All-cause mortality*

184 SLRs of cohort studies and RCTs provided unclear consensus on fatty acid categories and all-
185 cause mortality; with study duration ranging from 12 months to 8 years. In one review of
186 cohort studies, TFAs were positively associated and SFAs had no association (De Souza et
187 al., 2015); whereas in a second review, SFAs were positively associated (Brennan, Woodside,
188 Lunny, Cardwell, & Cantwell, 2017). A third review of cohort studies found linolenic acid
189 and gamma linolenic acid (GLA) had no association with all-cause mortality (Farvid et al.,
190 2014). A review of RCTs found replacing SFA with MUFA and/or PUFA did not reduce
191 total mortality (Hooper et al., 2012), nor did the substitution of SFAs and TFAs with omega-
192 6 PUFA (Ramsden, Hibbeln, Majchrzak, & Davis, 2010).

193 *Cardiovascular outcomes*

194 There is a substantial amount of SLR research on fatty acid categories and cardiovascular
195 outcomes. The most researched is the effect of SFAs via cohort studies and its manipulation
196 with unsaturated fatty acids in RCTs. Cohort studies provided conflicting evidence, more
197 frequently finding no association with cardiovascular outcomes (Chowdhury et al., 2014;
198 Harcombe, Baker, & Davies, 2017; Siri-Tarino, Sun, Hu, & Krauss, 2010; Te Morenga &
199 Montez, 2017; Zhu, Bo, & Liu, 2019). SLRs of RCTs that manipulated the ratio of fatty acid
200 categories show strong evidence for the replacement of SFAs with PUFA, and potentially
201 MUFA. These findings have been synthesized in two recent umbrella reviews and are in line

202 with current dietary recommendations (Clifton & Keogh, 2017; Foster & Wilson, 2013).
203 Relevant to edible oils was a SLR and MA of RCTs that found no effect of replacing SFA
204 with omega-6 PUFA on coronary heart disease outcomes, with the length of the RCTs
205 ranging 1-8 years (Hamley, 2017).

206 The SLR evidence is progressing to an individual fatty acid level, demonstrating effects of
207 individual fatty acids which differ to that portrayed in the corresponding fatty acid category.
208 For example, one SLR found medium-chain SFAs improved HDL-C without affecting other
209 lipids (Panth, Abbott, Dias, Wynne, & Garg, 2018). Another SLR found stearic acid
210 improved the lipid profile more than TFAs but less than PUFA or MUFA (Hunter, Zhang, &
211 Kris-Etherton, 2010).

212 The evidence for TFA being detrimental to cardiovascular health is consistent in both SLRs
213 of cohort studies and SLRs of RCTs (Aronis, Khan, & Mantzoros, 2012; Chowdhury et al.,
214 2014; De Souza et al., 2015; Hunter et al., 2010; Mensink, Zock, Kester, & Katan, 2003; Zhu
215 et al., 2019). In contrast, a review of RCTs on ruminant TFAs found no effect on
216 cardiovascular risk factors (Gayet-Boyer et al., 2014).

217 The health benefits of non-marine PUFA compared to omega-3, or combined omega-3 and
218 omega-6 PUFA, were less clear as the majority of studies reported PUFA as a total, and
219 limited studies explored the health benefits of non-marine PUFA individually, which did not
220 suggest a clear health benefit or detriment (Chowdhury et al., 2014; Farvid et al., 2014;
221 Haghghatdoost & Gh, 2018; Hooper et al., 2018), critical to the interpretation for edible oils
222 and fats.

223 *Diabetes and glycaemia*

224 An SLR of cohort studies suggested SFAs and TFAs were not linked to T2DM incidence (De
225 Souza et al., 2015), but alpha-linolenic acid (ALA) and fatty fish were associated with lower
226 T2DM incidence (Muley, Muley, & Shah, 2014). In SLRs of RCTs, higher MUFA intake
227 was found to improve glucose outcomes in two SLRs (Qian, Korat, Malik, & Hu, 2016; L.
228 Schwingshackl, Strasser, & Hoffmann, 2011), one showing greater effect than PUFA (Qian
229 et al., 2016). Replacing SFA or carbohydrate with plant-derived PUFA had a favorable albeit
230 weak effect on glucose and insulin in predominantly healthy cohorts in a third review
231 (Wanders et al., 2019); a fourth showed no effect of PUFA on glucose or insulin for people
232 with T2DM (Telle-Hansen, Gaundal, & Myhrstad, 2019); and a fifth found replacement of
233 liquids oils with palm oil did not affect glucose or insulin levels (Zulkipli, Balasubramaniam,
234 Bakar, Rashed, & Ismail, 2019). TFAs did not affect glucose or insulin (Aronis et al., 2012).

235 *Cancer*

236 The evidence for fatty acid categories and cancer was predominantly reliant on reviews of
237 cohort studies. In one review, positive associations were found for total fatty acids, SFAs,
238 and TFAs on ovarian cancer, whereas PUFA and MUFA had no association (Qiu, Lu, Qi, &
239 Wang, 2016). In a second SLR, MUFA was inversely associated with endometrial cancer
240 incidence, whereas PUFA had no association (Zhao et al., 2016). No associations were found
241 for PUFA with lung cancer in one review (Zhang, Lu, Yu, Gao, & Zhou, 2014); or fatty acid
242 categories with breast, colorectal, or prostate cancer in other reviews (Cao, Hou, & Wang,
243 2016; M. Kim & Park, 2018; C. Xu et al., 2015). One SLR found SFA positively associated
244 with breast cancer mortality (Xia, Ma, Wang, & Sun, 2015).

245 *Inflammation*

246 One SLR was identified for inflammation on RCTs, and found that conjugated linolenic acid
247 increased inflammation (Haghighatdoost & Gh, 2018).

248 ***Health effects of tocopherols***

249 Twenty-one SLRs were identified that examined the health effects of tocopherols including
250 SLRs and MAs of cohort studies (N=8), SLRs and MAs of both RCTs and cohort studies
251 (N=3), and SLRs and MAs of RCTs (N=10) (Table S12). Tocopherol studies focused on α -
252 tocopherol and γ -tocopherol. Cohort studies measured tocopherols through dietary intake
253 and/or blood levels. Intervention studies generally used vitamin E (α -tocopherol) as a
254 supplement and the dose ranged from 30mg/day to 5,500IU/day, while the intervention
255 duration ranged from 1 month to 10 years.

256 The evidence demonstrates an inverse relationship between blood α -tocopherol and all-cause
257 mortality (Aune et al., 2018; Jayedi, Rashidy-Pour, Parohan, Zargar, & Shab-Bidar, 2018),
258 CVD mortality (Jayedi, Rashidy-Pour, Parohan, Zargar, & Shab-Bidar, 2019), and risk of
259 stroke (Aune et al., 2018). The results for the association between blood α -tocopherol and
260 cancer were conflicting across different types, but tended to have relevant associations:
261 inverse relationship for total cancer, bladder, and colorectal cancer (marginal significance),
262 and no association with gastric cancer in the single cohort study (Nurses Health Study) (Aune
263 et al., 2018; Li et al., 2014; Longnecker et al., 1992; Miura & Green, 2015). Blood γ -
264 tocopherol was positively associated with coronary heart disease (Irawati et al., 2019) and
265 bladder cancer (Chen et al., 2015) in two separate studies, and had no association with all-
266 cause or cardiovascular-specific mortality, or risk of coronary heart disease, stroke, or total
267 cancer in a third study (Aune et al., 2018).

268 Dietary vitamin E intake was associated with all-cause mortality and CVD in one SLR in a
269 non-linear analysis (Aune et al., 2018), but not associated with all-cause mortality (Jayedi et
270 al., 2018) or CVD- mortality (Jayedi et al., 2019) in other reviews. Dietary vitamin E was
271 inversely associated with coronary heart disease in one SLR (Ye & Song, 2008), but had no

272 association in a more recent SLR (Aune et al., 2018). Dietary intake of vitamin E was
273 inversely associated with bladder cancer but there was no association when including both
274 dietary and supplemental vitamin E intake (Chen et al., 2015), and was marginally significant
275 for increased risk of gastric cancer (Li et al., 2014). A review of intervention and
276 observational studies that included a single cohort study (the Nurses Health Study) did not
277 find an association between dietary vitamin E intake and total cancer incidence (Miura &
278 Green, 2015).

279 ***Health effects of biophenols***

280 The search found 15 SLRs and MAs of RCTs, 6 SLRs of RCTs, 2 SLRs of RCTs and cohort
281 studies, 12 SLRs and MAs of cohort studies, and 1 SLR of cohort studies that examined the
282 health effects of biophenols (Table S13). Of the 36 included SLRs, 16 specifically examined
283 the effect of flavonoids, two examined phenols; and one examined flavonoids and lignans.
284 None examined secoiridoids nor single biophenol chemicals. Additional SLRs with and
285 without MAs of either RCTs or cohort studies were identified for the following individual
286 biophenols: curcumin (N=3); hesperidin (N=4); anthocyanin (N=3); flavan-3-ols (N=1);
287 flavonoid subclasses (N=1); quercetin (N=2); resveratrol (N=3). Additional SLRs and MAs
288 of RCTs or cohort studies were identified for one-specific food or beverage rich in
289 biophenols: pomegranate juice (N=3), tea (N=1), green tea (N=1), green coffee bean (N=1),
290 grapes (N=1), cocoa/chocolate (N=4).

291 Identified studies explored potential health benefits of biophenols through typical dietary
292 intake, circulating blood levels, and supplementation in the form of capsules/tablets, fortified
293 beverage, or high biophenol food or beverage in adults ≥ 20 years. Cohort studies generally
294 included $\geq 100,000$ people and $>10,000$ cases. Intervention reviews were mainly in healthy
295 populations and less frequently in people with metabolic abnormalities such as

296 hypercholesterolemia. Intervention duration ranged from acute effects (testing within hours
297 of intervention consumption) to 3 years. The range of dose was broad (1.55-1500mg/day),
298 but most SLRs reported a minimum dose of ≥ 28 mg/day. Findings are reported according to
299 the health outcome below.

300

301 *All-cause and cardiovascular-specific mortality*

302 All-cause and CVD-mortality were assessed in SLRs and MAs of cohort studies focused on
303 flavonoids (Grosso, Micek, et al., 2017; Y. Kim & Je, 2017; X. m. Liu et al., 2017; Wang,
304 Ouyang, Liu, & Zhao, 2014). Flavonoid intake consistently had an inverse relationship with
305 all-cause mortality across SLRs with MAs (Grosso, Micek, et al., 2017; Y. Kim & Je, 2017;
306 X. m. Liu et al., 2017); however, an SLR without MA reported conflicting results (Del Bo et
307 al., 2019). One SLR also assessed lignan intake and all-cause mortality for which there was
308 no association found (Grosso, Micek, et al., 2017).

309 *Effect on cardiovascular outcomes*

310 There was a significant risk reduction for incidence of CVD, stroke, and hypertension when
311 highest flavonoid intakes were compared to the lowest; and significant inverse relationships
312 in some dose-response SLRs and MAs (Godos et al., 2019; Y. Kim & Je, 2017; X. m. Liu et
313 al., 2017; Tang, Li, Zhang, & Hou, 2016; Wang et al., 2014). Contrary to the majority, one
314 SLR only detected a significant relationship with CVD risk through sensitivity analysis
315 (Grosso, Micek, et al., 2017) and an SLR without MA reported inconclusive results (Del Bo
316 et al., 2019).

317 Evidence from SLRs of RCTs suggested olive oil specific biophenols improved
318 cardiovascular risk factors, particularly oxidized-LDL and blood pressure, with mixed effects

319 on other outcomes (George et al., 2019; Hohmann et al., 2015; Sahebkar et al., 2017).
320 Additional SLRs for RCTs of high-biophenol foods such as ginger, turmeric, green tea, and
321 pomegranate skins suggest a beneficial effect of biophenols on blood pressure, triglycerides,
322 and flow mediated dilation. However, evidence appeared conflicting and dependent, at least
323 in part, on the food source of the biophenols (e.g. turmeric versus ginger versus
324 pomegranate), and possibly the dose and concentration of active components, which is often
325 not tested nor reported (Amiot, Riva, & Vinet, 2016; Ellwood, Torun, Bahar, & Fernandez,
326 2019; Hooper et al., 2008; Marx et al., 2017). SLRs using supplements found improved blood
327 pressure and HDL cholesterol, flow mediated dilation, blood pressure, weight, and waist
328 circumference; however, there was some inconsistency (i.e. some studies reported a
329 significant effect; others reported no effect) for most of these outcomes, likely related to
330 variations in sample and intervention characteristics (Akhlaghi, Ghobadi, Hosseini, Gholami,
331 & Mohammadian, 2018; Amiot et al., 2016; Farhat, Drummond, & Al-Dujaili, 2017; Kay,
332 Hooper, Kroon, Rimm, & Cassidy, 2012; Potì, Santi, Spaggiari, Zimetti, & Zanotti, 2019).

333 *Effect on diabetes and glycaemia*

334 Total biophenols and the flavonoid subclass had inverse relationships with T2DM risk across
335 three SLRs (Y.-J. Liu et al., 2014; Rienks, Barbaresko, Oluwagbemigun, Schmid, &
336 Nöthlings, 2018; H. Xu, Luo, Huang, & Wen, 2018). However, a fourth SLR found
337 inconclusive results (Del Bo et al., 2019). There was no relationship overall in the one SLR
338 which examined gestational diabetes; except for the drupes subgroup (nectarine, plum,
339 cherry), which was associated with a higher risk of gestational diabetes (Pham, Van Do, &
340 Lee, 2019).

341 For trials, one SLR found lower acute phase responses to glucose after consuming biophenol-
342 containing foods or beverages with a source of carbohydrate, and the second, found

343 reductions in glycated haemoglobin (longer term response) through extracts, supplements, or
344 foods (Coe & Ryan, 2016; Palma-Duran, Vlassopoulos, Lean, Govan, & Combet, 2017).

345 *Effect on risk of cancer*

346 There was preliminary evidence suggesting a relationship between total biophenol intake or
347 biophenol subclasses, and risk of various cancers (Grosso, Godos, et al., 2017); however, no
348 association was found between flavonoid intake and colorectal cancer in another SLR (He &
349 Sun, 2016).

350 *Effect on cognition and mental health*

351 Supplementation of biophenols frequently resulted in improved cognitive performance and
352 neuroprotective components, but effect sizes differed and may be related to variations in the
353 age of participants and intervention dose regimens (Ammar, Trabelsi, Boukhris, et al., 2020;
354 Ammar, Trabelsi, Müller, et al., 2020; Hein, Whyte, Wood, Rodriguez-Mateos, & Williams,
355 2019; Travica et al., 2019). The single SLR of RCTs and cohort studies on mental health
356 explored the effect of supplements and specific biophenol-containing food categories within
357 the Mediterranean diet, and found significant reductions in depressive symptoms (Bayes,
358 Schloss, & Sibbritt, 2020). A single SLR of RCTs found curcumin reduced depressive
359 symptoms (Ng, Koh, Chan, & Ho, 2017)

360 *Effect on immune function and inflammation*

361 The effect of supplementation with or without biophenol-rich foods on immune function and
362 inflammation was predominantly based on flavonoid-specific interventions (Peluso,
363 Raguzzini, & Serafini, 2013; Somerville, Braakhuis, & Hopkins, 2016; Speer et al., 2019;
364 Suen, Thomas, Kranz, Vun, & Miller, 2016). The effects of flavonoids tended to favor
365 reductions in at least one inflammatory and or oxidative stress markers analyzed (Peluso et

366 al., 2013; Speer et al., 2019; Suen et al., 2016); however, one meta-analysis found no
367 difference between intervention and control for immune function (Somerville et al., 2016).

368 *Individual biophenols*

369 Briefly, regarding SLRs solely on individual biophenols: curcumin reduced depressive
370 symptoms (Ng et al., 2017) and TNF- α concentration (Sahebkar, Cicero, Simental-Mendía,
371 Aggarwal, & Gupta, 2016), but did not affect lipid levels (Sahebkar, 2014). Hesperidin
372 improved vascular cell adhesion molecule 1 but no other inflammatory markers (Lorzadeh,
373 Ramezani-Jolfaie, Mohammadi, Khoshbakht, & Salehi-Abargouei, 2019), improved
374 endothelial function but no other biomarkers (Pla-Pagà et al., 2019), and had no effect on
375 lipids, blood pressure (Mohammadi, Ramezani-Jolfaie, Lorzadeh, Khoshbakht, & Salehi-
376 Abargouei, 2019), or blood glucose (Shams-Rad et al., 2020). Anthocyanin was inversely
377 associated with both coronary heart disease and cardiovascular disease mortality but not
378 myocardial infarction, stroke, or total cardiovascular disease in cohort studies (Kimble,
379 Keane, Lodge, & Howatson, 2019), it improved markers of cardiovascular disease in RCTs
380 (Wallace, Slavin, & Frankenfeld, 2016), and showed promising results on cognitive function
381 (Kent, Charlton, Netzel, & Fanning, 2017). Flavan-3-ols improved cardiometabolic outcomes
382 (Raman et al., 2019). Specifically, flavanols, flavanols, flavan-3-ols and isoflavones were
383 inversely associated with T2DM risk (H. Xu et al., 2018); quercetin reduced blood pressure
384 (Serban et al., 2016) but did not affect lipid levels (Sahebkar, 2017); resveratrol did not
385 improve markers of oxidative stress apart from improving total antioxidant capacity (Koushki
386 et al., 2020), but found improvements in cardiometabolic biomarkers as an adjunct to
387 pharmacological management of T2DM (Hausenblas, Schoulda, & Smoliga, 2015), and did
388 not reduce weight in overweight/obese people, but provided anti-inflammatory effects
389 (Christenson et al., 2016).

390 ***Health effects of phytosterols***

391 24 SLRs were identified and included: two SLRs of cohort and case/control studies, and 22
392 SLRs of RCTs (Table S14). Included studies ranged in duration from 3 weeks up to a year,
393 and most studies included foods fortified with plant sterols, or a tablet or capsule based
394 supplement of either plant sterols or plant stanols. Doses ranged from 0.1 to 9.0 g/day, with
395 the majority using doses between 1.5 and 4.0 g/day. Findings are reported according to the
396 health outcome below.

397 *Effect on cardiovascular outcomes*

398 Supplementation with phytosterols had a strong and consistent improvement on LDL
399 cholesterol where most SLRs reported a decrease of LDL-cholesterol of 0.31-0.38 mmol/L.
400 Effect sizes for LDL-cholesterol were comparable when phytosterols were delivered as
401 fortified foods or as capsules consumed with food (AbuMweis, Barake, & Jones, 2008; Amir
402 Shaghaghi, Abumweis, & Jones, 2013). The effect size in participants on statins was similar
403 to those not on statins (Han et al., 2016; Scholle, Baker, Talati, & Coleman, 2009). There was
404 a marginal decrease in triglycerides in one SLR (Wu, Fu, Yang, Zhang, & Han, 2009) but
405 more frequently no effect was found (Baker, Baker, & Coleman, 2009; Chung et al., 2020;
406 Del Bo et al., 2019; Han et al., 2016; Huang, Frohlich, & Ignaszewski, 2011; Moruisi,
407 Oosthuizen, & Opperman, 2006; Scholle et al., 2009), and no effect on HDL was noted in
408 any of the SLRs.

409 Two SLRs reported dose-response relationships between phytosterols and LDL-cholesterol
410 (Demonty et al., 2009; Ras, Geleijnse, & Trautwein, 2014), and one SLR compared high
411 (>2.5 g/day) vs low (<1.5 g/day) dose in a sub-group analysis (AbuMweis et al., 2008). There
412 was evidence of a dose-response reduction in LDL cholesterol up to doses of 3 g/day, where

413 effects appeared to plateau, and no further reductions in LDL cholesterol were observed. A
414 minimum effective dose could not be determined from the included SLRs.

415 There was some evidence that plant sterols delivered in solid foods or foods which are higher
416 in fat (e.g. fat spreads, yoghurt, salad dressings) may be more efficacious than liquid
417 mediums at lowering LDL cholesterol; however, this was inconsistent and subject to
418 heterogeneity (AbuMweis et al., 2008; Ras et al., 2014). One SLR found that phytosterols
419 fortified in a rapeseed (canola) oil medium lowered LDL cholesterol by an additional 0.1
420 mmol/L compared to a sunflower oil medium (Ferguson, Stojanovski, MacDonald-Wicks, &
421 Garg, 2016).

422 One SLR directly compared the effect of plant sterols versus plant stanols on LDL
423 cholesterol levels (Talati, Sobieraj, Makanji, Phung, & Coleman, 2010). At doses of up to
424 2.5g/day, there was no evidence of a statistical or clinical difference in their efficacy of
425 lowering LDL cholesterol levels. There was also no evidence that plant sterol structure (e.g.
426 ester, free sterols) influenced the effect size or function (AbuMweis et al., 2008; Amir
427 Shaghaghi et al., 2013).

428 Only one SLR investigated the contribution of individual plant sterols in sub-group analysis,
429 and compared high sitosterol/stanol (>80% sitosterol/sitostanol content) to low
430 sitosterol/stanol phytosterols. Both formations lowered LDL cholesterol, with the high
431 sitosterol/stanol group showing a significantly greater reduction.

432 *Effect on body composition*

433 One SLR investigated phytosterol effects on body composition and found there was no
434 evidence of an effect of plant sterols on body weight, fat mass, or waist circumference
435 (Ghaedi, Varkaneh, et al., 2019). There was a small decrease in BMI in the meta-analysis;

436 however, this was largely driven by only two studies, with the majority of studies showing no
437 effect (Ghaedi, Varkaneh, et al., 2019).

438 *Effect on blood pressure.* One SLR investigated phytosterol effects on blood pressure
439 (Ghaedi, Foshati, et al., 2019). There were small significant reductions in both systolic (-
440 1.55mmHg, 95%CI: -2.67, -0.42) and diastolic (-0.84mmHg, 95%CI: -1.6, -0.08) blood
441 pressure observed. However, the effects were largely driven by only a few included studies,
442 and thus should be interpreted cautiously.

443 *Effect on inflammation*

444 C-reactive protein (CRP) was the only inflammatory marker reported but an effect was not
445 seen in the healthy sample (Rocha et al., 2016).

446 *Effect on cancer risk*

447 There was a decreased incidence of cancer in adults with the highest dietary intake of
448 phytosterols reported in a single SLR (Jiang et al., 2019).

449 ***Health effects of squalene***

450 No SLRs and one 20-week double-blind placebo-controlled RCT was identified (Chan,
451 Tomlinson, Lee, & Lee, 1996) (Table S15). The trial included four study arms: i) Squalene
452 stand-alone (860mg/day), ii) Pravastatin stand-alone (10mg/day), iii) Combination of Squalene
453 and Pravastatin, iv) placebo.

454

455 Squalene consumed in capsule form reduced total cholesterol (17% compared to baseline, $p <$
456 0.05) and LDL cholesterol (22% compared baseline, $p < 0.05$) significantly more than
457 placebo but less than Pravastatin as stand-alone treatments (Chan et al., 1996). The
458 combination of squalene and Pravastatin had greatest effect on total cholesterol, LDL
459 cholesterol, and HDL cholesterol than stand-alone treatments or placebo.

460 **Discussion**

461 This critical review describes the key nutrients and bioactive components in edible oils and
462 fats and their associations with high burden chronic diseases. The results show that edible oils
463 and fats contain chemical properties which affect human health well beyond their SFA
464 content; therefore, the findings demand dietary guidelines reconsider how edible oils and fats
465 are judged. The total fatty acid composition, biophenols, and phytosterols all have well
466 established favorable associations on chronic disease outcomes. There is further emerging
467 evidence that dietary α -tocopherol, but not γ -tocopherol, and squalene may have beneficial
468 effects on risk of chronic disease.

469 The greatest limitation within identified studies for fatty acids is conflicting results,
470 particularly between SLRs of cohort studies and SLRs of RCTs. RCTs and SLRs are needed
471 which compare MUFA (particularly oleic acid) against non-marine PUFA (particularly LA).
472 In addition, a shift is required from viewing fatty acids, and their categories, as only
473 influencing cardiovascular risk, and understanding their potential influence on other high-
474 burden diseases such as diabetes, mental health, and dementia.

475 The literature around dietary intake and blood levels of tocopherols, particularly of α -
476 tocopherol, is promising. For example, dose-response meta-analyses of dietary vitamin E
477 cohort studies suggest that 30IU/day (20-27mg/day) incremental increases are associated
478 with a 4% decreased risk of coronary heart disease (Ye & Song, 2008), and 10mg/day
479 incremental increases are associated with a 17% reduced risk of bladder cancer (Chen et al.,
480 2015). These values suggest edible oils could contribute to the health benefits of vitamin E/ α -
481 tocopherol as sunflower, rice bran, cottonseed, corn kernel, safflower, and extra virgin olive
482 oil (EVOO) all have >20mg/100ml (range 22.4 to 51.5mg/100ml; Table S5) of α -tocopherol.
483 Consideration is also needed for γ -tocopherol content, which is present in substantial

484 quantities in canola, soybean and corn oils, as this was linked to an increased risk of both
485 coronary heart disease and bladder cancer (Chen et al., 2015; Irawati et al., 2019). However,
486 further research is needed to examine the effect of increasing dietary α -tocopherol and
487 decreasing γ -tocopherol on blood levels and subsequent disease risk.

488 Total biophenols and flavonoids were consistently linked with beneficial health outcomes in
489 SLRs across a range of high-burden health diseases. Greater exploration into the dose
490 requirements is needed given the large range of doses reported. The SLRs of RCTs which
491 utilized supplements may not be directly applicable to the biophenol content in edible oils;
492 however, are supported cohort study evidence. Despite potential accuracy limitations for
493 biophenol intake assessment within cohort studies, strong favourable evidence was found for
494 high biophenol olive oil compared to low biophenol olive oil across three SLRs (George et
495 al., 2019; Hohmann et al., 2015; Lukas Schwingshackl et al., 2019). Directly applicable to
496 judging edible oils, 25ml-70g per day of high biophenol olive oil or 3.4-31mg biophenols
497 from extra virgin olive oil had clear health benefits to cardiovascular health compared to
498 refined olive oil (George et al., 2019; Hohmann et al., 2015).

499 There was strong and consistent evidence of an LDL-lowering effect of phytosterols in a
500 dose-dependent manner for up to 3g/day delivered in food or supplements. These findings
501 were consistent in SLRs which included only high-quality studies. As some of the SLRs
502 included people without hypercholesterolemia, the findings on LDL cholesterol are largely
503 generalizable, but the doses identified (>1000mg/day) were generally well above that
504 obtained from consuming edible oils (\leq 185mg/100g). However, it is possible that an effect is
505 seen at lower doses, as an SLR of phytosterols in tree nuts, which used a dose range of 4.8-
506 279mg/day, lowered LDL cholesterol, and phytosterol intake was inversely correlated with
507 the change in LDL cholesterol (Del Gobbo, Falk, Feldman, Lewis, & Mozaffarian, 2015).

508 Further, edible oils and fats are a part of the whole diet, and should be considered together
509 with other sources of phytosterols recommended in dietary guidelines, such as fruits and
510 vegetables.

511 The literature on squalene was mostly limited to theoretical models, in-vitro studies, and
512 animal studies (Ibrahim, Fairus, Zulfarina, & Naina Mohamed, 2020; Lou-Bonafonte et al.,
513 2018). This pre-clinical evidence suggested a role for squalene in humans as an antioxidant,
514 anticancer, anti-atherosclerotic, and anti-inflammatory agent, but human data are lacking.

515 While squalene may hold promise for human health, there is currently insufficient evidence
516 to confirm health effects and dosage required; and if it has any effect when consumed as part
517 of the diet as opposed to a pharmaceutical agent. The dosage used in the single identified
518 RCT (Nergiz & Çelikkale, 2011) was substantially higher than that which would be typically
519 obtained from edible oils: 175g of EVOO per day would be required. Further, outside edible
520 oils, the only known dietary source is shark liver oil, and therefore intake from edible oils and
521 fats would not be supported by intakes from other food groups in the dietary guidelines.

522 Although SLRs of RCTs which used fortification- or supplementation-based interventions
523 frequently used doses which could not be achieved through usual dietary intake; though
524 dietary guidelines typically do not only include foods which provide 100% of requirements.
525 Demonstrating positive associations of edible oil components with health outcomes
526 strengthens the argument that edible oils and fats form part of a healthy diet for populations
527 and could be considered a core food rather than an allowance if judged on their full fatty acid
528 profile, α -tocopherol, biophenol, and phytosterol content.

529 **Limitations**

530 This umbrella review was not able to draw upon all available literature, using a hierarchy of
531 study designs, and a limited search strategy so as to focus the vast and exhaustive research

532 available. This umbrella review used transparent and comprehensive methodology; however,
533 due to the broad searching and reviewing required to answer the research questions, did not
534 use systematic review methodology such as searching four or more databases or duplicate
535 screening. Methodology within studies and food composition databases appeared to differ for
536 the different sources, and some may be outdated as highlighted summary tables.

537 **Conclusion**

538 A shift in how we judge edible oils and fats is required from judging based on their SFA
539 content alone, to instead considering if they may be included as part of a healthy diet based
540 on the full nutrient and bioactive component profile of each edible oil and fat; supported by
541 potential health benefits beyond CVD including mortality, T2DM, cancer, inflammation,
542 mental health, and cognition. This may also have flow on effects on how diet quality is
543 judged in clinical practice, in research, and in epidemiology; and in how nutrient profiling
544 and food rating systems are applied globally.

545

546 **Acknowledgements:** The authors would like to acknowledge Jacqui Plozza, Sarah Gray , and
547 Leandro Ravetti from Boundary Bend Ltd their contribution to the stakeholder consultation
548 and for providing top suggestions on the proposed methodology.

549

550 **Disclaimer:** All authors work independently work for Nutrition Research Australia, which is
551 funded by government, not-for-profits, professional, community, and industry organisations.
552 All authors declare no conflicts of interest. The funding body, Boundary Bend Pty Ltd
553 contributed to the study concept, provided stakeholder consultation, and advised on the top
554 line eligibility criteria; but had no role in the drafting or revision of the manuscript.

References

- (FSANZ), F. S. A. a. N. Z. (2019). Australian Food Composition Database (Publication no. <https://www.foodstandards.gov.au/science/monitoringnutrients/afcd/Pages/default.aspx>). from FSANZ
- (NHMRC), N. H. a. M. R. C. (2013). *National Dietary Guidelines*. Retrieved from Canberra: www.eatforhealth.gov.au
- (USDA), U. S. D. o. A. (2019). Agricultural Research Service: FoodData Central. Retrieved from <https://fdc.nal.usda.gov>. from USDA <https://fdc.nal.usda.gov>
- AbuMweis, S. S., Barake, R., & Jones, P. J. H. (2008). Plant sterols/stanols as cholesterol lowering agents: A meta-analysis of randomized controlled trials. *Food & Nutrition Research, 0*(52). doi:10.3402/fnr.v52i0.1811
- Afshin, A., Sur, P. J., Fay, K. A., Cornaby, L., Ferrara, G., Salama, J. S., . . . Abebe, Z. (2019). Health effects of dietary risks in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet, 393*(10184), 1958-1972.
- Agriculture., U. S. D. o. H. a. H. S. a. U. S. D. o. (2015). 2015–2020 Dietary Guidelines for Americans. 8th Edition. December 2015. Available at <http://health.gov/dietaryguidelines/2015/guidelines/>.
- Akhlaghi, M., Ghobadi, S., Hosseini, M. M., Gholami, Z., & Mohammadian, F. (2018). Flavanols are potential anti-obesity agents, a systematic review and meta-analysis of controlled clinical trials. *Nutr Metab Cardiovasc Dis, 28*(7), 675-690.
- Amiot, M. J., Riva, C., & Vinet, A. (2016). Effects of dietary polyphenols on metabolic syndrome features in humans: a systematic review. *Obes Rev, 17*(7), 573-586.
- Amir Shaghghi, M., Abumweis, S. S., & Jones, P. J. (2013). Cholesterol-lowering efficacy of plant sterols/stanols provided in capsule and tablet formats: results of a systematic review and meta-analysis. *J Acad Nutr Diet, 113*(11), 1494-1503. doi:10.1016/j.jand.2013.07.006 %M 24144075
- Ammar, A., Trabelsi, K., Boukhris, O., Bouaziz, B., Müller, P., M Glenn, J., . . . Driss, T. (2020). Effects of Polyphenol-Rich Interventions on Cognition and Brain Health in Healthy Young and Middle-Aged Adults: Systematic Review and Meta-Analysis. *J Clin Med, 9*(5), 1598.

- Ammar, A., Trabelsi, K., Müller, P., Bouaziz, B., Boukhris, O., Glenn, J. M., . . . Müller, N. (2020). The Effect of (Poly) phenol-Rich Interventions on Cognitive Functions and Neuroprotective Measures in Healthy Aging Adults: A Systematic Review and Meta-Analysis. *J Clin Med*, *9*(3), 835.
- Aronis, K. N., Khan, S. M., & Mantzoros, C. S. (2012). Effects of trans fatty acids on glucose homeostasis: a meta-analysis of randomized, placebo-controlled clinical trials. *Am J Clin Nutr*, *96*(5), 1093-1099.
- Aune, D., Keum, N., Giovannucci, E., Fadnes, L. T., Boffetta, P., Greenwood, D. C., . . . Norat, T. (2018). Dietary intake and blood concentrations of antioxidants and the risk of cardiovascular disease, total cancer, and all-cause mortality: a systematic review and dose-response meta-analysis of prospective studies. *Am J Clin Nutr*, *108*(5), 1069-1091.
- Australian Dietary Guidelines*. (2013). Retrieved from Canberra:
- Baker, W. L., Baker, E. L., & Coleman, C. I. (2009). The effect of plant sterols or stanols on lipid parameters in patients with type 2 diabetes: a meta-analysis. *Diabetes Res Clin Pract*, *84*(2), e33-37.
doi:10.1016/j.diabres.2009.01.015 %M 19243852
- Bayes, J., Schloss, J., & Sibbritt, D. (2020). Effects of Polyphenols in a Mediterranean Diet on Symptoms of Depression: A Systematic Literature Review. *Adv Nutr*, *11*(3), 602-615.
- Bedell, B. A., & Shackleton, P. A. (1989). The relationship between a nutrition education program and nutrition knowledge and eating behaviors of the elderly. *Journal of Nutrition for the Elderly*, *8*(3-4), 35-45.
Retrieved from <http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/052/CN-00062052/frame.html>. (Accession No. CN-00062052)
- Brennan, S. F., Woodside, J. V., Lunny, P. M., Cardwell, C. R., & Cantwell, M. M. (2017). Dietary fat and breast cancer mortality: a systematic review and meta-analysis. *Crit Rev Food Sci Nutr*, *57*(10), 1999-2008.
- Cao, Y., Hou, L., & Wang, W. (2016). Dietary total fat and fatty acids intake, serum fatty acids and risk of breast cancer: A meta-analysis of prospective cohort studies. *Int J Cancer*, *138*(8), 1894-1904.
- Chan, P., Tomlinson, B., Lee, C. B., & Lee, Y. S. (1996). Effectiveness and safety of low-dose pravastatin and squalene, alone and in combination, in elderly patients with hypercholesterolemia. *J Clin Pharmacol*, *36*(5), 422-427.
- Chen, F., Li, Q., Yu, Y., Yang, W., Shi, F., & Qu, Y. (2015). Association of vitamin C, vitamin D, vitamin E and risk of bladder cancer: a dose-response meta-analysis. *Sci Rep*, *5*, 9599.

- Chowdhury, R., Warnakula, S., Kunutsor, S., Crowe, F., Ward, H. A., Johnson, L., . . . Thompson, S. G. (2014). Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. *Ann Intern Med*, *160*(6), 398-406.
- Christenson, J., Whitby, S. J., Mellor, D., Thomas, J., McKune, A., Roach, P. D., & Naumovski, N. (2016). The effects of resveratrol supplementation in overweight and obese humans: a systematic review of randomized trials. *Metab Syndr Relat Disord*, *14*(7), 323-333.
- Chung, M., Zhao, N., Wang, D., Shams-White, M., Karlsen, M., Cassidy, A., . . . Wallace, T. C. (2020). Dose–response relation between tea consumption and risk of cardiovascular disease and all-cause mortality: a systematic review and meta-analysis of population-based studies. *Adv Nutr*, [Epub ahead of print 19 Feb 2020; doi: 10.1093/advances/nmaa010].
- Clifton, P. M., & Keogh, J. B. (2017). A systematic review of the effect of dietary saturated and polyunsaturated fat on heart disease. *Nutr Metab Cardiovasc Dis*, *27*(12), 1060-1080.
- Coe, S., & Ryan, L. (2016). Impact of polyphenol-rich sources on acute postprandial glycaemia: a systematic review. *J Nutr Sci*, *5* e24.
- Committee, D. G. A. (2020). Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.
- de Oliveira, B. G. R. B. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.
- De Souza, R. J., Mente, A., Maroleanu, A., Cozma, A. I., Ha, V., Kishibe, T., . . . Beyene, J. (2015). Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *BMJ*, *351*, h3978.
- Del Bo, C., Bernardi, S., Marino, M., Porrini, M., Tucci, M., Guglielmetti, S., . . . Kroon, P. (2019). Systematic review on polyphenol intake and health outcomes: is there sufficient evidence to define a health-promoting polyphenol-rich dietary pattern? *Nutrients*, *11*(6), 1355.
- Del Gobbo, L. C., Falk, M. C., Feldman, R., Lewis, K., & Mozaffarian, D. (2015). Are Phytosterols Responsible for the Low-Density Lipoprotein-Lowering Effects of Tree Nuts?: A Systematic Review and Meta-Analysis. *J Am Coll Cardiol*, *65*(25), 2765-2767. doi:10.1016/j.jacc.2015.03.595 %M 26112204

- Demonty, I., Ras, R. T., van der Knaap, H. C., Duchateau, G. S., Meijer, L., Zock, P. L., . . . Trautwein, E. A. (2009). Continuous dose-response relationship of the LDL-cholesterol-lowering effect of phytosterol intake. *J Nutr*, *139*(2), 271-284. doi:10.3945/jn.108.095125 %M 19091798
- Ellwood, L., Torun, G., Bahar, Z., & Fernandez, R. (2019). Effects of flavonoid-rich fruits on hypertension in adults: a systematic review. *JBI Database System Rev Implement Rep*, *17*(10), 2075-2105.
- England, P. H. (2018). The Eatwell Guide. Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/742750/Eatwell_Guide_booklet_2018v4.pdf
- Farhat, G., Drummond, S., & Al-Dujaili, E. A. S. (2017). Polyphenols and their role in obesity management: a systematic review of randomized clinical trials. *Phytother Res*, *31*(7), 1005-1018.
- Farvid, M. S., Ding, M., Pan, A., Sun, Q., Chiuve, S. E., Steffen, L. M., . . . Hu, F. B. (2014). Dietary linoleic acid and risk of coronary heart disease: a systematic review and meta-analysis of prospective cohort studies. *Circulation*, *130*(18), 1568-1578.
- Ferguson, J. J., Stojanovski, E., MacDonald-Wicks, L., & Garg, M. L. (2016). Fat type in phytosterol products influence their cholesterol-lowering potential: A systematic review and meta-analysis of RCTs. *Prog Lipid Res*, *64*, 16-29. doi:10.1016/j.plipres.2016.08.002 %M 27497855
- Foster, R. H., & Wilson, N. (2013). Review of the evidence for the potential impact and feasibility of substituting saturated fat in the New Zealand diet. *Aust N Z J Pub Health*, *37*(4), 329-336.
- Gayet-Boyer, C., Tenenhaus-Aziza, F., Prunet, C., Marmonier, C., Malpuech-Brugere, C., Lamarche, B., & Chardigny, J.-M. (2014). Is there a linear relationship between the dose of ruminant trans-fatty acids and cardiovascular risk markers in healthy subjects: results from a systematic review and meta-regression of randomised clinical trials. *Br J Nutr*, *112*(12), 1914-1922.
- George, E. S., Marshall, S., Mayr, H. L., Trakman, G. L., Tatucu-Babet, O. A., Lassemillante, A.-C. M., . . . Tierney, A. C. (2019). The effect of high-polyphenol extra virgin olive oil on cardiovascular risk factors: A systematic review and meta-analysis. *Crit Rev Food Sci Nutr*, *59*(17), 2772-2795.
- Ghaedi, E., Foshati, S., Ziaei, R., Beigrezaei, S., Kord-Varkaneh, H., Ghavami, A., & Miraghajani, M. (2019). Effects of phytosterols supplementation on blood pressure: A systematic review and meta-analysis. *Clin Nutr*. doi:10.1016/j.clnu.2019.12.020

- Ghaedi, E., Varkaneh, H. K., Rahmani, J., Mousavi, S. M., Mohammadi, H., Fatahi, S., . . . Zhang, Y. (2019). Possible anti-obesity effects of phytosterols and phytostanols supplementation in humans: A systematic review and dose-response meta-analysis of randomized controlled trials. *Phytother Res*, 33(5), 1246-1257. doi:10.1002/ptr.6319
- Glanz, K., & Scharf, M. (1985). A nutrition training program for social workers serving the homebound elderly. *Gerontologist*, 25(5), 455-459. Retrieved from <http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=1986049959&site=ehost-live>
- Godos, J., Vitale, M., Micek, A., Ray, S., Martini, D., Del Rio, D., . . . Grosso, G. (2019). Dietary polyphenol intake, blood pressure, and hypertension: A systematic review and Meta-Analysis of observational studies. *Antioxidants*, 8(6), 152.
- Government, A. (2020). Review of the Australian Dietary Guidelines: living well for longer. Retrieved from <https://www.health.gov.au/ministers/the-hon-greg-hunt-mp/media/review-of-the-australian-dietary-guidelines-living-well-for-longer>
- Grosso, G., Godos, J., Lamuela-Raventos, R., Ray, S., Micek, A., Pajak, A., . . . Galvano, F. (2017). A comprehensive meta-analysis on dietary flavonoid and lignan intake and cancer risk: Level of evidence and limitations. *Mol Nutr Food Res*, 61(4), 1600930.
- Grosso, G., Micek, A., Godos, J., Pajak, A., Sciacca, S., Galvano, F., & Giovannucci, E. L. (2017). Dietary flavonoid and lignan intake and mortality in prospective cohort studies: Systematic review and dose-response meta-analysis. *Am J Epidemiol*, 185(12), 1304-1316.
- Haghighatdoost, F., & Gh, B. F. N. M. (2018). Effect of conjugated linoleic acid on blood inflammatory markers: a systematic review and meta-analysis on randomized controlled trials. *Eur J Clin Nutr*, 72(8), 1071-1082.
- Hamley, S. (2017). The effect of replacing saturated fat with mostly n-6 polyunsaturated fat on coronary heart disease: a meta-analysis of randomised controlled trials. *Nutr J*, 16(1), 30.
- Han, S., Jiao, J., Xu, J., Zimmermann, D., Actis-Goretta, L., Guan, L., . . . Qin, L. (2016). Effects of plant stanol or sterol-enriched diets on lipid profiles in patients treated with statins: systematic review and meta-analysis. *Sci Rep*, 6, 31337. doi:10.1038/srep31337 %2 PMC4990897 Lausanne. L. Guan and Y.Y. Zhao

are employees of Nestlé Research Centre Beijing. The other authors declare that they have no competing financial interest. %M 27539156

- Harcombe, Z., Baker, J. S., & Davies, B. (2017). Evidence from prospective cohort studies does not support current dietary fat guidelines: a systematic review and meta-analysis. *Br J Sports Med*, *51*(24), 1743-1749.
- Hausenblas, H. A., Shoulada, J. A., & Smoliga, J. M. (2015). Resveratrol treatment as an adjunct to pharmacological management in type 2 diabetes mellitus—systematic review and meta-analysis. *Mol Nutr Food Res*, *59*(1), 147-159.
- He, X., & Sun, L.-m. (2016). Dietary intake of flavonoid subclasses and risk of colorectal cancer: evidence from population studies. *Oncotarget*, *7*(18), 26617.
- Hein, S., Whyte, A. R., Wood, E., Rodriguez-Mateos, A., & Williams, C. M. (2019). Systematic review of the effects of blueberry on cognitive performance as we age. *J Gerontol A Biol Sci Med Sci*, *74*(7), 984-995.
- Hohmann, C.-D., Cramer, H., Michalsen, A., Kessler, C., Steckhan, N., Choi, K., & Dobos, G. (2015). Effects of high phenolic olive oil on cardiovascular risk factors: A systematic review and meta-analysis. *Phytomedicine*, *22*(6), 631-640.
- Hooper, L., Al-Khudairy, L., Abdelhamid, A. S., Rees, K., Brainard, J. S., Brown, T. J., . . . Donaldson, D. H. (2018). Omega-6 fats for the primary and secondary prevention of cardiovascular disease. *Cochrane Database Syst Rev*, *7*(7), CD011094.
- Hooper, L., Kroon, P. A., Rimm, E. B., Cohn, J. S., Harvey, I., Le Cornu, K. A., . . . Cassidy, A. (2008). Flavonoids, flavonoid-rich foods, and cardiovascular risk: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*, *88*(1), 38-50.
- Hooper, L., Summerbell, C. D., Thompson, R., Sills, D., Roberts, F. G., Moore, H. J., & Davey, S. G. (2012). Reduced or modified dietary fat for preventing cardiovascular disease. *Cochrane Database of Systematic Reviews*, (5). doi:10.1002/14651858.CD002137.pub3. (Accession No. CD002137)
- Huang, J., Frohlich, J., & Ignaszewski, A. P. (2011). The impact of dietary changes and dietary supplements on lipid profile. *Can J Cardiol*, *27*(4), 488-505. doi:10.1016/j.cjca.2010.12.077 %M 21801978

- Hunter, J. E., Zhang, J., & Kris-Etherton, P. M. (2010). Cardiovascular disease risk of dietary stearic acid compared with trans, other saturated, and unsaturated fatty acids: a systematic review. *Am J Clin Nutr*, *91*(1), 46-63.
- Ibrahim, N. I., Fairus, S., Zulfarina, M. S., & Naina Mohamed, I. (2020). The Efficacy of Squalene in Cardiovascular Disease Risk-A Systematic Review. *Nutrients*, *12*(2), 414.
- INRA. (2015). Phenol-Explorer 3.6: Polyphenols. Retrieved from <http://phenol-explorer.eu>. from INRA <http://phenol-explorer.eu>
- Irawati, S., Wasir, R., Floriaan Schmidt, A., Islam, A., Feenstra, T., Buskens, E., . . . Hak, E. (2019). Long-term incidence and risk factors of cardiovascular events in Asian populations: systematic review and meta-analysis of population-based cohort studies. *Curr Med Res Opin*, *35*(2), 291-299.
- Jayedi, A., Rashidy-Pour, A., Parohan, M., Zargar, M. S., & Shab-Bidar, S. (2018). Dietary antioxidants, circulating antioxidant concentrations, total antioxidant capacity, and risk of all-cause mortality: a systematic review and dose-response meta-analysis of prospective observational studies. *Adv Nutr*, *9*(6), 701-716.
- Jayedi, A., Rashidy-Pour, A., Parohan, M., Zargar, M. S., & Shab-Bidar, S. (2019). Dietary and circulating vitamin C, vitamin E, β -carotene and risk of total cardiovascular mortality: a systematic review and dose-response meta-analysis of prospective observational studies. *Pub Health Nutr*, *22*(10), 1872-1887.
- JBIM Manual for Evidence Synthesis*. (2020). JBI.
- Jiang, L., Zhao, X., Xu, J., Li, C., Yu, Y., Wang, W., & Zhu, L. (2019). The Protective Effect of Dietary Phytosterols on Cancer Risk: A Systematic Meta-Analysis. *J Oncol*, *2019*, 7479518. doi:10.1155/2019/7479518 %2 pmc6612402 %m 31341477
- Kay, C. D., Hooper, L., Kroon, P. A., Rimm, E. B., & Cassidy, A. (2012). Relative impact of flavonoid composition, dose and structure on vascular function: a systematic review of randomised controlled trials of flavonoid-rich food products. *Mol Nutr Food Res*, *56*(11), 1605-1616.
- Kent, K., Charlton, K. E., Netzel, M., & Fanning, K. (2017). Food-based anthocyanin intake and cognitive outcomes in human intervention trials: a systematic review. *J Hum Nutr Diet*, *30*(3), 260-274.
- Kim, M., & Park, K. (2018). Dietary fat intake and risk of colorectal cancer: a systematic review and meta-analysis of prospective studies. *Nutrients*, *10*(12), 1963.

- Kim, Y., & Je, Y. (2017). Flavonoid intake and mortality from cardiovascular disease and all causes: A meta-analysis of prospective cohort studies. *Clin Nutr ESPEN*, 20, 68-77.
- Kimble, R., Keane, K. M., Lodge, J. K., & Howatson, G. (2019). Dietary intake of anthocyanins and risk of cardiovascular disease: A systematic review and meta-analysis of prospective cohort studies. *Crit Rev Food Sci Nutr*, 59(18), 3032-3043.
- Koushki, M., Lakzaei, M., Khodabandehloo, H., Hosseini, H., Meshkani, R., & Panahi, G. (2020). Therapeutic effect of resveratrol supplementation on oxidative stress: a systematic review and meta-analysis of randomised controlled trials. *Postgrad Med J*, 96(1134), 197-205.
- Kris-Etherton, P. M., Hecker, K. D., Bonanome, A., Coval, S. M., Binkoski, A. E., Hilpert, K. F., . . . Etherton, T. D. (2002). Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. *The American journal of medicine*, 113(9), 71-88.
- Kyu, H. H., Abate, D., Abate, K. H., Abay, S. M., Abbafati, C., Abbasi, N., . . . Abdelalim, A. (2018). Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*, 392(10159), 1859-1922.
- Li, P., Zhang, H., Chen, J., Shi, Y., Cai, J., Yang, J., & Wu, Y. (2014). Association between dietary antioxidant vitamins intake/blood level and risk of gastric cancer. *Int J Cancer*, 135(6), 1444-1453.
- Liu, X. m., Liu, Y. j., Huang, Y., Yu, H. j., Yuan, S., Tang, B. w., . . . He, Q. q. (2017). Dietary total flavonoids intake and risk of mortality from all causes and cardiovascular disease in the general population: A systematic review and meta-analysis of cohort studies. *Mol Nutr Food Res*, 61(6), 1601003.
- Liu, Y.-J., Zhan, J., Liu, X.-L., Wang, Y., Ji, J., & He, Q.-Q. (2014). Dietary flavonoids intake and risk of type 2 diabetes: a meta-analysis of prospective cohort studies. *Clin Nutr*, 33(1), 59-63.
- Longnecker, M. P., Martin-Moreno, J.-M., Knekt, P., Nomura, A. M. Y., Schober, S. E., Stähelin, H. B., . . . Willett, W. C. (1992). Serum α -tocopherol concentration in relation to subsequent colorectal cancer: pooled data from five cohorts. *J Natl Cancer Inst*, 84(6), 430-435.
- Lorzadeh, E., Ramezani-Jolfaie, N., Mohammadi, M., Khoshbakht, Y., & Salehi-Abargouei, A. (2019). The effect of hesperidin supplementation on inflammatory markers in human adults: A systematic review and meta-analysis of randomized controlled clinical trials. *Chem Biol Interact*, 307, 8-15.

- Lou-Bonafonte, J. M., Martínez-Beamonte, R., Sanclemente, T., Surra, J. C., Herrera-Marcos, L. V., Sanchez-Marco, J., . . . Osada, J. (2018). Current insights into the biological action of squalene. *Mol Nutr Food Res*, *62*(15), 1800136.
- Marx, W., Kelly, J., Marshall, S., Nakos, S., Campbell, K., & Itsiopoulos, C. (2017). The effect of polyphenol-rich interventions on cardiovascular risk factors in haemodialysis: A systematic review and meta-analysis. *Nutrients*, *9*(12), 1345.
- Mensink, R. P., Zock, P. L., Kester, A. D. M., & Katan, M. B. (2003). Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr*, *77*(5), 1146-1155.
- Miura, K., & Green, A. C. (2015). Dietary antioxidants and melanoma: evidence from cohort and intervention studies. *Nutr Cancer*, *67*(6), 867-876.
- Mohammadi, M., Ramezani-Jolfaie, N., Lorzadeh, E., Khoshbakht, Y., & Salehi-Abargouei, A. (2019). Hesperidin, a major flavonoid in orange juice, might not affect lipid profile and blood pressure: A systematic review and meta-analysis of randomized controlled clinical trials. *Phytother Res*, *33*(3), 534-545.
- Moruisi, K. G., Oosthuizen, W., & Opperman, A. M. (2006). Phytosterols/stanols lower cholesterol concentrations in familial hypercholesterolemic subjects: a systematic review with meta-analysis. *J Am Coll Nutr*, *25*(1), 41-48. doi:10.1080/07315724.2006.10719513 %m 16522931
- Muley, A., Muley, P., & Shah, M. (2014). ALA, fatty fish or marine n-3 fatty acids for preventing DM?: a systematic review and meta-analysis. *Curr Diab Rev*, *10*(3), 158-165.
- Nergiz, C., & Çelikkale, D. (2011). The effect of consecutive steps of refining on squalene content of vegetable oils. *J Food Sci Technol*, *48*(3), 382-385.
- Ng, Q. X., Koh, S. S. H., Chan, H. W., & Ho, C. Y. X. (2017). Clinical use of curcumin in depression: a meta-analysis. *J Am Med Direct Assoc*, *18*(6), 503-508.
- Palma-Duran, S. A., Vlassopoulos, A., Lean, M., Govan, L., & Combet, E. (2017). Nutritional intervention and impact of polyphenol on glycohemoglobin (HbA1c) in non-diabetic and type 2 diabetic subjects: Systematic review and meta-analysis. *Crit Rev Food Sci Nutr*, *57*(5), 975-986.

- Panth, N., Abbott, K. A., Dias, C. B., Wynne, K., & Garg, M. L. (2018). Differential effects of medium-and long-chain saturated fatty acids on blood lipid profile: a systematic review and meta-analysis. *Am J Clin Nutr*, *108*(4), 675-687.
- Peluso, I., Raguzzini, A., & Serafini, M. (2013). Effect of flavonoids on circulating levels of TNF- α and IL-6 in humans: A systematic review and meta-analysis. *Mol Nutr Food Res*, *57*(5), 784-801.
- Pham, N. M., Van Do, V., & Lee, A. H. (2019). Polyphenol-rich foods and risk of gestational diabetes: a systematic review and meta-analysis. *Eur J Clin Nutr*, *73*(5), 647-656.
- Pla-Pagà, L., Companys, J., Calderón-Pérez, L., Llauradó, E., Solà, R., Valls, R. M., & Pedret, A. (2019). Effects of hesperidin consumption on cardiovascular risk biomarkers: a systematic review of animal studies and human randomized clinical trials. *Nutr Rev*, *77*(12), 845-864.
- Potì, F., Santi, D., Spaggiari, G., Zimetti, F., & Zanotti, I. (2019). Polyphenol health effects on cardiovascular and neurodegenerative disorders: A review and meta-analysis. *Int J Mol Sci*, *20*(2), 351.
- Qian, F., Korat, A. A., Malik, V., & Hu, F. B. (2016). Metabolic effects of monounsaturated fatty acid-enriched diets compared with carbohydrate or polyunsaturated fatty acid-enriched diets in patients with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. *Diab Care*, *39*(8), 1448-1457.
- Qiu, W., Lu, H., Qi, Y., & Wang, X. (2016). Dietary fat intake and ovarian cancer risk: a meta-analysis of epidemiological studies. *Oncotarget*, *7*(24), 37390.
- Raman, G., Avendano, E. E., Chen, S., Wang, J., Matson, J., Gayer, B., . . . Cassidy, A. (2019). Dietary intakes of flavan-3-ols and cardiometabolic health: systematic review and meta-analysis of randomized trials and prospective cohort studies. *Am J Clin Nutr*, *110*(5), 1067-1078.
- Ramsden, C. E., Hibbeln, J. R., Majchrzak, S. F., & Davis, J. M. (2010). n-6 fatty acid-specific and mixed polyunsaturate dietary interventions have different effects on CHD risk: a meta-analysis of randomised controlled trials. *Br J Nutr*, *104*(11), 1586-1600.
- Ras, R. T., Geleijnse, J. M., & Trautwein, E. A. (2014). LDL-cholesterol-lowering effect of plant sterols and stanols across different dose ranges: a meta-analysis of randomised controlled studies. *Br J Nutr*, *112*(2), 214-219. doi:10.1017/s0007114514000750 %2 PMC4071994 %M 24780090

- Rienks, J., Barbaresko, J., Oluwagbemigun, K., Schmid, M., & Nöthlings, U. (2018). Polyphenol exposure and risk of type 2 diabetes: dose-response meta-analyses and systematic review of prospective cohort studies. *Am J Clin Nutr*, *108*(1), 49-61.
- Rocha, V. Z., Ras, R. T., Gagliardi, A. C., Mangili, L. C., Trautwein, E. A., & Santos, R. D. (2016). Effects of phytosterols on markers of inflammation: A systematic review and meta-analysis. *Atherosclerosis*, *248*, 76-83. doi:10.1016/j.atherosclerosis.2016.01.035 %M 26987068
- Sahebkar, A. (2014). A systematic review and meta-analysis of randomized controlled trials investigating the effects of curcumin on blood lipid levels. *Clin Nutr*, *33*(3), 406-414.
- Sahebkar, A. (2017). Effects of quercetin supplementation on lipid profile: A systematic review and meta-analysis of randomized controlled trials. *Crit Rev Food Sci Nutr*, *57*(4), 666-676.
- Sahebkar, A., Cicero, A. F. G., Simental-Mendía, L. E., Aggarwal, B. B., & Gupta, S. C. (2016). Curcumin downregulates human tumor necrosis factor- α levels: A systematic review and meta-analysis of randomized controlled trials. *Pharmacol Res*, *107*, 234-242.
- Sahebkar, A., Ferri, C., Giorgini, P., Bo, S., Nachtigal, P., & Grassi, D. (2017). Effects of pomegranate juice on blood pressure: A systematic review and meta-analysis of randomized controlled trials. *Pharmacol Res*, *115*, 149-161.
- Scholle, J. M., Baker, W. L., Talati, R., & Coleman, C. I. (2009). The effect of adding plant sterols or stanols to statin therapy in hypercholesterolemic patients: systematic review and meta-analysis. *J Am Coll Nutr*, *28*(5), 517-524. doi:10.1080/07315724.2009.10719784 %m 20439548
- Schwingshackl, L., Krause, M., Schmucker, C., Hoffmann, G., Rucker, G., & Meerpohl, J. J. (2019). Impact of different types of olive oil on cardiovascular risk factors: A systematic review and network meta-analysis. *Nutr Metab Cardiovasc Dis*, *29*(10), 1030-1039.
- Schwingshackl, L., Strasser, B., & Hoffmann, G. (2011). Effects of monounsaturated fatty acids on glycaemic control in patients with abnormal glucose metabolism: a systematic review and meta-analysis. *Ann Nutr Metab*, *58*(4), 290-296.
- Serban, M. C., Sahebkar, A., Zanchetti, A., Mikhailidis, D. P., Howard, G., Antal, D., . . . Muntner, P. (2016). Effects of quercetin on blood pressure: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc*, *5*(7), e002713.

- Shams-Rad, S., Mohammadi, M., Ramezani-Jolfaie, N., Zarei, S., Mohsenpour, M., & Salehi-Abargouei, A. (2020). Hesperidin supplementation has no effect on blood glucose control: a systematic review and meta-analysis of randomized controlled clinical trials. *Br J Clin Pharmacol*, *86*(1), 13-22.
- Siri-Tarino, P. W., Sun, Q., Hu, F. B., & Krauss, R. M. (2010). Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *Am J Clin Nutr*, *91*(3), 535-546.
- Somerville, V. S., Braakhuis, A. J., & Hopkins, W. G. (2016). Effect of flavonoids on upper respiratory tract infections and immune function: A systematic review and meta-analysis. *Adv Nutr*, *7*(3), 488-497.
- Speer, H., D’Cunha, N. M., Botek, M., McKune, A. J., Sergi, D., Georgousopoulou, E., . . . Naumovski, N. (2019). The Effects of Dietary Polyphenols on Circulating Cardiovascular Disease Biomarkers and Iron Status: A Systematic Review. *Nutr Metab Insights*, *12*, 117863881988273.
- Suen, J., Thomas, J., Kranz, A., Vun, S., & Miller, M. (2016). Effect of flavonoids on oxidative stress and inflammation in adults at risk of cardiovascular disease: a systematic review. *Healthcare*, *4*(3), 69.
- Talati, R., Sobieraj, D. M., Makanji, S. S., Phung, O. J., & Coleman, C. I. (2010). The comparative efficacy of plant sterols and stanols on serum lipids: a systematic review and meta-analysis. *J Am Diet Assoc*, *110*(5), 719-726. doi:10.1016/j.jada.2010.02.011 %M 20430133
- Tang, Z., Li, M., Zhang, X., & Hou, W. (2016). Dietary flavonoid intake and the risk of stroke: a dose-response meta-analysis of prospective cohort studies. *BMJ Open*, *6*(6), e008680.
- Te Morenga, L., & Montez, J. M. (2017). Health effects of saturated and trans-fatty acid intake in children and adolescents: systematic review and meta-analysis. *PloS one*, *12*(11), e0186672.
- Telle-Hansen, V. H., Gaundal, L., & Myhrstad, M. C. W. (2019). Polyunsaturated Fatty Acids and Glycemic Control in Type 2 Diabetes. *Nutrients*, *11*(5), 1067.
- Travica, N., D’Cunha, N. M., Naumovski, N., Kent, K., Mellor, D. D., Firth, J., . . . Jacka, F. (2019). The effect of blueberry interventions on cognitive performance and mood: A systematic review of randomized controlled trials. *Brain Behav Immun*, *85*, 96-105.
- Wallace, T. C., Slavin, M., & Frankenfeld, C. L. (2016). Systematic review of anthocyanins and markers of cardiovascular disease. *Nutrients*, *8*(1), 32.

- Wanders, A. J., Blom, W. A. M., Zock, P. L., Geleijnse, J. M., Brouwer, I. A., & Alsema, M. (2019). Plant-derived polyunsaturated fatty acids and markers of glucose metabolism and insulin resistance: a meta-analysis of randomized controlled feeding trials. *BMJ Open Diabetes Res Care*, *7*(1), e000585.
- Wang, X., Ouyang, Y. Y., Liu, J., & Zhao, G. (2014). Flavonoid intake and risk of CVD: a systematic review and meta-analysis of prospective cohort studies. *Br J Nutr*, *111*(1), 1-11.
- Wu, T., Fu, J., Yang, Y., Zhang, L., & Han, J. (2009). The effects of phytosterols/stanols on blood lipid profiles: a systematic review with meta-analysis. *Asia Pac J Clin Nutr*, *18*(2), 179-186.
- Xia, H., Ma, S., Wang, S., & Sun, G. (2015). Meta-analysis of saturated fatty acid intake and breast cancer risk. *Medicine*, *94*(52), e2391.
- Xu, C., Han, F.-F., Zeng, X.-T., Liu, T.-Z., Li, S., & Gao, Z.-Y. (2015). Fat intake is not linked to prostate cancer: a systematic review and dose-response meta-analysis. *PloS one*, *10*(7), e0131747.
- Xu, H., Luo, J., Huang, J., & Wen, Q. (2018). Flavonoids intake and risk of type 2 diabetes mellitus: A meta-analysis of prospective cohort studies. *Medicine*, *97*(19), e0686.
- Ye, Z., & Song, H. (2008). Antioxidant vitamins intake and the risk of coronary heart disease: meta-analysis of cohort studies. *Eur J Cardiovasc Prev Rehabil*, *15*(1), 26-34.
- Zhang, Y.-F., Lu, J., Yu, F.-F., Gao, H.-F., & Zhou, Y.-H. (2014). Polyunsaturated fatty acid intake and risk of lung cancer: a meta-analysis of prospective studies. *PloS one*, *9*(6), e99637.
- Zhao, J., Lyu, C., Gao, J., Du, L., Shan, B., Zhang, H., . . . Gao, Y. (2016). Dietary fat intake and endometrial cancer risk: A dose response meta-analysis. *Medicine*, *95*(27), e4121.
- Zhu, Y., Bo, Y., & Liu, Y. (2019). Dietary total fat, fatty acids intake, and risk of cardiovascular disease: a dose-response meta-analysis of cohort studies. *Lipids Health Dis*, *18*(1), 91.
- Zulkipli, S. H., Balasubramaniam, V., Bakar, N. A. A., Rashed, A. A., & Ismail, S. R. (2019). Effects of palm oil consumption on biomarkers of glucose metabolism: A systematic review. *PloS one*, *14*(8), e0220877.

1 **Table 1. Inclusion criteria according to PICOS format**

PICOS element	Inclusion Criteria
Participant	<ul style="list-style-type: none"> • Human • General population, ‘high-risk’ disease groups, and groups with a unifying health condition
Intervention	Edible oils and fats which were “high priority”: <ul style="list-style-type: none"> • Fatty acids: MUFA, PUFA, SFA, TFA categories • Tocopherols: Total and individual tocopherols (focus on α-tocopherol) • Biophenols (a.k.a. polyphenols): total and subcategories (flavonoids, phenolic acids, lignans, secoiridoids (oleuropein and ligstroside derivatives including oleocanthal) • Phytosterols: total level • Squalene
Comparator	<ul style="list-style-type: none"> • Placebo (for RCTs or SLR of RCTs) • Presence of the nutritional component versus no nutritional component • Varying levels of the nutritional component (high vs low)
Outcome	<ul style="list-style-type: none"> • Disease/disorder risk factors (all studies): Total cholesterol, low- and high-density lipoproteins, triglycerides, blood pressure, inflammatory (CRP, IL-6, IL-8, IL-10, TNF-α) and oxidative markers (8-iso PGF_{2a}, ORAC, TBARS, FRAP, GSH-Px, SOD), blood glucose, insulin, glycated haemoglobin, body weight/composition change, mental health/wellbeing assessments, common mental illness symptomatology, measures of cognition. • Disease/disorder and event prevalence /incidence (cohort studies): Cardiovascular disease (CVD), CVD-event, CVD-death, T2DM, obesity, cancer, cancer-death, mental disorders, cognitive impairment/dementia.
Sources	<ul style="list-style-type: none"> • Umbrella reviews of SLRs of RCTs and/or cohort studies • SLRs of RCTs and/or cohort studies (with and without meta-analysis) • RCTs • Cohort studies

2 CRP: C-reactive protein, CVD: cardiovascular disease, FRAP: Ferric reducing antioxidant power assay, GSH:
 3 Glutathione, IL: Interleukin, MUFA: Monounsaturated fatty acids, ORAC: Oxygen radical absorbance capacity,
 4 PUFA: Polyunsaturated fatty acids, RCT: Randomized-controlled trial, SFA: Saturated fatty acids, SLR:
 5 Systematic literature review, SOD: Superoxide dismutase, T2DM: Type-II diabetes mellitus, TBARS:
 6 Thiobarbituric acid reactive substances, TFA: Trans-fatty acids, TNF: Tumor-necrosis factor

7 **Table 2. Key summary of the differences in nutritional components across edible fats and oils**

Fats & oils	Vitamins and minerals^a	Fatty acids	Phytosterols	Biophenols	Squalene^b
EVOO	Highest in Fe for all oils. Moderate in tocopherol.	High in MUFA, Low in PUFA, Low in SFA.	Moderate content.	High content.	High content.
Olive Oil (refined)	N/A	N/A	Moderate content.	Moderate content.	High content.
Canola oil	High in tocopherol. High in Al, Moderate in Cr, Cl, F & Ni.	High in MUFA, Moderate in PUFA, Low in SFA.	High content.	Moderate content.	Low content.
Palm oil	Low- Moderate in tocopherol. Minimal vit/min.	Moderate in MUFA, Low in PUFA, High in SFA.	N/A.	N/A	Low content.
Soybean oil	High in tocopherol. Presence of Cl.	Moderate in MUFA, High in PUFA, Low in SFA.	Moderate content.	Low content.	Low content.
Sunflower oil	High in tocopherol.	Moderate in MUFA, High in PUFA, Low in SFA.	Moderate content.	Low content.	Low content.
Rice bran oil	Moderate in tocopherol.	Moderate in MUFA, Moderate in PUFA, Moderate in SFA.	High content.	N/A	Low content.
Peanut oil	Moderate in tocopherol.	High in MUFA, Moderate in PUFA, Moderate in SFA.	Moderate content.	Not detectable.	Low content.
Coconut oil	Low in tocopherol.	Moderate in MUFA, Low in PUFA, High in SFA.	Low content.	HE- High content. CE- Moderate content	Low content.
Cottonseed oil	Moderate in tocopherol.	Moderate in MUFA, High in PUFA, Moderate in SFA.	N/A.	N/A.	Low content.
Grapeseed oil	Low in tocopherol.	Moderate in MUFA, High in PUFA, Low in SFA.	Moderate content.	Moderate content.	Low content.
Butter	Low in tocopherol.	Moderate in MUFA,	N/A..	N/A.	N/A.

Fats & oils	Vitamins and minerals ^a	Fatty acids	Phytosterols	Biophenols	Squalene ^b
Avocado oil	Low- Moderate in tocopherol.	Low in PUFA, High in SFA. High in MUFA, Low in PUFA, Low in SFA.	Moderate content.	High content.	Low content.
Corn oil	Very high in kernel and wet milled germ High in bran Moderate in dry milled germ	Moderate in MUFA, High in PUFA, Low in SFA.	High content.	Total content NI	Low content.
Tallow/lard	Tocopherol NI	High in MUFA, Low in PUFA, High in SFA.	N/A.	N/A.	N/A.
Sesame oil	Tocopherol NI Low in Vitamin E	Moderate in MUFA Moderate in PUFA Low in SFA	High content	Low content.	N/A.
Safflower oil	Moderate in tocopherol	High in MUFA Low in PUFA Low in SFA	N/A.	Low content.	Low content.
Mustard seed oil	Low in tocopherol	High in MUFA Moderate in PUFA Low in SFA	N/A.	N/A.	N/A.
Almond oil	Moderate in tocopherol.	High in MUFA, Moderate in PUFA, Low in SFA.	Low-moderate content.	Not detectable.	Low content.
Walnut oil	Tocopherol NI	Moderate in MUFA, High in PUFA, Low in SFA.	Moderate content.	Not detectable.	Low content.
Flaxseed oil	Moderate in tocopherol.	Moderate in MUFA, High in PUFA, Low in SFA.	Moderate content.	N/A.	N/A.
Macadamia oil	Low- Moderate in tocopherol.	High in MUFA, Low in PUFA, Low in SFA.	Moderate content.	High content.	Low content.

Fats & oils	Vitamins and minerals ^a	Fatty acids	Phytosterols	Biophenols	Squalene ^b
Hemp seed oil	High in tocopherol.	Low in MUFA, High in PUFA, Low in SFA.	Moderate content.	High in total phenols and very high in total flavonoids.	Low content.
Apricot seed oil	Moderate -High in tocopherol.	High in MUFA, Moderate in PUFA, Low in SFA.	N/A	Low content.	N/A.

8 N/A- not applicable symbol is used when data were not obtained from the literature search.

9 Olive oil is reported as a combination of multiple grades in the Food Standards Australia and New Zealand database. Data on refined olive oil were identified for
10 Phytosterols, Biophenols and Squalene.

11 Cr- Chromium; Cl- Chloride; F- Fluoride; Ni- Nickel; Al- Aluminium; Fe- iron; MUFA- monounsaturated fatty acids; PUFA- polyunsaturated fatty acids; SFA- saturated
12 fatty acids.

13 a. Clinical relevance of most levels is questionable.

14 b. Note. Amaranth oil is reported to have significantly higher squalene than all other oils reviewed in this matrix.

15 **Table 3: Number of studies included according to each component**

Component	Umbrella reviews	Number of SLRs	Number of RCTs ^a	Number of cohort studies
Fatty acid categories				
Total	2	51	N/A	N/A
Multiple FA categories	1	19	N/A	N/A
MUFA	0	3	N/A	N/A
PUFA	0	8	N/A	N/A
SFA	1	10	N/A	N/A
SFA + TFA	0	2	N/A	N/A
TFA	0	2	N/A	N/A
Edible oils/fats ^b	0	9	N/A	N/A
Tocopherols	0	21	N/A	N/A
Biophenols^c				
Total	0	36 (+ 27 related ^d)	N/A	N/A
Flavonoids	0	16	N/A	N/A
Phenolic acids	0	2	N/A	N/A
Lignans	0	1	N/A	N/A
Secoiridoids	0	0	N/A	N/A
Phytosterols	0	32	N/A	N/A
Squalene	0	0	1	0

16 N/A: not applicable, PUFA: polyunsaturated fatty acids, RCT: randomized controlled trial, SFA: saturated fatty
 17 acids, TSFA: trans saturated fatty acid, SLR: systematic literature review

- 18 a. If sufficient SLRs were identified for a nutritional component, the number of RCTs and cohort studies
 19 were not quantified; as per the methodology on page 8.
- 20 b. Edible oil/fat studies identified in the FA search were noted and added to the end of the table. This is
 21 not a comprehensive list; however, may provide insight into the evidence base.
- 22 c. Some biophenol studies explored more than one subclass. These studies were tallied in each of the
 23 respective subclass categories.
- 24 d. Studies identified which were specific to one individual phenol-containing food such as cacao, or an
 25 individual biophenol were documented to further describe the breadth of the literature.