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Dietary fiber intervention on gut microbiota composition in healthy adults: a systematic review and meta-analysis

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Short running head

Dietary fiber interventions on the gut microbiota

Abbreviations

CI – Confidence intervals

FISH – Fluorescence *in situ* hybridization

GI – Gastrointestinal

HMO – Human Milk Oligosaccharide

ICTRP – International Clinical Trials Register

MD – Mean difference

OTU – Operational taxonomic unit

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analysis

PROSPERO – The International Prospective Register of Systematic Reviews

qPCR – Quantitative polymerase chain reaction

RCT – Randomized controlled trial

SCFA – Short chain fatty acid

SD – Standard deviation

SE – Standard error

SMD – Standardized mean difference

Clinical trial registry number

Not required. PROSPERO registration (CRD42016053101)

URL: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016053101

1 ABSTRACT

2 **Background:** Dysfunction of the gut microbiota is frequently reported as a manifestation of
3 chronic disease, and therefore presents as a modifiable risk factor in their development. Diet is
4 a major regulator of the gut microbiota and certain types of dietary fiber may modify bacterial
5 numbers and metabolism, including short-chain fatty acid (SCFA) generation.

6 **Objective:** A systematic review and meta-analysis were undertaken to assess the effect of
7 dietary fiber interventions on gut microbiota composition in healthy adults.

8 **Design:** A systematic search was conducted across MEDLINE, EMBASE, CENTRAL and
9 CINAHL for randomized controlled trials using culture and/or molecular microbiological
10 techniques evaluating the effect of fiber intervention on gut microbiota composition in healthy
11 adults. Meta-analyses using random-effects model were performed on alpha diversity, pre-
12 specified bacterial abundances including *Bifidobacterium* and *Lactobacillus* spp., and fecal
13 SCFA concentrations comparing dietary fiber intervention with placebo/low fiber
14 comparators.

15 **Results:** A total of 64 studies involving 2099 participants were included. Dietary fiber
16 intervention resulted in higher abundance of *Bifidobacterium* spp. [Standardized Mean
17 Difference (SMD) 0.64 (95% Confidence Interval: 0.42, 0.86]; $P < 0.00001$] and *Lactobacillus*
18 spp. [SMD: 0.22 (0.03, 0.41), $P = 0.02$] as well as fecal butyrate concentration [SMD: 0.24
19 (0.00, 0.47), $P = 0.05$] compared with placebo/low fiber comparators. Subgroup analysis
20 revealed fructans and galacto-oligosaccharides led to significantly greater abundance of both
21 *Bifidobacterium* spp. and *Lactobacillus* spp. compared with comparators ($P < 0.00001$ and $P =$
22 0.002 respectively). No differences in effect were found between fiber intervention and
23 comparators for α -diversity, abundances of other pre-specified bacteria, or other SCFA
24 concentrations.

25 **Conclusion:** Dietary fiber intervention, particularly involving prebiotic fibers, leads to higher
26 fecal abundance of *Bifidobacterium* and *Lactobacillus* spp. but does not impact α -diversity.
27 Further research is required to better understand the role of individual fiber types on the
28 growth of microbes and the overall gut microbial community.

29 **KEYWORDS**

30 Diet, dietary fiber, gastrointestinal microbiome, gastrointestinal microbiota, gut microbiota,
31 prebiotic

32 BACKGROUND

33 The gut microbiota is a highly diverse and metabolically active community, consisting of
34 approximately 3.9×10^{13} microbial cells (1). These microbes participate in several functions
35 beneficial to the host, including the fermentation of undigested nutrients (2, 3), synthesis of
36 vitamins (4) and interaction with the immune system (5, 6). A number of disorders, including
37 irritable bowel syndrome and type 2 diabetes mellitus, have been linked with disturbances in
38 gut microbiota composition (2, 7-9). Such an association presents the gut microbiota as a
39 potentially modifiable risk factor in the etiology of these conditions.

40 The gut microbiota can be detected and enumerated using different methods ranging from
41 culture to next-generation sequencing (6, 10, 11), and can be characterized by measures of
42 diversity and bacterial abundances (12, 13). Alpha diversity of the gut microbiota describes the
43 richness (number of taxonomically distinct organisms present) and evenness (relative
44 abundances of organisms) of its composition (12, 13), with cross-sectional studies
45 demonstrating inverse associations between α -diversity and disease states (7-9). Specific
46 bacteria shown to be more abundant in health compared with disease states include
47 *Bifidobacterium* and *Lactobacillus* spp. (2, 7, 14), whose functions include carbohydrate
48 fermentation and vitamin synthesis (15-18). Furthermore, increasing evidence supports the
49 importance of 'keystone' bacterial species, whose absence may have profound consequences
50 for the host, as well as other members of the microbial community and their metabolic outputs,
51 including the short-chain fatty acid (SCFA) butyrate (19-23). Butyrate is of particular interest
52 to health due to its beneficial properties such as its immunomodulatory effects (24, 25).

53 Dietary fiber is defined as non-digestible carbohydrates of ≥ 3 monomeric units found
54 inherently in foods, and also includes isolated or synthetic fibers with demonstrated
55 physiological benefits (26-28). It is a key candidate in facilitating changes in the gut
56 microbiota, as it escapes digestion by the host in the small intestine to pass into the colon

57 where it is available to the microbial community. Dietary fiber encompasses an array of
58 heterogeneous compounds whose physicochemical properties vary based on their particle size,
59 chemical structure, solubility, viscosity and fermentability (29, 30). Fiber with fermentable
60 characteristics are substrates for the microbial population in the colon, stimulating growth of
61 specific organisms and leading to production of various metabolites including SCFA (19, 29,
62 31). Indeed, some fibers can be further classified as ‘prebiotic’ (e.g. fructans) if they have been
63 shown to be selectively utilized by host microorganisms conferring a health benefit (32).
64 The current body of evidence regarding the effect of dietary fiber on the gut microbiota is
65 informed via specific prebiotic fiber interventions (33, 34), whole-diet interventions (35-37)
66 and cross-sectional associations (38, 39). However, these investigations are limited in that
67 prebiotic fibers represent only a subset of total dietary fiber, and confounding factors such as
68 disease states and intake of other fermentable substrates, are unaccounted for in whole diet
69 studies and cross-sectional studies (40). Therefore, there is a gap in knowledge regarding the
70 precise impact of dietary fiber intervention on the gut microbiota in healthy subjects, and this
71 is the focus on the systematic review.

72 **METHODS**

73 This systematic review was conducted in line with the guidelines of the Preferred Reporting
74 Items for Systematic Reviews and Meta-Analysis: The PRISMA statement (41), and the
75 guidelines of the Cochrane Handbook for Systematic Reviews and Interventions (42). The
76 methods including the eligibility criteria, search strategy, extraction process and analysis were
77 pre-specified and documented in a protocol that was published in the International Prospective
78 Register of Systematic Reviews (CRD42016053101).

79 **Literature search**

80 A literature search was performed in the electronic databases MEDLINE, EMBASE,
81 CENTRAL and CINAHL (from inception to October 4, 2017), using a combination of subject

82 headings, free text terms and synonyms relevant to this review, in consultation with an
83 experienced systematic review search librarian (**Supplemental Tables 1-4**). There was no date
84 or language restriction in the search strategy. A multi-step search approach was taken to
85 retrieve relevant studies through additional hand-searching; contacting field experts; searching
86 conference abstracts; theses and dissertations (ProQuest); and the International Clinical Trials
87 Register (ICTRP) Search Portal and ClinicalTrials.gov to identify ongoing trials. Two review
88 authors (DS and HS) screened articles in a blinded, standardized manner, with disagreements
89 in judgement resolved by consensus or a third reviewer (KC).

90 **Study selection**

91 Search results were merged into reference management software Endnote (X7; Thomson
92 Reuters) and de-duplicated prior to screening using Rayyan (Qatar Computing Research
93 Institute) (43). Full text articles of potentially relevant studies were sought and reviewed.
94 Attempts were made to contact the corresponding author where the full text article provided
95 inadequate information to assess eligibility or extract relevant data. Studies were included if
96 they met all of the following criteria: 1) randomized controlled trial (RCT), cluster RCT, or
97 quasi-RCT; 2) inclusion of healthy adult participants (≥ 18 years of age); 3) intervention aimed
98 at increasing fiber intake; 4) inclusion of a placebo for supplement interventions (e.g.
99 maltodextrin), and either low fiber control (e.g. white bread) or habitual diet group for food
100 interventions as comparators; 5) measured fecal microbiota related outcomes at the end of
101 intervention.

102 Studies that were solely investigating enteral nutrition and those that included participants with
103 an acute or chronic disease, including gastrointestinal (GI) conditions such as coeliac disease,
104 inflammatory bowel disease, irritable bowel syndrome and other functional gastrointestinal
105 disorders were excluded. Studies including mixed population groups where the healthy sub-
106 group was not reported separately were also excluded. Studies that included overweight and

107 obese participants who were otherwise healthy and without any abnormal clinical parameters
108 (e.g. elevated blood pressure) were included. Interventions eligible for inclusion provided an
109 increase in fiber intake achieved through 1) dietary counselling to increase dietary fiber intake
110 from food 2) food intervention (e.g. added cereals); or 3) fiber supplementation. Dietary
111 counselling studies or food interventions were only included if fiber modification was the
112 primary aim of the intervention.

113 The primary outcome was between-group differences in α -diversity of fecal microbiota at the
114 end of the intervention. Measures of α -diversity included the total number of observed
115 operational taxonomic units (OTUs) (the number of taxonomically-related groups of bacteria,
116 evaluating richness); Chao1 Index (a non-parametric richness estimator); Shannon diversity
117 index (a metric combining richness and evenness, with equal weighting to abundant and rare
118 species); and Simpson diversity index (metric of richness and evenness, where more weighting
119 is given to abundant species). Secondary outcomes were between-group differences in
120 abundances of the following commonly measured bacterial groups: *Bifidobacterium* spp.;
121 *Lactobacillus* spp.; *Roseburia* spp.; *Akkermansia muciniphila*; *Eubacterium hallii*;
122 *Eubacterium rectale*; *Faecalibacterium prausnitzii*; and *Ruminococcus bromii*. Studies were
123 included if they reported on either primary or secondary outcomes. Between-group differences
124 in fecal SCFAs (total SCFAs and butyrate) were included as an exploratory outcome.

125 **Data extraction and management**

126 Two reviewers (DS and HS) independently extracted the data from eligible studies. Data
127 extracted included: study design (duration, location, details of 'run-in' and 'wash-out'
128 periods); participant characteristics, intervention details (fiber type, fiber dose, intervention
129 delivery, compliance, assessment and control of dietary intake); and other information
130 including antibiotic or probiotic use.

131 For all pre-specified primary, secondary and exploratory outcome data, the mean, standard
132 deviation (SD), standard error (SE) or 95% confidence intervals (CI) that were reported at end
133 of intervention were extracted for analysis. Where studies used multiple intervention groups of
134 different fiber doses, data for the highest intervention dose was extracted. Where studies used
135 multiple intervention groups of different fibers at the same dose compared with a single
136 control group, data was extracted from each intervention group and pooled together. A
137 weighted average of the intervention groups and the study variance was then calculated (44).
138 Risk of bias was independently assessed by two reviewers (DS and HS) using Cochrane
139 methodology (45). The review assessed “other bias” regarding the control of dietary intake
140 during the study. This included examining whether dietary advice (e.g. to maintain dietary
141 intake or avoid probiotic food sources) was provided, whether dietary compliance and/or
142 intake were measured and reported, and if adjustments in statistical analysis were made if
143 differences in dietary intake were found.

144 **Statistical analysis**

145 The overall treatment effect of fiber on primary and secondary outcomes was calculated using
146 the difference between the end of intervention values for the intervention and comparator
147 groups. Data reported as median and interquartile range were converted to mean and SD as
148 previously described (46). Variance was calculated from the SD and SE of end of intervention
149 values, or from the confidence intervals (CI) where these values were not available (46). In
150 crossover studies, the mean and SD, SE or CI of intervention and control periods were
151 extracted and analyzed separately (47). Where end of intervention endpoint data was unable to
152 be obtained, the results were described in text only.

153 Meta-analysis was performed where outcomes were reported in at least two studies using
154 Revman (Version 5.3; Cochrane Collaboration). The mean difference (MD) was used to
155 calculate effect sizes where outcome data were presented in the same units (Shannon diversity

156 index, total number of observed OTUs). Where outcome data were reported using different
157 units, effect sizes were calculated using the standardized mean difference (SMD) (bacterial
158 abundances, fecal SCFA concentration).

159 A random-effects model was used to produce a pooled estimate of the MD or SMD, and the
160 fixed-effects model was used to check for robustness and potential outliers. Inconsistencies
161 between studies were assessed using the I^2 statistic, where significant heterogeneity was
162 defined as $I^2 \geq 50\%$.

163 Pre-defined subgroup analyses were undertaken for primary and secondary outcomes that were
164 reported in at least two studies in each subgroup. Pre-defined subgroup analyses included
165 intervention types (supplements and dietary interventions), fiber types (accepted and candidate
166 prebiotic fibers defined by Roberfroid et al., and general fibers defined by the review) (34),
167 dose-response (comparing difference in fiber intake between intervention and control group of
168 $\leq 5\text{g/d}$, $5\text{-}10\text{g/d}$, and $>10\text{g/d}$), trial design (parallel and crossover), and microbial analysis
169 method (e.g. culture, sequencing). Post hoc subgroup analyses were undertaken for exploratory
170 outcomes based on reporting method of fecal SCFA concentrations (dry weight of feces and
171 wet weight of feces). Fructans and galacto-oligosaccharides were classified as ‘accepted
172 prebiotic’ fibers, while ‘candidate prebiotic’ fibers included a broader range of fibers including
173 polydextrose and resistant starch (34). The term ‘general fiber’ was used by the review to
174 describe fibers not classified as either accepted or candidate prebiotics, and is not a formal
175 term used to describe fibers in the literature.

176 For the fiber type subgroup analysis only, the fiber arm with the highest prebiotic classification
177 (e.g. accepted prebiotic as opposed to a general fiber) was selected if multiple intervention
178 groups were reported. Where multiple arms of the same prebiotic classification were
179 presented, the interventions were pooled together and a weighted average of the intervention
180 arms and study variance were calculated (44). Significant outliers were determined by visual

181 inspection as well as through a study-by-study sensitivity analysis, where each study was
182 sequentially omitted and the remaining data re-assessed. If a study contributed to over 30%
183 heterogeneity (based on changes to the I^2 statistic) then it was removed from the analysis in the
184 sensitivity analysis. Funnel plots were generated for outcomes where at least 10 studies were
185 included in meta-analysis (48) and reporting bias detected by assessment of funnel plot
186 asymmetry by visual inspection.

187 **RESULTS**

188 **Study characteristics**

189 Study identification and selection are detailed in the PRISMA flow chart (**Figure 1**). The
190 initial electronic and manual search generated 3829 records. After review of full texts
191 (**Supplemental Table 5**), 64 publications, along with three secondary studies (49-51)
192 reporting additional outcomes from the primary publications, fulfilled the inclusion criteria
193 and were included in the review.

194 The 64 included primary studies that analyzed a total of 2099 participants. Of these 64 studies,
195 29 were parallel RCTs (52-80) and 35 were crossover RCTs (81-115). Five crossover trials did
196 not include a wash out period (84, 93, 95, 105, 108). The majority of studies (52 studies) used
197 fiber supplementation, including: accepted prebiotic fiber (26 studies) (52, 54-58, 61, 62, 65,
198 67, 70, 74, 86, 90, 92, 95, 97, 100, 102, 103, 105, 107, 109-111, 115); candidate prebiotic fiber
199 (18 studies) (53, 63, 64, 66, 68, 69, 73, 77, 81, 83, 84, 87, 88, 91, 99, 101, 112, 113); general
200 fiber (seven studies) (59, 60, 72, 76, 80, 93, 94); and a fiber mix (108). The remaining 12
201 studies used food intervention by providing key food items (e.g. wholegrain cereal) to
202 supplement the diet (71, 78, 82, 85, 89, 96, 98) or provided all food and fluid to participants
203 (75, 79, 104, 106, 114). Intervention doses ranged from 1.2 g/d to 50 g/d, while treatment
204 periods ranged from five days to three months, with a median length of three weeks.

205 Analysis techniques used to characterize fecal microbiota included: culture (15 studies) (52,
206 54-58, 65, 66, 69, 71, 73, 96, 98, 105, 114); fluorescence *in situ* hybridization (FISH) (20
207 studies) (53, 70, 74, 76, 82, 85, 89-92, 94, 99, 100, 103, 106, 108-110, 112, 113); quantitative
208 polymerase chain reaction (qPCR) (11 studies) (60, 63, 68, 81, 86, 87, 95, 102, 104, 107, 111);
209 and next-generation sequencing (including 454 pyrosequencing and Illumina sequencing) (12
210 studies) (59, 62, 64, 72, 75, 77-80, 97, 101, 115). A combination of techniques were used in
211 six studies (49, 61, 67, 83, 84, 88, 93).

212 The outcomes of each meta-analysis are reported in **Table 1**. Results from subgroup analyses
213 performed are included in **Supplemental Table 6**. Overall, outcome data from 56 studies were
214 suitable for meta-analysis; results from the following studies were unable to be statistically
215 pooled and are presented narratively under their respective sub-headings (59, 62, 69, 77-79,
216 83, 93, 95, 97, 101, 113, 115). The characteristics of included studies are presented in **Tables**
217 **2-3**.

218 **Dietary fiber and gut microbiota diversity (α -diversity)**

219 Alpha-diversity was measured in 13 studies involving 393 participants (49, 59, 64, 72, 75, 77,
220 79, 80, 83, 88, 93, 97, 101).

221 Ten studies reported α -diversity using Shannon diversity index. Of these, six reported the
222 metric in a form suitable for inclusion in the meta-analysis (49, 64, 72, 75, 80, 88). Dietary
223 fiber intervention had no effect on α -diversity compared with placebo/low fiber comparators
224 [MD: -0.06 Shannon diversity index (95% CI: -0.25, 0.12), $P = 0.48$], albeit with substantial
225 heterogeneity ($I^2 = 53\%$). In two of the studies not included in the meta-analysis, raffinose and
226 resistant starch interventions did not lead to significant difference in α -diversity compared with
227 placebo (93, 101). A significant reduction in the α -diversity of fecal microbiota from baseline
228 was detected in a trial involving flaxseed mucilage, measured by both the exponential of
229 Shannon diversity index [-38010 (95% CI: -64473, -11546, $P = 0.007$)] as well as through

230 Simpson's inverse index [-17515 (95% CI: -30992, -4038, $P = 0.014$)], although a between-
231 group comparison was not reported (59). Conversely, significant end of intervention
232 differences in α -diversity measured by Shannon diversity index ($P = 0.013$) and inverse
233 Simpson index ($P = 0.004$) were detected between intervention and comparator groups in a
234 supplementation trial involving resistant starch type 2 (77).

235 A study evaluating α -diversity through Simpson's index found it was significantly higher in
236 the intervention group receiving polydextrose compared with placebo after 21 days ($P =$
237 0.014) (88). A trial involving 15 g/d arabinoxylan supplementation reported variable
238 intervention effects when α -diversity was evaluated using different metrics: α -diversity was
239 significantly lower compared with placebo when measured through observed species ($P =$
240 0.029), but there were no significant differences when assessed by Simpson's evenness ($P =$
241 0.063) (80).

242 A separate meta-analysis was performed for the three studies reporting α -diversity measured
243 by total number of observed OTUs (49, 72, 75). Dietary fiber had no effect on α -diversity
244 compared with placebo/low fiber comparators [MD: -4.37 OTUs (95% CI: -42.92, 34.19), $P =$
245 0.82], with no heterogeneity ($I^2 = 0\%$). The Chao1 index was used to report α -diversity in two
246 studies, although there was insufficient data available precluding meta-analysis. Neither trial
247 reported significant differences between fiber intervention and placebo or low fiber control
248 (49, 83). A feeding trial comparing wholegrain and refined grain diets found no difference in
249 α -diversity at end of intervention between the two groups, although the metric used to measure
250 α -diversity was not reported (79).

251 **Dietary fiber and bacterial abundances**

252 Reporting of bacterial abundances differed across studies. Of the taxa of interest in this review,
253 abundances of *Bifidobacterium* spp. (59 studies) and *Lactobacillus* spp. (28 studies) were most
254 commonly reported. No studies reported on the abundance of *Akkermansia muciniphila*.

255 A total of 59 studies including 1896 participants reported the effect of dietary fiber on
256 *Bifidobacterium* spp. abundance and of these, 51 trials (1629 participants) reported data in a
257 form suitable for meta-analysis (53-58, 60, 61, 63-68, 70, 71, 73-76, 81, 82, 84-94, 96-112,
258 114). Dietary fiber led to a significantly greater *Bifidobacterium* spp. abundance compared
259 with placebo/low fiber comparators [SMD: 0.64 (95% CI: 0.42, 0.86), $P < 0.00001$], albeit
260 with considerable heterogeneity ($I^2 = 85\%$) (**Figure 2**).

261 However, subgroup analysis showed fiber interventions delivered through supplements
262 resulted in a significantly higher *Bifidobacterium* spp. abundance compared with placebo/low
263 fiber controls [SMD: 0.75 (95% CI: 0.52, 0.98), $P < 0.00001$, $I^2 = 83\%$], whereas no
264 differences were found between food interventions and comparators [SMD: 0.20 (95% CI: -
265 0.36, 0.76), $P = 0.49$, $I^2 = 88\%$], although considerable heterogeneity persisted in both
266 analyses.

267 Subgroup analysis demonstrated interventions investigating fibers classified as accepted
268 prebiotics and candidate prebiotics resulted in a significantly higher *Bifidobacterium* spp.
269 abundance compared with placebo/low fiber controls [Accepted prebiotic fiber SMD: 0.68
270 (95% CI: 0.38, 0.98), $P < 0.00001$, $I^2 = 81\%$; Candidate prebiotic fiber SMD: 0.77 (95% CI:
271 0.30, 1.24), $P < 0.00001$, $I^2 = 86\%$] (**Figure 2**). However, there was no difference in effect
272 between the general fiber subgroup compared with comparators [SMD: 0.25 (95% CI: -0.16,
273 0.65), $P = 0.24$, $I^2 = 86\%$]. This subgroup analysis did not reduce the considerable
274 heterogeneity across each subgroup.

275 Subgroup analysis of dose-response showed dietary fiber led to significantly higher
276 *Bifidobacterium* spp. abundance compared with placebo/low fiber comparators at all pre-
277 defined dosage [≤ 5 g/d fiber SMD: 0.51 (95% CI: 0.18, 0.84), $P = 0.003$, $I^2 = 70\%$; 5-10g/d
278 SMD: 0.48 (95% CI: 0.13, 0.83), $P = 0.007$, $I^2 = 87\%$ >10g/d SMD: 0.85 (95% CI: 0.45, 1.25),

279 $P < 0.00001$, $I^2 = 85\%$]. No differences were found in subgroup analyses of trial design or
280 microbiota analysis method (**Supplemental Table 6**).

281 Eight trials were not included in the meta-analysis. In the supplement trials of accepted
282 prebiotics, a significantly higher *Bifidobacterium* spp. abundance was reported following
283 supplementation involving inulin (115) and human milk oligosaccharides (HMO) (62)
284 compared with placebo at the end of intervention, while a significant within-group increase
285 from baseline was detected following 10g/d inulin supplementation (95). In the candidate
286 prebiotic trial of resistant starch supplementation, *Bifidobacterium* spp. abundance was
287 significantly higher in the intervention group compared with placebo at end of intervention
288 (77). In the supplement studies of general fiber, *Bifidobacterium* spp. abundance was higher
289 following after xylo-oligosaccharide supplementation compared with placebo (69) while
290 manno-oligosaccharides had no effect on *Bifidobacterium* spp. compared with placebo (113).

291 The third supplement trial of general fiber (resistant maltodextrin) reported no change in
292 *Bifidobacterium* spp. abundance within groups using FISH, although a significant increase
293 from baseline was reported for the intervention group on qPCR analysis (83). Finally, a food
294 study comparing intakes of wholegrains to refined grain products found no significant
295 difference in *Bifidobacterium* spp. abundance at the end of intervention period (78).

296 *Lactobacillus* spp. abundance was measured in 28 studies involving 867 participants. Data
297 from 24 studies (730 participants) was reported in a form suitable for meta-analysis (52, 55,
298 56, 60, 63-68, 73, 75, 76, 84, 87, 93, 96, 97, 99, 104, 105, 107, 111, 114). Dietary fiber led to a
299 significantly greater *Lactobacillus* spp. abundance compared with placebo/low fiber
300 comparators [SMD: 0.37 (95% CI: 0.07, 0.68), $P = 0.02$]. However, heterogeneity was
301 considerable ($I^2 = 80\%$), and was skewed by results from a single outlier study (66) [4.70 (95%
302 CI: 3.69, 5.70)]. A sensitivity analysis excluding this study produced a more homogenous
303 study population ($I^2 = 49\%$), with a modest impact on the result [SMD: 0.22 (95% CI: 0.03,

304 0.41), $P = 0.02$] (**Figure 3**). The outlier study (66) was excluded from subsequent subgroup
305 analyses.

306 Subgroup analysis demonstrated interventions involving fiber supplements resulted in a
307 significantly higher *Lactobacillus* spp. abundance compared with placebo/low fiber controls
308 while substantially reducing study heterogeneity [SMD: 0.16 (95% CI: 0.01, 0.31), $P = 0.04$, I^2
309 = 7%]. No significant differences in effect were found between food interventions and
310 comparators [SMD: 0.35 (95% CI: -0.46, 1.16), $P = 0.40$, $I^2 = 84\%$].

311 Subgroup analysis of fiber types showed accepted prebiotic fiber interventions led to a
312 significantly greater *Lactobacillus* spp. abundance compared with placebo/low fiber controls
313 and further reduced heterogeneity [SMD: 0.34 (95% CI: 0.13, 0.55), $P = 0.002$, $I^2 = 0\%$]
314 (**Figure 3**). There were no differences in effect in the candidate prebiotic [SMD: -0.06 (95%
315 CI: -0.29, 0.16), $P = 0.58$, $I^2 = 0\%$] and general fiber [SMD: 0.22 (95% CI: -0.31, 0.75), $P =$
316 0.42, $I^2 = 74\%$] subgroups when compared with comparators.

317 Subgroup analysis of analysis method demonstrated dietary fiber led to significantly higher
318 *Lactobacillus* spp. abundance compared with placebo/low fiber comparators when enumerated
319 via culture [SMD: 0.61 (95% CI: 0.13, 1.08), $P = 0.01$]. There were no significant differences
320 between intervention and comparator when *Lactobacillus* spp. was detected using FISH, qPCR
321 or sequencing (**Supplemental Table 6**). There were no differences in effect when sub-
322 analyzing by intervention type or dose-response (**Supplemental Table 6**).

323 There were four studies that could not be pooled into the meta-analysis. A prebiotic
324 supplementation trial of HMOs reported no difference in *Lactobacillus* spp. abundance
325 between intervention and control groups (62). There was also no significant difference in
326 *Lactobacillus* spp. reported in a wholegrain food intervention study compared with controls
327 (78). Of the two remaining studies, there was higher *Lactobacillus* spp. abundance following
328 xylo-oligosaccharide supplementation compared with placebo (69), and significant within-

329 group increases in *Lactobacillus* spp. abundance was demonstrated following manno-
330 oligosaccharide supplementation (113).

331 Abundance of *F. prausnitzii* was measured in 15 studies investigating 566 participants.
332 Thirteen studies (519 participants) were able to be meta-analyzed (53, 61, 67, 68, 74, 84, 88,
333 94, 99-101, 110, 112). There was no difference between dietary fiber compared with
334 placebo/low fiber comparators for *F. prausnitzii* abundance [SMD: 0.14 (95% CI: -0.12, 0.39),
335 $P = 0.29$], with substantial heterogeneity between studies ($I^2 = 68\%$) (**Figure 4**). Aside from
336 trial design, no differences with respect to the pre-specified subgroups were found
337 (**Supplemental Table 6**). Two studies reporting abundances of *F. prausnitzii* were unable to
338 be pooled into the meta-analysis. Both studies measured the relative abundance of *F.*
339 *prausnitzii* and reported only within-group changes, with one study reporting a decrease in
340 abundance following supplementation of flaxseed mucilage (59), and the other reporting an
341 increase in abundance following inulin supplementation (50).

342 Seven studies including 261 participants measured *Roseburia* spp. abundance. Four studies
343 (189 participants) were included in the meta-analysis (49, 68, 79, 97). Dietary fiber had no
344 effect on *Roseburia* spp. abundance compared with placebo/low fiber comparators [SMD: 0.33
345 (95% CI: -0.14, 0.80), $P = 0.17$] although substantial heterogeneity was detected ($I^2 = 70\%$)
346 (**Figure 4**). Similar results were reported in the studies excluded from meta-analysis. No
347 between or within-group differences were detected between intervention and placebo groups in
348 two prebiotic fiber supplement trials (50, 62). A third trial found the relative abundance of
349 *Roseburia* spp. was lower following inulin supplementation compared with control at end of
350 intervention, although significance was not reported (115).

351 Two studies of 32 participants measured *E. hallii* abundance. These results could not be
352 statistically pooled because one study did not report data in a suitable form. One study

353 reported no within-group difference in *E. hallii* abundance (50, 62), the other reported a
354 significant decrease in *E. hallii* abundance compared with placebo (49).

355 *E. rectale* was measured in three studies including 42 participants. Two studies (30
356 participants) were suitable for meta-analysis (84, 101). Dietary fiber did not impact on *E.*
357 *rectale* abundance compared with placebo/low fiber comparators [SMD: -0.26 (95% CI: -1.20,
358 0.67), $P = 0.58$] and substantial heterogeneity was detected ($I^2 = 75\%$) (**Figure 4**). The study
359 not eligible for meta-analysis was an inulin supplementation trial which reported no difference
360 for within-group effects for *E. rectale* abundance (50).

361 *R. bromii* abundance was measured in three studies encompassing 76 participants, of which all
362 were suitable for meta-analysis (49, 81, 101). Dietary fiber had no effect on *R. bromii*
363 abundance compared with placebo/low fiber comparators [SMD: 0.15 (95% CI: -0.15, 0.45), P
364 = 0.33], with no heterogeneity detected ($I^2 = 0\%$) (**Figure 4**).

365 **Dietary fiber and short-chain fatty acids**

366 A total of 25 studies of 870 participants reported between-group differences in fecal SCFA
367 concentration following fiber intervention (52, 53, 55, 59, 63, 64, 66-68, 71, 73, 74, 77, 80, 82,
368 84, 86, 90, 91, 93, 94, 96, 103, 112, 115). Fecal SCFA concentration was determined through
369 gas-liquid chromatography in all but one study (90) where high-performance liquid
370 chromatography was used.

371 Total fecal SCFA concentration was measured in 13 studies encompassing 406 participants
372 (52, 55, 59, 63, 64, 67, 73, 80, 82, 84, 86, 91, 94). Dietary fiber had no effect on total SCFA
373 concentration compared with placebo/low fiber comparators [SMD: 0.11 (95% CI: -0.05,
374 0.27), $P = 0.19$], with similar intervention effects across studies ($I^2 = 0\%$).

375 Fecal acetate concentration was reported in 18 studies involving 657 participants (52, 53, 63,
376 66, 71, 74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112). There was no difference in fecal

377 acetate following fiber intervention compared with placebo/low fiber comparators [SMD: 0.28
378 (95% CI: -0.08, 0.63), $P = 0.13$] with substantial heterogeneity between studies ($I^2 = 86$).

379 The effect of fiber intervention on fecal propionate concentration was reported in 19 studies of
380 677 participants (52, 53, 63, 66, 71, 74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112, 115).

381 No differences were found between fecal propionate and comparators [SMD: -0.01 (95% CI: -
382 0.20, 0.22), $P = 0.95$], with moderate heterogeneity detected ($I^2 = 61\%$).

383 The effect of fiber intervention on fecal butyrate concentration was reported in 20 studies of
384 712 participants (52, 53, 59, 63, 66, 71, 74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112,
385 115). Fecal butyrate was significantly higher following fiber intervention compared with
386 placebo/low fiber comparators [SMD: 0.24 (95% CI: 0.00, 0.47), $P = 0.05$], although
387 considerable heterogeneity was present ($I^2 = 70\%$).

388 Of the studies evaluating differences in fecal SCFA concentration following fiber intervention
389 compared with placebo/low fiber comparators, 13 studies expressed mean SCFA
390 concentrations per wet weight of feces (52, 53, 66, 67, 71, 73, 74, 77, 82, 90, 91, 96, 115), 10
391 studies as dry weight of feces (55, 59, 63, 64, 68, 80, 93, 94, 103, 112), one study as molar
392 ratio (84), and one study as a combination of wet weight of feces and molar ratio (86).

393 Additional subgroup analyses were performed to compare differences in fecal SCFA
394 concentrations when expressed as wet weight compared with dry weight (**Supplemental**
395 **Table 7**). Fiber intervention led to significantly higher fecal concentrations of total SCFA,
396 acetate and butyrate compared with comparators when expressed per wet weight of feces.

397 However, there were no significant differences when mean SCFA concentrations were
398 expressed per dry weight of feces. Study heterogeneity was considerably greater for fecal
399 acetate and butyrate, but not total fecal SCFA concentrations when expressed as wet compared
400 with dry wet of feces. There were no differences in effect based on analysis method for fecal

401 propionate concentrations, although heterogeneity was greater when results were expressed per
402 wet weight of feces (**Supplemental Table 7**).

403 **Differences in intervention effects based on trial design**

404 There were differences in intervention effects in subgroup analyses depending upon trial
405 design. Dietary fiber led to significantly lower α -diversity compared with placebo/low fiber
406 comparators in crossover design trials, where α -diversity was reported using Shannon diversity
407 index [MD: -0.10 (95% CI: -0.19, -0.01), $P = 0.03$], while there was no difference in α -
408 diversity in parallel design trials [MD: -0.03 (95% CI: -0.57, 0.51), $P = 0.91$] (**Supplemental**
409 **Table 6**). The presence and duration of washout periods were inconsistent across the three
410 crossover trials included this analysis. One study did not include a wash out period (84), and
411 wash out periods lasted 14 (75) and 21 days (88) in the other two. Regarding bacterial
412 abundances however, intervention effects were significant in parallel trials but not in crossover
413 trials for *Lactobacillus* and *Roseburia* spp. and *F. prausnitzii*, but not for *Bifidobacterium* spp.
414 (**Supplemental Table 6**). Statistical heterogeneity was lower in crossover trials compared with
415 parallel trials for α -diversity reported using Shannon diversity index, *Bifidobacterium* and
416 *Lactobacillus* spp., as well as *F. prausnitzii*, but there was no difference in statistical
417 heterogeneity for *Roseburia* spp. (**Supplemental Table 6**).

418 **Risk of bias**

419 The risk of bias was low-to-moderate across the 64 included studies (**Supplemental Figure 1**).
420 Selection bias was unclear in most studies. Random sequence generation and allocation
421 concealment were adequately described by 26% (59-62, 70-72, 77, 79, 80, 84, 86, 94, 103,
422 113-115) and 16% (59, 61, 62, 70, 77, 79, 80, 86, 94, 115) of studies, respectively. There was
423 low risk of bias across included studies regarding performance and detection bias, as most
424 trials investigated objective outcomes and incorporated a double-blind design. Attrition bias
425 was adequately addressed by only 41% (54-58, 62, 67, 69, 71, 74-76, 79, 82, 86-89, 92, 93, 98,

426 99, 105, 107, 108, 110) of the included studies. Selective reporting was unclear in the majority
427 of studies. Published protocols or clinical registrations were reported by only 26% (59, 61, 68-
428 70, 75, 77-80, 86, 97, 100-102, 110, 115) of included studies. Bias related to control of dietary
429 intake was unclear in half of included studies (55%) (54, 56-60, 62, 64-67, 71, 72, 74, 78, 80,
430 81, 83, 85-93, 96, 98, 102, 103, 105, 108, 110, 115), while even fewer studies were judged to
431 have a low risk of bias regarding dietary advice and assessment of dietary compliance (33%)
432 (52, 55, 63, 68, 69, 73, 75, 76, 79, 82, 84, 94, 97, 99, 104, 106, 107, 111-114). Furthermore,
433 13% (53, 61, 70, 77, 95, 100, 101, 109) of studies did not provide dietary advice or assess
434 intake, and were judged to have a high risk of bias relating to the potential influence of
435 background dietary intake.

436 **Reporting bias**

437 Funnel plots were generated for abundances of *Bifidobacterium* spp.; *Lactobacillus* spp.; *F.*
438 *prausnitzii*; and total SCFA; acetate; propionate; and butyrate concentrations. Visual
439 inspection found no evidence of funnel plot asymmetry, indicating reporting bias was unlikely
440 (**Supplemental Figures 2-7**).

441 **DISCUSSION**

442 This systematic review and meta-analysis found dietary fiber intervention had no effect on the
443 diversity of the gut microbiota but did increase abundance of *Bifidobacterium* and
444 *Lactobacillus* spp. as well as fecal butyrate concentration in healthy adults.

445 The lack of effect on α -diversity of the gut microbiota found in this review is similar to other
446 dietary interventions documented in the literature. For instance, controlled feeding studies
447 lasting four days to three weeks found that despite significant changes to fiber intake, there
448 was no effect on microbial diversity (35-37). These findings suggest that short-term dietary
449 interventions are unlikely to facilitate changes in the α -diversity of the gut microbiota. Indeed,
450 study design is likely important, as subgroup analysis demonstrated different effects between
451 crossover and parallel trials. The lower α -diversity between fiber and control groups in
452 crossover trials may be related to a lack of or insufficient wash-out between interventions, as
453 well as potential differences in the microbiota and habitual diet of individuals at baseline.
454 These null findings are in contrast to the findings from observational studies that report a
455 correlation between fiber intakes in habitual diet and diversity of the gut microbiota, for
456 example in studies comparing agrarian dietary habits with Western populations (38, 39).
457 Interestingly, a positive correlation has also been reported between dietary diversity and
458 microbiota diversity (116). Taken together, long term dietary diversity as opposed to changes
459 in isolated nutrients or foods over a short period of time may be a stronger driver of microbial
460 diversity. It must also be noted that the stability of the gut microbiota, as well as the
461 abundances and metabolites of the individual members of the microbial community, also
462 contribute to maintaining an ecosystem that promotes health (117, 118). Therefore, the totality
463 of findings here, including that microbial diversity was not compromised, support the
464 favorable effects of dietary fiber on the gut microbiota.

465 In regard to particular bacterial groups, this review demonstrated dietary fiber interventions
466 involving accepted prebiotic fibers led to higher abundance of *Bifidobacterium* and
467 *Lactobacillus* species. These results support the selectivity criteria of the prebiotic concept,
468 where the host microorganisms selectively utilize the prebiotic fibers as substrates, which may
469 confer health benefits to the host (32). However, candidate prebiotic interventions produced
470 different effects on the abundance of these two genera, with significant effects demonstrated
471 for *Bifidobacterium* but not *Lactobacillus* species. This may represent differences in substrate
472 preferences between the two genera, where *Bifidobacterium* spp. may be less discriminating
473 than *Lactobacillus* spp. regarding fermentation substrates (119, 120). Conversely, fibers not
474 classified as accepted or candidate prebiotics, here termed general fibers, did not impact the
475 abundance of these taxa. This may be due to the heterogeneity of the general fibers, including
476 their degree of polymerization, viscosity and fermentability, whereas accepted and candidate
477 prebiotic fibers are mostly highly fermentable oligosaccharides (29, 30).

478 Subgroup analysis separating the effect of food vs supplement interventions showed food
479 interventions had no effect on *Bifidobacterium* and *Lactobacillus* species. This result may be
480 attributed to a lack of statistical power, due to the food interventions comprising a relatively
481 small number of low sample size studies (10 studies, 301 participants; 4 studies, 127
482 participants). It must also be noted that most of the trials employing food interventions
483 supplemented with grain and cereal foods to increase fiber intake (71, 78, 79, 82, 85, 89, 96,
484 98, 104). Therefore, the food interventions evaluated may be more representative of grains and
485 cereals *per se* rather than a diverse range of fibrous foods.

486 Interestingly, there were no differences in the effect of dietary fiber interventions on
487 *Bifidobacterium* spp. abundance with varying doses of fiber. Dietary fiber intervention led to
488 an effect at all levels of consumption in subgroup analysis (≤ 5 g, 5-10g, >10 g) with no
489 discernible gradient in effectiveness, suggesting fewer than 5 grams of dietary fiber is

490 sufficient. This may represent a potential limit to the amount of fiber that can be fermented by
491 *Bifidobacterium* species. The lack of a dose-response effect may also be attributed to the
492 percentage increase in fiber intake from baseline rather than the intervention dose, which was
493 unable to be accounted for in this review due to the inconsistent reporting of baseline values
494 across included studies. This requires further clarification but lower dose supplementation may
495 be advantageous in patients who experience GI symptoms with higher fiber loads.

496 There was more variability in intervention effects for abundances of *Bifidobacterium* spp. ($I^2 =$
497 85%) compared with *Lactobacillus* spp. ($I^2 = 49%$). While this may be related to differences in
498 the accuracy of techniques used to determine specific bacterial abundances (121, 122), there
499 were no differences in effect based on analysis method for *Bifidobacterium* species. Another
500 plausible explanation is the differences in nutrient requirements of these taxa as discussed
501 previously. Furthermore, ‘responder and non-responder’ effects for *Bifidobacterium* spp.
502 abundance, which have been shown previously (97, 123, 124), may be impacted by individual
503 host factors, such as differences in baseline abundances (124), or the presence/absence of
504 specific strains of *Bifidobacterium* able to utilize the particular fiber under investigation.

505 There were differences in intervention effects based on trial design, with parallel design
506 studies demonstrating stronger intervention effects and greater statistical heterogeneity
507 compared with crossover design studies for several outcomes. This may in part be due to inter-
508 individual differences in microbiota composition as well as carry-over effects from a lack of or
509 insufficient wash-out periods in the crossover studies as discussed previously.

510 There was no effect of dietary fiber interventions on abundance of other commonly measured
511 bacterial groups (e.g. *F. prausnitzii*), suggesting these species may be stimulated by dietary
512 components other than fiber, such as polyols and polyphenols (125). However, the number of
513 studies evaluating species of other bacterial groups was small, and therefore further studies are
514 needed to investigate the effect of fiber and other dietary components on these groups.

515 The higher fecal concentration of butyrate following fiber intervention highlights the ability of
516 dietary fiber to beneficially modulate the metabolic outputs of the gut microbiota. This is
517 likely due to cross-feeding interactions between butyrate producers with *Bifidobacterium* and
518 *Lactobacillus* species, which are noted lactate and acetate producers (25, 120, 126). As the
519 preferred energy source for colonic epithelial cells, butyrate is a microbial by-product that is of
520 particular interest to host health, exhibiting a wide spectrum of positive effects, such as
521 inhibiting colonic carcinogenesis and ameliorating mucosal inflammation (31, 127, 128).
522 However, it is acknowledged that the variability in the reporting of SCFA results may limit the
523 applicability of these findings, particularly when considering the variance in results when
524 expressed as wet compared with dry weight of feces.

525 This study is the first systematic review and meta-analysis to assess the effect of dietary fiber
526 intervention on gut microbiota composition. Major strengths of this study include its robust
527 design, comprehensive search strategies, and the use of two independent reviewers.

528 It is acknowledged this study has some limitations. Firstly, there were only a limited number
529 of studies reporting the primary outcome of α -diversity, and a small proportion presenting data
530 using the same diversity indices. Secondly, baseline fiber intake was not able to be accounted
531 for due to the paucity of reporting by included studies. Furthermore, included studies sampled
532 feces as a surrogate for gut microbiota profile, and although feces are a common sampling
533 route, the microbial composition of feces differs from the mucosal microbiota (10, 11), which
534 is in closer contact with the host and may be more important when considering the relationship
535 between microbiota and disease pathophysiology or outcomes. Finally, the limited number of
536 taxa assessed in the review may not convey the overall effect elicited by dietary fiber
537 intervention on gut microbiota composition and metabolic outputs, although the selection of
538 taxa was guided by the available literature. Thus, the taxa selected may be more representative
539 of the scope of research in the field to date, rather than a limitation of the review.

540 Dietary fiber intervention leads to a higher abundance of fecal *Bifidobacterium* and
541 *Lactobacillus* spp., as well as higher fecal concentration of butyrate compared with
542 placebo/low fiber comparators. Accepted prebiotic fibers had an effect on the abundances of
543 both *Bifidobacterium* and *Lactobacillus* spp. while candidate prebiotic fibers had an effect on
544 *Bifidobacterium* spp. abundance but not *Lactobacillus* species. General fibers appear to have a
545 limited effect on gut microbiota composition. Although the diversity of the gut microbiota,
546 abundances of other commonly measured bacterial groups and concentration of other fecal
547 SCFAs were not significantly different compared with controls following dietary fiber
548 intervention, it is worth noting that a short-term increase in fiber intake does not appear to be
549 rate-limiting to these outcomes. These results further support the favorable effects of dietary
550 fiber and contribute to our understanding of its effect on the gut microbiota.

551 Future RCTs investigating the effect of fiber on the gut microbiota should adjust for
552 participants' baseline microbiota composition and dietary characteristics as well as controlling
553 for dietary intake in order to determine the precise effect of dietary fiber. Scope may also need
554 to be broadened to evaluate taxa than that considered here, including the eukaryote (e.g. fungi)
555 members of the gut microbiota. Additionally, longer duration studies are needed to better
556 assess the chronic effect of fiber on microbiota diversity.

557 **Author contributions**

558 The author's responsibilities were as follows – HS and KC: initiated the study; DS, KW, HS,
559 MR, KW and KC: developed the protocol; DS and HS: performed eligibility screening and
560 data extraction; DS and JK: analyzed the data and performed the statistical analysis; DS KW,
561 MR, MM, JK, ES, HS and KC: interpreted the data; DS: wrote the initial manuscript; and KW,
562 MR, MM, GH, JK, ES, HS and KC: critically revised the manuscript. All authors read and
563 approved the final manuscript.

564 **Competing interests**

565 None declared.

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Table 1: Statistical analysis for the outcomes reported in ≥ 2 randomized controlled trials and included in the meta-analysis.

Outcomes	No. of studies in meta-analysis (references)	n^I	Results		Heterogeneity		
			Meta-analysis overall estimate (95% CI)	P	Chi-square test	P	I^2 (%)
Shannon Diversity Index	6 (64, 72, 75, 80, 84, 88)	127	MD: -0.06 (95% CI: -0.25; 0.12)	0.48	10.73	0.06	53
Total number of observed OTUs	3 (72, 75, 84)	53	MD: -4.37 (95% CI: -42.92; 34.19)	0.82	0.07	0.97	0
<i>Bifidobacterium</i> spp.	51 (52-58, 60, 61, 63-68, 70-76, 82, 84-94, 96-112, 114)	1629	SMD: 0.64 (95% CI: 0.42; 0.86)	<0.00001	327.93	<0.00001	85
<i>Lactobacillus</i> spp.²	23 (52, 55, 56, 60, 63-65, 67, 68, 73, 75, 76, 84, 87, 93, 96, 97, 99, 104, 105, 107, 111, 114)	670	SMD: 0.22 (95% CI: 0.03; 0.41)	0.02	42.8	0.005	49
<i>Faecalibacterium prausnitzii</i>	13 (53, 61, 67, 68, 74, 84, 88, 94, 99-101, 110, 112)	519	SMD: 0.14 (95% CI: -0.12; 0.39)	0.29	37.53	0.0002	68
<i>Roseburia</i> spp.	4 (68, 79, 84, 97)	189	SMD: 0.33 (95% CI: -0.14; 0.80)	0.17	10.16	0.02	70
<i>Eubacterium rectale</i>	2 (84, 101)	30	SMD: -0.26 (95% CI: -1.20; 0.67)	0.58	3.94	0.05	75
<i>Ruminococcus bromii</i>	3 (81, 84, 101)	76	SMD: 0.15 (95% CI: -0.15; 0.45)	0.33	1.1	0.58	0
Total SCFA	13 (52, 55, 59, 63, 64, 67, 73, 80, 82, 84, 86, 91, 94)	406	SMD: 0.11 (95% CI: -0.05; 0.27)	0.19	6.46	0.89	0
Acetate	18 (52, 53, 63, 66, 71, 74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112)	657	SMD: 0.28 (95% CI: -0.08; 0.63)	0.13	119.36	<0.00001	86
Propionate	19 (52, 53, 63, 66, 71,	677	SMD: 0.01 (95% CI: -0.20; 0.22)	0.95	46.23	0.0003	61

Outcomes	No. of studies in meta-analysis (references)	<i>n</i> ¹	Results		Heterogeneity		
			Meta-analysis overall estimate (95% CI)	<i>P</i>	Chi-square test	<i>P</i>	I ² (%)
Butyrate	74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112, 115) 20 (52, 53, 59, 63, 66, 71, 74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112, 115)	712	SMD: 0.24 (95% CI: 0.00; 0.47)	0.05	64.21	<0.00001	70

Data was meta-analyzed using a random-effects model and presented as MDs or SMDs as appropriate. Statistical heterogeneity was assessed using the chi-square test and quantified using the I² statistic. ¹ Number of participants in meta-analysis. ² Results from outlier study excluded from this meta-analysis. Abbreviations: MD, Mean difference; OTU, Operational taxonomic unit; SCFA, Short chain fatty acid; SMD, Standardized mean difference.

Table 2: Characteristics of randomized controlled trials of fiber supplementation comparing dietary fiber with placebo or low fiber comparators in healthy adults

Study	Participants		Interventions			RCT Design				
	n; age ¹ ; % F	Fiber, daily dose	Prebiotic	Comparator; daily dose	Compliance ²	Design	Duration (days)	Run in	Wash out	Analysis
Abell 2008 (81)	46; 25-66; 65%	RS, 22 g	C	RS, 1 g	Y	Cross-over	28	Y	Y	qPCR
Alfa 2017 (77)	84; 32-96; 42%	RS2, 21 g	C	Corn starch, 21 g	Y	Parallel	72	Y	N	Illumina
Alles 1999 (52)	27.4; 40.4; 45%	TOS, 15 g	A	Glucose & lactose mix, 15 g	Y	Parallel	21	Y	N	Culture
Baer 2014 (83)	14; 47; 9%	Resistant maltodextrin, 50 g	C	Maltodextrin, 50 g	Y	Cross-over	21	N	Y	454 Pyrosequencing; DGGE; FISH; qPCR
Beards 2010 (53)	30; 33 ³ ; 66% ³	PDX; RS, 45.6 g	C	Maltitol, 45.6 g	N	Parallel	44	N	N	FISH
Blaedel 2016 (115)	21; 23-45; 100%	Inulin, 15 g	A	Placebo	Y	Cross-over	21	N	Y	Illumina
Boler 2011 (84); Hooda 2012 (49)⁴	21; 21-28; 0%	PDX⁵ ; Soluble maize fiber, 21 g	C	Placebo	N	Cross-over	21	N	N	qPCR; Pyrosequencing ⁴
Bouhnik 1996 (54)	10; 22-39; 50%	SC-FOS, 12.5 g	A	Saccharose, 10 g	N	Parallel	12	Y	Y	Culture
Bouhnik 1999 (58)	8; 29.6; 55%	SC-FOS, 20 g	A	Saccharose, 20 g	N	Parallel	7	N	N	Culture

Study	Participants		Interventions			RCT Design				
	n; age ¹ ; % F	Fiber, daily dose	Prebiotic	Comparator; daily dose	Compliance ²	Design	Duration (days)	Run in	Wash out	Analysis
Bouhnik 2004 (57)	64; 30 ³ ; 55% ³	SC-FOS ⁵ ; GOS ⁵ ; Isomalto-OS; Inulin ⁵ ; RS; Soybean-OS, 10 g	A	Sucrose & maltodextrin mix, 10 g	N	Parallel	7	Y	N	Culture
Bouhnik 2006 (56)	40; 29; 55%	SC-FOS (Actilight), 10 g	A	Sucrose & maltodextrin mix, 10 g	N	Parallel	7	Y	N	Culture
Bouhnik 2007 (55)	39; 33.9; NR	Inulin, 5 g	A	Sucrose & maltodextrin mix, 5 g	N	Parallel	28	Y	Y	Culture
Brahe 2015 (59)	35; 59.6 ³ ; 100%	Flaxseed mucilage, 10 g	G	Placebo	Y	Parallel	42	N	N	Quantitative metagenomics qPCR
Calame 2008 (60)	16; 30.9; NR	Arabic gum, 40 g	G	Placebo	Y	Parallel	28	N	N	
Clarke 2016 (86)	30; 27; 57%	Beta 2-1 fructan, 15 g	A	Maltodextrin, 15 g	Y	Cross-over	28	N	Y	qPCR
Cloetens 2010 (87)	20; 24; 70%	AXOS, 10 g	C	Maltodextrin, 20 g	N	Cross-over	21	N	Y	qPCR
Costabile 2010 (90)	31; 25; 56%	Very long chain inulin, 10 g	A	Maltodextrin, 10 g	N	Cross-over	21	N	Y	FISH
Costabile 2012 (88)	31; 33; 52%	PDX, 8 g	C	Maltodextrin, 8 g	N	Cross-over	21	N	Y	DGGE; FISH
Damen 2012 (91)	27; 25; 63%	AXOS, 2.14 g	C	Placebo	Y	Cross-over	21	Y	Y	FISH
Depeint 2008 (92)	30; 36.3; 60%	Beta-GOS, 7 g	A	Sucrose, 7 g	N	Cross-over	7	Y	Y	FISH

Study	Participants		Interventions			RCT Design				
	n; age ¹ ; % F	Fiber, daily dose	Prebiotic	Comparator; daily dose	Compliance ²	Design	Duration (days)	Run in	Wash out	Analysis
Dewulf 2013 (61)	30; 47.5; 100%	Inulin-type fructan (Synergy 1), 16 g	A	Maltodextrin, 16 g	N	Parallel	Reported as 3 months	N	N	qPCR; Phylogenetic microarray
Elison 2016 (62)	40; 22-57; 52%	HMO⁶ : 2'-O-fucosyllactose (2'FL); lacto-N-neotetraose (LNnT); Mixture (2:1 mixture of 2'FL + LNnT), 20 g	A	Glucose, 2 g	Y	Parallel	14	Y	N	Illumina
Fastinger 2008 (63)	25; 26.7; 50%	Resistant maltodextrin, 15 g	C	Maltodextrin, 15 g	N	Parallel	21	Y	Y	qPCR
Fernando 2010 (93)	12; 25.6; 42%	Raffinose, 5 g	G	Placebo	N	Cross-over	21	N	N	qPCR; T-RLFP
Finegold 2014 (64)	16; 21-49 ³ ; 66% ³	XOS, 2.8 g	C	Maltodextrin, 2.8 g	N	Parallel	56	Y	Y	Pyrosequencing
Francois 2012 (94)	52; 42; 48%	Wheat bran extract, 10 g	G	Placebo	N	Cross-over	21	Y	Y	FISH
Fuller 2007 (95); Ramirez-Farias 2009 (50)⁴	12; 38.1; 75%	Inulin, 10 g	A	Nil	Y	Cross-over	16	N	N	qPCR
Gopal 2003 (65)	19; 20-60 ³ ; 44% ³	GOS, 2.4 g	A	Placebo	Y	Parallel	28	Y	Y	Culture
Holscher 2015 (97)	29; 27; 52%	Agave inulin, 7.5 g	A	Placebo	N	Cross-over	21	Y	Y	Illumina

Study	Participants		Interventions			RCT Design				
	n; age ¹ ; % F	Fiber, daily dose	Prebiotic	Comparator; daily dose	Compliance ²	Design	Duration (days)	Run in	Wash out	Analysis
Jie 2000 (66)	30; 29.9; 45%	PDX, 12 g	C	Nil	N	Parallel	28	Y	N	Culture
Kleesen 2007 (67)	45; 23.5; 55%	Inulin⁶ : Chicory inulin; Jerusalem artichoke inulin, 15.4 g	A	Placebo	N	Parallel	21	Y	N	Culture; FISH
Lecerf 2012 (68)	59; 20.1; 57%	XOS⁵ ; Inulin-XOS mix, 6.64 g	C	Wheat dextrin, 6.64 g	N	Parallel	28	N	N	qPCR
Lin 2016 (69)	20; 24.2; 80%	XOS, 1.2 g	C	Placebo	N	Parallel	42	Y	Y	Culture
Lomax 2012 (70)	43; 55; 74%	Beta 2-1 fructan, 8 g	A	Maltodextrin, 8 g	Y	Parallel	28	Y	N	FISH
Maki 2012 (99)	55; 35.1 ³ ; 54% ³	AXOS, 2.4 g	C	Placebo	N	Cross-over	21	N	Y	FISH
Maneerat 2013 (100)	35; 67.4 ³ ; 53% ³	GOS, 8 g	A	Maltodextrin, 8 g	N	Cross-over	21	N	Y	FISH
Martinez 2010 (101)	10; 23-38; 50%	RS⁶ : RS2; RS4, 33.2 g	C	Native wheat starch, 33.2 g	N	Cross-over	21	Y	Y	Pyrosequencing
Pallav 2014 (72)	14; 31.4 ³ ; 65%	Polysaccharidepeptide (I'm-Yunity), 3.6 g	G	Nil	N	Parallel	14	N	N	Pyrosequencing
Pasman 2006 (73)	29; 34.1; 0%	Nutriose FB (dextrin), 45 g	A	Maltodextrin, 22.5 g	Y	Parallel	35	Y	N	Culture
Petry 2012 (102)	32; 18-40; 100%	Inulin, 20 g	A	Maltodextrin, 20 g	N	Cross-over	28	N	Y	qPCR
Ramnani 2010 (74)	66; 32.9; 50%	Inulin, 5 g	A	Placebo	Y	Parallel	21	Y	Y	FISH

Study	Participants		Interventions			RCT Design				
	n; age ¹ ; % F	Fiber, daily dose	Prebiotic	Comparator; daily dose	Compliance ²	Design	Duration (days)	Run in	Wash out	Analysis
Ramnani 2015 (103)	38; 35.1 ³ ; 50%	Agave inulin, 5 g	A	Maltodextrin, 5 g	Y	Cross-over	21	Y	Y	FISH
Salden 2017 (80)	27; 48; 48%	Arabinoxylans, 15 g	G	Maltodextrin, 15 g	Y	Parallel	42	N	N	Illumina
Slavin 2011 (105)	10; 27-49 ³ ; 0%	Chicory inulin, 20 g	A	Placebo	Y	Cross-over	21	N	N	Culture
Ten Bruggencaete 2006 (107)	29; 22.7; 0%	FOS, 20 g	A	Sucrose, 6 g	Y	Cross-over	14	N	Y	qPCR
Tuohy 2011 (108)	NR; NR; 55%	Mix:(FOS & PHGG), 10 g	Mix	Placebo	Y	Cross-over	21	N	N	FISH
Vulevic 2008 (109)	41; 69.3 ³ ; 64% ³	GOS (Bimuno), 5.5 g	A	Maltodextrin, 5.5 g	Y	Cross-over	70	N	Y	FISH
Vulevic 2015 (110)	40; 70.4; 62%	GOS (Bimuno), 5.5 g	A	Maltodextrin, 5.5 g	Y	Cross-over	70	N	Y	FISH
Walton 2010 (113)	31; 21; 58%	MOS, 5 g	C	Placebo	Y	Cross-over	21	N	Y	FISH
Walton 2012 (111)	37; 58.9 ³ ; 57% ³	GOS, 8 g	A	Placebo	N	Cross-over	21	Y	Y	qPCR
Walton 2012 (112)	40; 31.4 ³ ; 60% ³	AXOS, 2.2 g	C	Placebo	Y	Cross-over	21	Y	Y	FISH
Wu 2011 (76)	15; 40.6; 93%	Konjac glucomannan, 4.5 g	G	Nil	N	Parallel	28	N	N	FISH

¹ Age expressed as mean years; age range provided where means were not obtainable. ² Compliance to intervention; assessed by primary study. ³ Refers to randomized population rather than actual population. Compliance to intervention; assessed by primary study. ⁴ Secondary publication reporting additional outcomes from the primary study. ⁵ Refers to analyzed intervention arm with the highest prebiotic classification (accepted prebiotic fiber > candidate prebiotic fiber > general fiber) selected for fiber type subgroup analysis. ⁶ Refers to intervention fibers that have been pooled together for meta-analyses. Abbreviations: A; Accepted prebiotic fiber; AXOS; Arabinoxylan-oligosaccharide; C; Candidate prebiotic fiber; DGGE; Denaturing gradient gel electrophoresis; FISH; Fluorescent *in situ* hybridization; G; General fiber; GOS; Galacto-oligosaccharide; HMO; Human milk oligosaccharide; MOS; Manno-oligosaccharide; NR; Not reported by study; OS; Oligosaccharide; PDX; Polydextrose; PHGG; Partially hydrolyzed guar gum; qPCR; Quantitative polymerase chain reaction; RS; Resistant starch; RS2; Resistant starch 2; RS4; Resistant starch 4; SC-FOS; Short chain fructo-oligosaccharide; TOS; Trans-galacto-oligosaccharide; XOS; Xylo-oligosaccharide.

Table 3: Characteristics of randomized controlled trials of food interventions comparing dietary fiber with low fiber comparators in healthy adults

Study	Participants	Interventions					RCT Design				
	n; age ¹ ; % F	Intervention	Comparator	Daily fiber difference	Study diet ²	Compliance ³	Design	Duration (days)	Run in	Wash out	Analysis
Ampatzoglou 2008 (82)	33; 48.8; 64%	WG diet	RG diet	10 g	N	Y	Cross-over	14	Y	Y	FISH
Carvalho-Wells 2010 (85)	32; 31.6; 66%	WG cereal	Non-WG cereal	6.5 g	N	N	Cross-over	21	Y	Y	FISH
Cooper 2017 (78)	46; 25.8; 46%	WG market basket	RG market basket	5 g	N	Y	Parallel	42	N	N	Illumina
Costabile 2008 (89)	31; 25; 52%	WG cereal	Wheat bran cereal	7.4 g	N	N	Cross-over	21	Y	Y	FISH
Grasten 2007 (96)	14; 59.7 ⁴ ; 100%	Rye bread	White wheat bread	19 g	N	Y	Cross-over	56	Y	Y	Culture
Jenkins 1999 (98)	24; 33; 50%	Wheat bran	Wheat flour	19 g	N	Y	Cross-over	14	N	Y	Culture
Karl 2017 (79); Vanegas 2017 (51)⁵	81; 40-65 ⁴ ; 60%	WG diet	RG diet	8 g	Y	Y	Parallel	42	Y	N	Illumina
Nemoto 2011 (71)	36; 22-67; 63%	Fermented brown rice	"Non-functional food"	4.62 g	N	Y	Parallel	14	N	N	Culture
Ross 2011	17; 35; 65%	WG diet	RG diet	13 g	Y	Y	Cross-	14	Y	Y	qPCR

Study	Participants		Interventions				RCT Design				
	n; age ¹ ; % F	Intervention	Comparator	Daily fiber difference	Study diet ²	Compliance ³	Design	Duration (days)	Run in	Wash out	Analysis
(104)							over				
Smith 2006 (106)	18; 42.8; 0%	Lupin kernal fiber diet	Control diet	22 g	Y	N	Cross-over	28	N	Y	FISH
Tap 2015 (75)	19; 19-25; 53%	High fiber diet	Low fiber diet	30 g	Y	Y	Cross-over	5	N	Y	454 Pyrosequencing Culture
Zeng 2015 (114)	77; 63.4; 70%	Whole cereal legume diet	Control diet	14.5 g	Y	Y	Parallel	90	N	N	

¹ Age expressed as mean years; age range provided where means were not obtainable. ² Whether the participant's entire diet was provided by the study. ³ Compliance to intervention; assessed by primary study. ⁴ Refers to randomized population rather than actual population. ⁵ Secondary publication reporting additional outcomes from the primary study. Abbreviations: FISH; Fluorescent *in situ* hybridization; qPCR; Quantitative polymerase chain reaction; RG; Refined grain; WG; Whole grain.

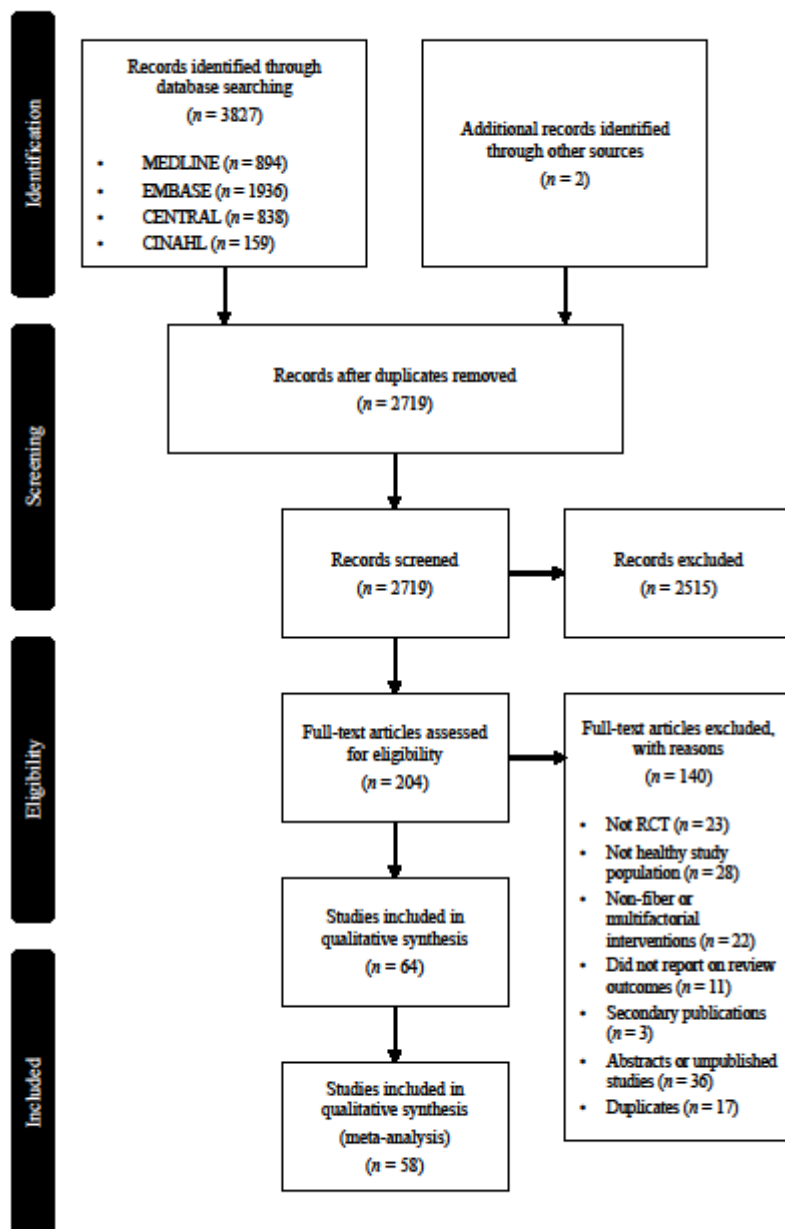


Figure 1: Flow diagram of studies evaluated in the systematic review.

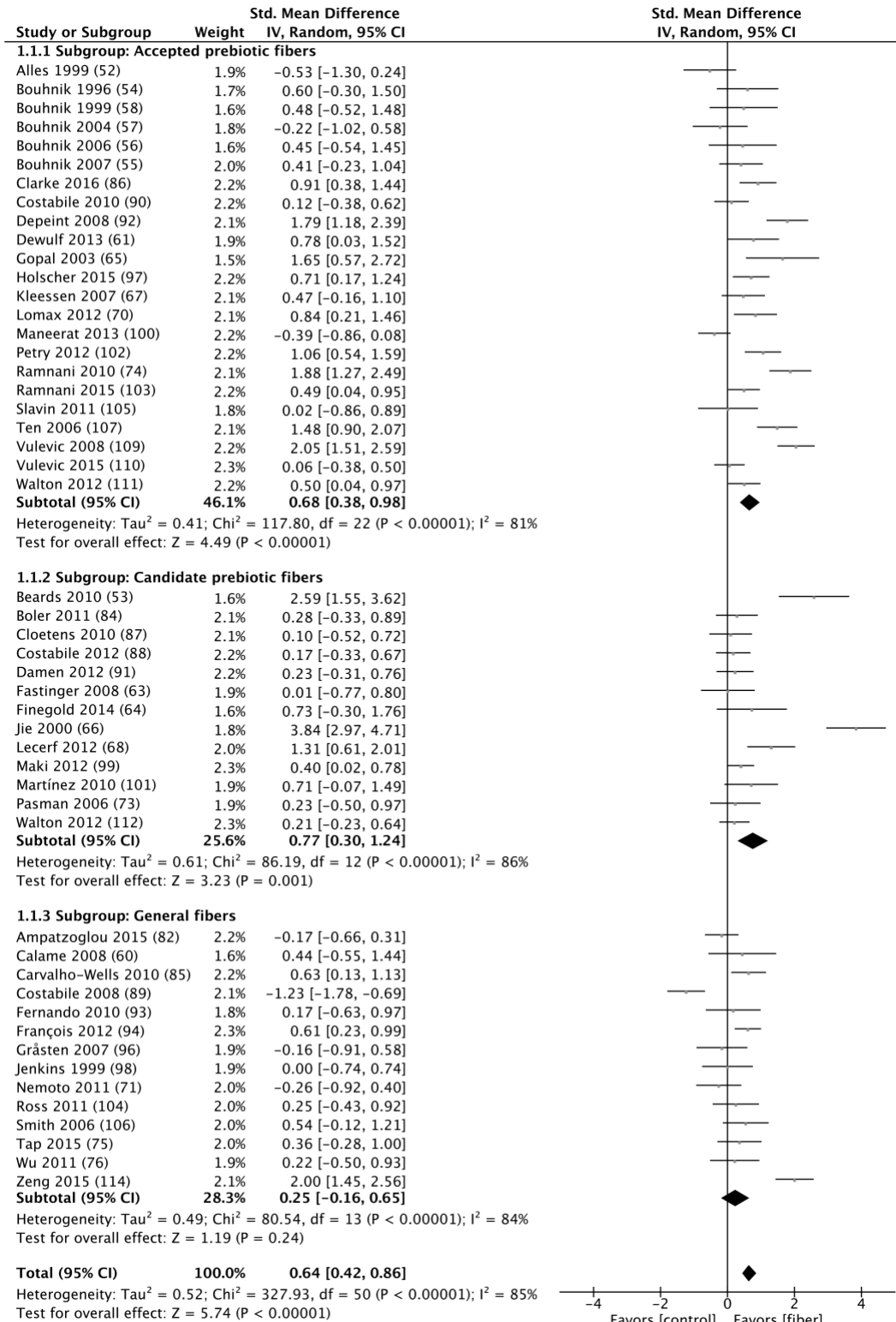


Figure 2: Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low fiber comparators. Studies are sub-grouped by fiber type, with the overall effect included at the bottom. Data are presented as means and SDs of *Bifidobacterium* spp. abundance at end of intervention. Effects of trials are presented as weights (percentages) and SMD (95% CI). CI, confidence interval; IV, inverse variance; SD, standard deviation; SMD, standardized mean difference.

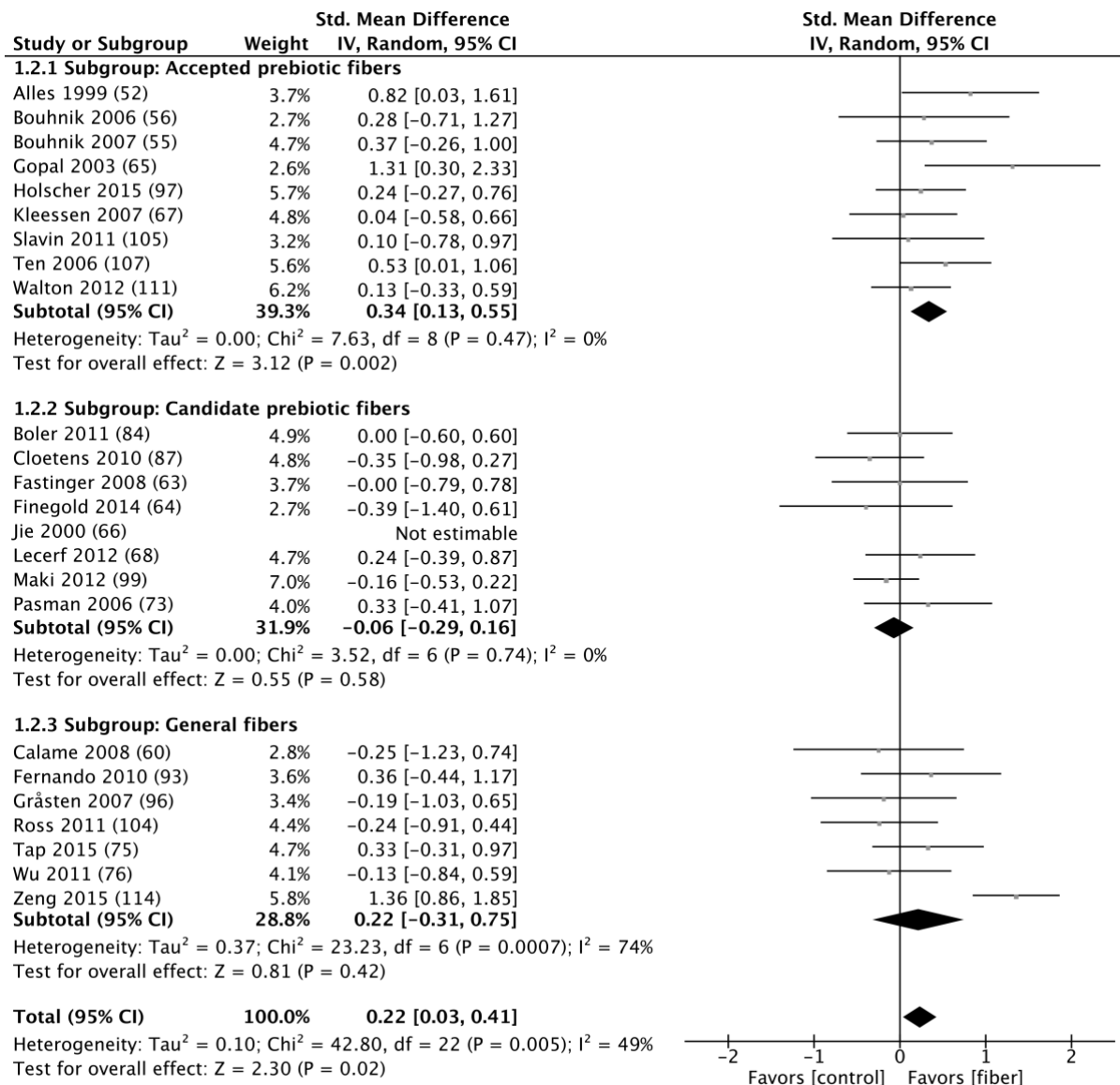


Figure 3: Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low fiber comparators. Studies are sub-grouped by fiber type, with the overall effect included at the bottom. Data are presented as means and SDs of *Lactobacillus* spp. abundance at end of intervention are reported for trials. Effects of trials are presented as weights (percentages) and SMD (95% CI). CI, confidence interval; IV, inverse variance; SD, standard deviation; SMD, standardized mean difference.

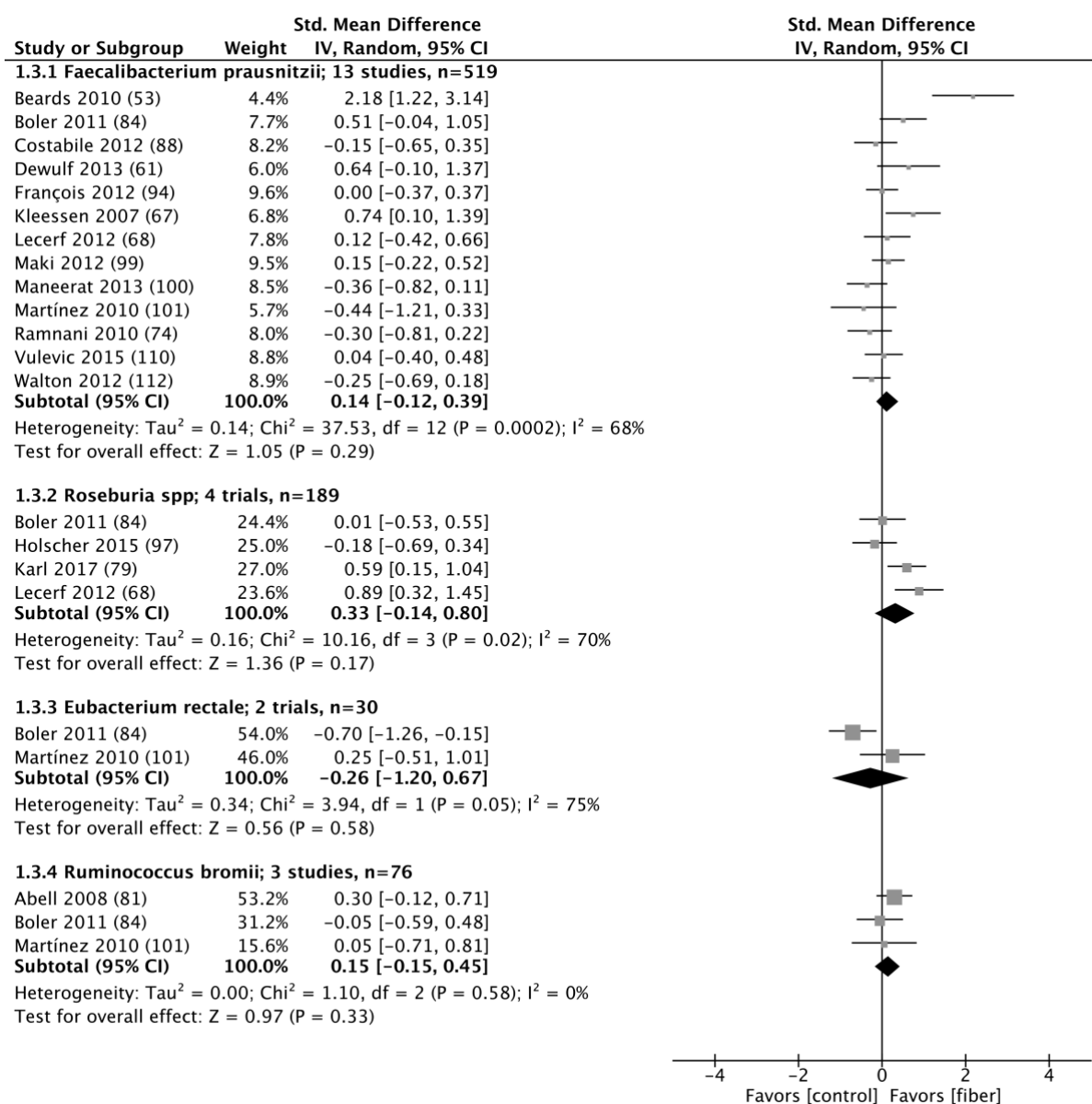


Figure 4: Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low fiber comparators. The means and SDs of *Faecalibacterium prausnitzii*, *Roseburia* spp., *Eubacterium rectale* and *Ruminococcus bromii* abundance at end of intervention are reported for trials. Effects of trials are presented as weights (percentages) and SMD (95% CI). CI, confidence interval; IV, inverse variance; SD, standard deviation; SMD, standardized mean difference.

Supplemental Table 1: Search algorithm: MEDLINE via OVID

Supplemental Table 2: Search algorithm: EMBASE

Supplemental Table 3: Search algorithm: CENTRAL

Supplemental Table 4: Search algorithm: CINAHL

Supplemental Table 5: Reasons for excluding studies from full text analysis

Supplemental Table 6: Outcomes of pre-defined subgroup analyses undertaken

Supplemental Table 7: Outcomes of post hoc subgroup analyses undertaken

Supplemental Figure 1: Risk of bias across the included studies showing the summary percentage in each domain

Supplemental Figure 2: Funnel plot for the effect of dietary fiber on Bifidobacterium spp. abundance

Supplemental Figure 3: Funnel plot for the effect of dietary fiber on Lactobacillus spp. abundance

Supplemental Figure 4: Funnel plot for the effect of dietary fiber on total fecal SCFA

Supplemental Figure 5: Funnel plot for the effect of dietary fiber on fecal acetate

Supplemental Figure 6: Funnel plot for the effect of dietary fiber on fecal propionate

Supplemental Figure 7: Funnel plot for the effect of dietary fiber on fecal butyrate

Supplemental Table 1: Search algorithm: MEDLINE via OVID

1. exp Dietary Fiber/ 2. roughage*.tw. 3. exp Prebiotics/ 4. prebiotic*.tw. 5. (carbohydrate adj2 polymer*).tw. 6. ((non-starch or nonstarch) adj (poly-saccharide* or polysaccharide*)).tw. 7. 1 or 2 or 3 or 4 or 5 or 6 8. Diet/ 9. diet*.tw. 10. consum*.tw. 11. eat*.tw. 12. food*.tw. 13. nutri*.tw. 14. 8 or 9 or 10 or 11 or 12 or 13 15. Agar/ 16. agar*.tw. 17. Alginates/ 18. alginate*.tw. 19. (alginic adj2 acid*).tw. 20. Carrageenan/ 21. carrageen*.tw. 22. exp Cellulose/ 23. cellulose*.tw. 24. exp Chitin/ 25. chitin*.tw. 26. hemicellulose*.tw. 27. hexosan*.tw. 28. Lignin/ 29. lignin*.tw. 30. Pectins/ 31. pectin*.tw. 32. pentosan*.tw. 33. polydextrose*.tw. 34. polyuronide*.tw. 35. Raffinose/ 36. raffinose*.tw. 37. xanthan*.tw. 38. Xylose/ 39. xylose*.tw. 40. exp Galactans/ 41. galactan*.tw. 42. (galactooligosaccharide* or galacto-oligosaccharide* or gos or tos).tw. 43. exp Fructans/ 44. fructan*.tw. 45. (fructooligosaccharide* or fructo-oligosaccharide* or fos or oligofructose or oligo-fructose).tw.	46. exp Inulin/ 47. Inulin*.tw. 48. (gentiooligosaccharide* or gentio-oligosaccharide*).tw. 49. (isomalto oligosaccharide* or isomalto-oligosaccharide* or imo).tw. 50. (mannanooligosaccharide* or mannano-oligosaccharide*).tw. 51. (N-acetylchitooligosaccharide* or N-acetylchito-oligosaccharide*).tw. 52. (pectic oligosaccharide* or pectic-oligosaccharide*).tw. 53. (resistant starch* or resistant-starch*).tw. 54. (soybean oligosaccharide* or soybean-oligosaccharide*).tw. 55. (xylooligosaccharide* or xylo-oligosaccharide*).tw. 56. exp Oligosaccharides/ 57. Oligosaccharide*.tw. 58. (fiber* or fiber* or high-fiber* or high-fiber*).tw. 59. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 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 39 or 40 or 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 57 or 58 60. 14 and 59 61. 7 or 60 62. exp Gastrointestinal Microbiome/ 63. (microbiota or microbiome).tw. 64. bifido*.tw. 65. lactobacill*.tw. 66. 62 or 63 or 64 or 65 67. (faecal or fecal).tw. 68. (bacteri* or flora).tw. 69. 67 and 68 70. exp Dysbiosis/ 71. 66 or 69 or 70 72. 61 and 71 73. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or randomised.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) 74. 72 and 73
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Supplemental Table 2: Search algorithm: EMBASE

1. exp Dietary Fiber/ 2. roughage*.tw. 3. exp Prebiotics/ 4. prebiotic*.tw. 5. (carbohydrate adj2 polymer*).tw. 6. ((non-starch or nonstarch) adj (poly-saccharide* or polysaccharide*)).tw. 7. 1 or 2 or 3 or 4 or 5 or 6 8. Diet/ 9. diet*.tw. 10. consum*.tw. 11. eat*.tw. 12. food*.tw. 13. nutri*.tw. 14. 8 or 9 or 10 or 11 or 12 or 13 15. Agar/ 16. agar*.tw. 17. Alginates/ 18. alginate*.tw. 19. (alginic adj2 acid*).tw. 20. Carrageenan/ 21. carrageen*.tw 22. exp Cellulose/ 23. cellulose*.tw. 24. exp Chitin/ 25. chitin*.tw. 26. hemicellulose*.tw. 27. hexosan*.tw. 28. Lignin/ 29. lignin*.tw. 30. Pectins/ 31. pectin*.tw. 32. pentosan*.tw. 33. polydextrose*.tw. 34. polyuronide*.tw. 35. Raffinose/ 36. raffinose*.tw. 37. xanthan*.tw. 38. Xylose/ 39. xylose*.tw. 40. exp Galactans/ 41. galactan*.tw. 42. (galactooligosaccharide* or galactooligosaccharide* or gos or tos).tw. 43. exp Fructans/ 44. fructan*.tw. 45. (fructooligosaccharide* or fructooligosaccharide* or fos or oligofructose or oligofructose).tw.	46. exp Inulin/ 47. Inulin*.tw. 48. (gentiooligosaccharide* or gentiooligosaccharide*).tw. 49. (isomalto oligosaccharide* or isomalto oligosaccharide* or imo).tw. 50. (mannanooligosaccharide* or mannooligosaccharide*).tw. 51. (N-acetylchitooligosaccharide* or N-acetylchitooligosaccharide*).tw. 52. (pectic oligosaccharide* or pectic oligosaccharide*).tw. 53. (resistant starch* or resistant-starch*).tw. 54. (soybean oligosaccharide* or soybean oligosaccharide*).tw. 55. (xylooligosaccharide* or xylooligosaccharide*).tw. 56. exp Oligosaccharides/ 57. Oligosaccharide*.tw. 58. (fiber* or fiber* or high-fiber* or high-fiber*).tw. 59. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 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 39 or 40 or 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 57 or 58 60. 14 and 59 61. 7 or 60 62. exp Gastrointestinal Microbiome/ 63. (microbiota or microbiome).tw. 64. bifido*.tw. 65. lactobacill*.tw. 66. 62 or 63 or 64 or 65 67. (faecal or fecal).tw. 68. (bacteri* or flora).tw. 69. 67 and 68 70. exp Dysbiosis/ 71. 66 or 69 or 70 72. 61 and 71 73. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or randomised.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.) 74. 72 and 73
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Supplemental Table 3: Search algorithm: CENTRAL

#1	MeSH descriptor: [Dietary Fiber] explode all trees	#40	MeSH descriptor: [Galactans] explode all trees
#2	roughage*	#41	galactan*
#3	MeSH descriptor: [Prebiotics] explode all trees	#42	(galactooligosaccharide* or galacto- oligosaccharide* or gos or tos)
#4	prebiotic*	#43	MeSH descriptor: [Fructans] explode all trees
#5	carbohydrate near/2 polymer*	#44	fructan*
#6	((non-starch or nonstarch) near (poly- saccharide* or polysaccharide*))	#45	(fructooligosaccharide* or fructo- oligosaccharide* or fos or oligofructose* or oligo- fructose*)
#7	#1 or #2 or #3 or #4 or #5 or #6	#46	MeSH descriptor: [Inulin] explode all trees
#8	MeSH descriptor: [Diet] this term only	#47	inulin*
#9	diet*	#48	(gentiooligosaccharide* or gentio- oligosaccharide*)
#10	consum*	#49	(isomalto oligosaccharide* or isomalto- oligosaccharide* or imo)
#11	eat*	#50	(mannanooligosaccharide* or mannano- oligosaccharide*)
#12	food*	#51	(N-acetylchitooligosaccharide* or N-acetylchito- oligosaccharide*)
#13	nutri*	#52	(pectic oligosaccharide* or pectic- oligosaccharide*)
#14	#8 or #9 or #10 or #11 or #12 or #13	#53	(resistant starch* or resistant-starch*)
#15	MeSH descriptor: [Agar] this term only	#54	(soybean oligosaccharide* or soybean- oligosaccharide*)
#16	agar*	#55	(xylooligosaccharide* or xylo-oligosaccharide*)
#17	MeSH descriptor: [Alginates] this term only	#56	MeSH descriptor: [Oligosaccharides] explode all trees
#18	alginate*	#57	oligosaccharide*
#19	alginic near/2 acid	#58	fiber* or fiber* or high-fiber* or high-fiber*
#20	MeSH descriptor: [Carrageenan] this term only	#59	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #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 #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #51 or #52 or #53 or #54 or #55 or #56 or #56 or #57 or #58
#21	carrageen*	#60	#14 and #59
#22	MeSH descriptor: [Cellulose] explode all trees	#61	#7 or #60
#23	cellulose*	#62	MeSH descriptor: [Gastrointestinal Microbiome] explode all trees
#24	MeSH descriptor: [Chitin] explode all trees	#63	(microbiota or microbiome)
#25	chitin*	#64	bifido*
#26	hemicellulose*	#65	lactobacill*
#27	hexosan*	#66	#62 or #63 or #64 or #65
#28	MeSH descriptor: [Lignin] this term only	#67	(faecal or fecal)
#29	lignin*	#68	(bacteri* or flora)
#30	MeSH descriptor: [Pectins] this term only	#69	#67 and #68
#31	pectin*	#70	MeSH descriptor: [Dysbiosis] explode all trees
#32	pentosan*	#71	#66 or #69 or #70
#33	polydextrose*	#72	#61 and #71
#34	polyuronide*		
#35	MeSH descriptor: [Raffinose] this term only		
#36	raffinose*		
#37	xanthan*		
#38	MeSH descriptor: [Xylose] this term only		
#39	xylose*		

Supplemental Table 4: Search algorithm: CINAHL

1. ((dietary fib* OR roughage* OR prebiotic*) OR (diet* OR consum* OR eat* OR food* OR nutri*) AND (agar* OR alginate* OR carrageen* OR cellulose* OR chitin* OR hemicellulose* OR hexosan* OR lignin* OR pectin* OR pentosan* OR polydextrose* OR polyuronide* OR raffinose* OR xanthan* OR xylose* OR galactan* OR galactooligosaccharde* OR galacto-oligosaccharide* OR gos OR tos OR fructan* OR fructooligosaccharide* OR fructo-oligosaccharide* OR fos OR oligofructose* OR oligo-fructose* OR inulin* OR gentiooligosaccharide* OR gentio-oligosaccharide* OR isomalto oligosaccharide* OR isomalto-oligosaccharide* OR imo OR mannanooligosaccharide* OR mannano-oligosaccharide* OR N-acetylchitooligosaccharide* OR N-acetylchito-oligosaccharide* OR pectic oligosaccharide* OR pectic-oligosaccharide* OR resistant starch* OR resistant-starch* OR soybean oligosaccharide* OR soybean-oligosaccharide* OR oligosaccharide* OR high-fib*))
2. ((MH "Microbiota") OR microbiota OR microbiome OR bifido* OR lactobacill*) OR ((faecal OR fecal) AND (bacteri* OR flora)) OR (dysbio*)
3. (MH "Clinical Trials+") OR (MH "Quantitative Studies") OR TI placebo* OR AB placebo* OR (MH "Placebos") OR (MH "Random Assignment") OR TI random* OR AB random* OR TI ((singl* or doubl* or tripl* or trebl*) W1 (blind* or mask*)) OR AB ((singl* or doubl* or tripl* or trebl*) W1 (blind* or mask*)) OR TI clinic* trial* OR AB clinic* trial* OR PT clinical trial

Supplemental Table 5: Reasons for excluding studies following full text analysis*

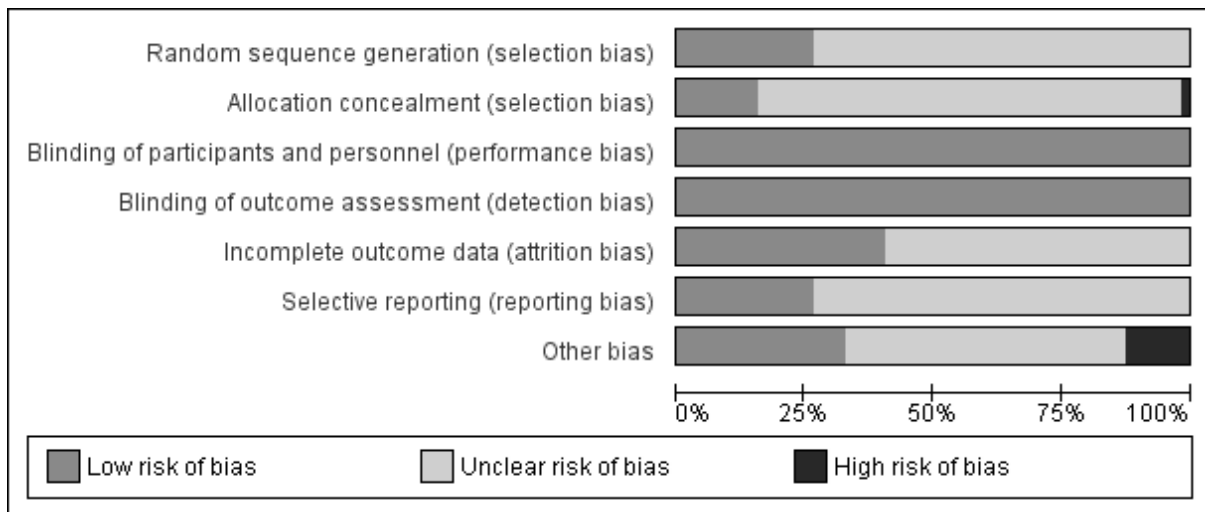
Study Citation	Reason for exclusion
Nil author 2013 (1)	Not RCT
Alfa 2017 (2)	Duplicate
Azcarate-Peril 2013 (3)	Not healthy study population
Azcarate-Peril 2016 (4)	Not healthy study population
Azcarate-Peril 2017 (5)	Not healthy study population
Azpiroz 2016 (6)	Not healthy study population
Baer 2009 (7)	Abstracts or unpublished studies
Benus 2010 (8)	Non-fiber or multifactorial intervention
Brahe 2014 (9)	Duplicate
Brejholt 2005 (10)	Non-fiber or multifactorial intervention
Brighenti 1999 (11)	Not RCT
Casellas 2007 (12)	Not healthy study population
Chen 2006 (13)	Not RCT
Chen 2008 (14)	Not healthy study population
Christensen 2013 (15)	Non-fiber or multifactorial intervention
Chung 2007 (16)	Not RCT
Clarke 2016 (17)	Duplicate
Clarke 2016 (18)	Duplicate
Clarke 2016 (19)	Duplicate
Cooper 2016 (20)	Abstracts or unpublished studies
Costabile 2016 (21)	Not RCT
Culpepper 2012 (22)	Abstracts or unpublished studies
Davis 2010 (23)	Not RCT
Davis 2011 (24)	Not RCT
De Preter 2007 (25)	Not RCT
Demircioglu 2008 (26)	Non-fiber or multifactorial intervention
Dewulf 2011 (27)	Abstracts or unpublished studies
Dewulf 2012 (28)	Abstracts or unpublished studies
Eastwood 1995 (29)	Non-fiber or multifactorial intervention
Eid 2015 (30)	Non-fiber or multifactorial intervention
Elison 2016 (31)	Duplicate
Famdodu 2016 (32)	Abstracts or unpublished studies
Famodu 2016 (33)	Abstracts or unpublished studies
Fava 2013 (34)	Non-fiber or multifactorial intervention
Finley 2007 (35)	Did not report on review outcomes
Ford 2017 (36)	Abstracts or unpublished studies
Gopal 2003 (37)	Duplicate
Gordon 2017 (38)	Abstracts or unpublished studies
Grasten 2000 (39)	Did not report on review outcomes
Guetterman 2016 (40)	Non-fiber or multifactorial intervention
Guglielmetti 2013 (41)	Non-fiber or multifactorial intervention
Hald 2016 (42)	Not healthy study population
Halmos 2013 (43)	Duplicate
Halmos 2014 (44)	Not healthy study population
Halmos 2015 (45)	Duplicate
Healey 2016 (46)	Abstracts or unpublished studies
Heiman 2014 (47)	Not healthy study population
Holscher 2014 (48)	Duplicate
Holscher 2015 (49)	Abstracts or unpublished studies
Hooda 2012 (50)	Secondary publication
Jalanka 2016 (51)	Abstracts or unpublished studies
Jenkins 1999 (52)	Did not report on review outcomes
Karl 2017 (53)	Duplicate
Kellow 2014 (54)	Not healthy study population
Klinder 2016 (55)	Non-fiber or multifactorial intervention

Study Citation	Reason for exclusion
Klosterbuer 2013 (56)	Did not report on review outcomes
Kolida 2007 (57)	Not RCT
Kovatcheva-Datchary 2015 (58)	Did not report on review outcomes
Kruse 1999 (59)	Not RCT
Lambert 2014 (60)	Abstracts or unpublished studies
Lambert 2015 (61)	Not healthy study population
Lamichhane 2014 (62)	Did not report on review outcomes
Langlands 2004 (63)	Not RCT
Lappi 2013 (64)	Not healthy study population
Lee 2016 (65)	Did not report on review outcomes
Lehtinen 2012 (66)	Abstracts or unpublished studies
Li 2009 (67)	Non-fiber or multifactorial intervention
Li 2014 (68)	Abstracts or unpublished studies
Li 2015 (69)	Abstracts or unpublished studies
Lin 2014 (70)	Not healthy study population
Lin 2016 (71)	Duplicate
Linetzky 2012 (72)	Not healthy study population
Lomax 2012 (73)	Duplicate
Lomax 2013 (74)	Duplicate
Lomax 2013 (75)	Abstracts or unpublished studies
Mai 2009 (76)	Abstracts or unpublished studies
Mai 2012 (77)	Non-fiber or multifactorial intervention
Maki 2011 (78)	Abstracts or unpublished studies
Marteau 2011 (79)	Not healthy study population
Matthan 2015 (80)	Abstracts or unpublished studies
Mayengbam 2017 (81)	Abstracts or unpublished studies
Medina-Vera 2017 (82)	Abstracts or unpublished studies
Mego 2017 (83)	Non-fiber or multifactorial intervention
Mitchell 2015 (84)	Not healthy study population
Mitsou 2009 (85)	Non-fiber or multifactorial intervention
Mitsou 2011 (86)	Non-fiber or multifactorial intervention
Orrhage 2000 (87)	Non-fiber or multifactorial intervention
Pantophlet 2017 (88)	Not RCT
Ramirez-Farias 2009 (89)	Secondary publication
Ramprasath 2015 (90)	Abstracts or unpublished studies
Rao 2001 (91)	Not RCT
Ravn-Haren 2013 (92)	Non-fiber or multifactorial intervention
Robinson 2001 (93)	Not RCT
Salazar 2013 (94)	Abstracts or unpublished studies
Salazar 2015 (95)	Abstracts or unpublished studies
Salden 2015 (96)	Abstracts or unpublished studies
Salonen 2014 (97)	Not healthy study population
Scarpellini 2012 (98)	Abstracts or unpublished studies
Scarpellini 2016 (99)	Did not report on review outcomes
Scholtens 2006 (100)	Did not report on review outcomes
Sloan 2016 (101)	Abstracts or unpublished studies
Smilowitz 2017 (102)	Not RCT
Song 2015 (103)	Non-fiber or multifactorial intervention
Souza 2015 (104)	Not healthy study population
Surakka 2009 (105)	Not healthy study population
Tannock 2004 (106)	Not RCT
Taylor 2016 (107)	Non-fiber or multifactorial intervention
Thompson 2016 (108)	Abstracts or unpublished studies
Thompson 2016 (109)	Abstracts or unpublished studies
Tomono 2010 (110)	Not healthy study population
Tuohy 2001 (111)	Not RCT
Tuohy 2001 (112)	Duplicate

Study Citation	Reason for exclusion
Ukhanova 2014 (113)	Non-fiber or multifactorial intervention
Upadhyaya 2016 (114)	Not healthy study population
Vanegas 2016 (115)	Abstracts or unpublished studies
Vanegas 2017 (116)	Secondary publication
Vanegas 2017 (117)	Duplicate
Vendrame 2011 (118)	Non-fiber or multifactorial intervention
Venkataraman 2016 (119)	Not RCT
Vitaglione 2015 (120)	Non-fiber or multifactorial intervention
Vulevic 2013 (121)	Not healthy study population
Walker 2011 (122)	Not healthy study population
Wallace 2015 (123)	Not RCT
Weickert 2011 (124)	Not healthy study population
West 2012 (125)	Not RCT
Westreich 2017 (126)	Abstracts or unpublished studies
Whisner 2016 (127)	Not healthy study population
Willis 2013 (128)	Did not report on review outcomes
Windey 2015 (129)	Did not report on review outcomes
Wong 2010 (130)	Not RCT
Wood 2017 (131)	Abstracts or unpublished studies
Wood 2017 (132)	Abstracts or unpublished studies
Worthley 2009 (133)	Not RCT
Worthley 2009 (134)	Abstracts or unpublished studies
Wutzke 2012 (135)	Abstracts or unpublished studies
Xiao 2014 (136)	Not RCT
Yang 2015 (137)	Not healthy study population
Yen 2011 (138)	Duplicate
Yen 2011 (139)	Not healthy study population
Yen 2011 (140)	Not healthy study population

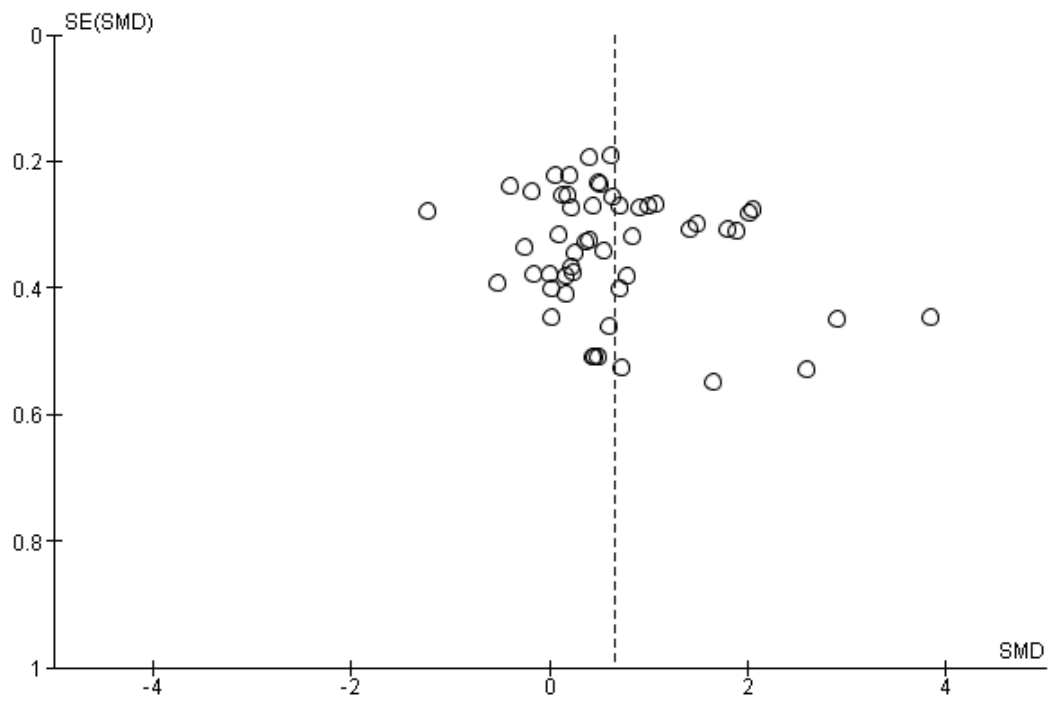
* Citation numbers do not correspond to citations in main manuscript, and are provided at the end of this document.

Risk of Bias

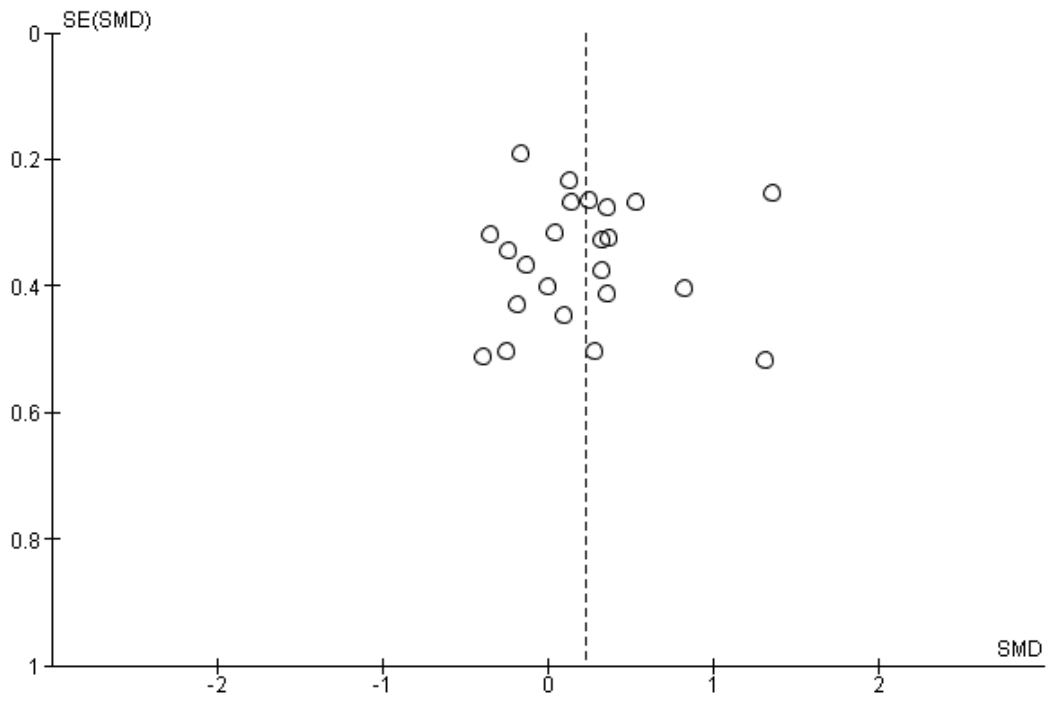


Supplemental Figure 1: Risk of bias across the included studies showing the summary percentage in each domain

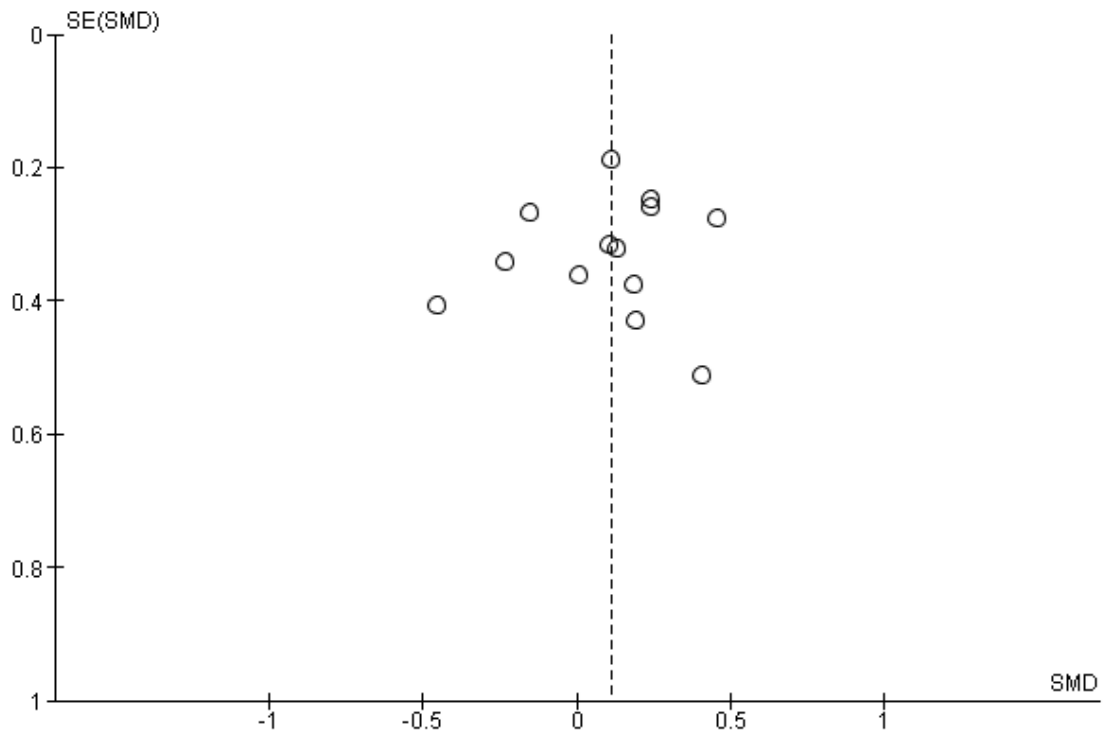
Reporting Bias



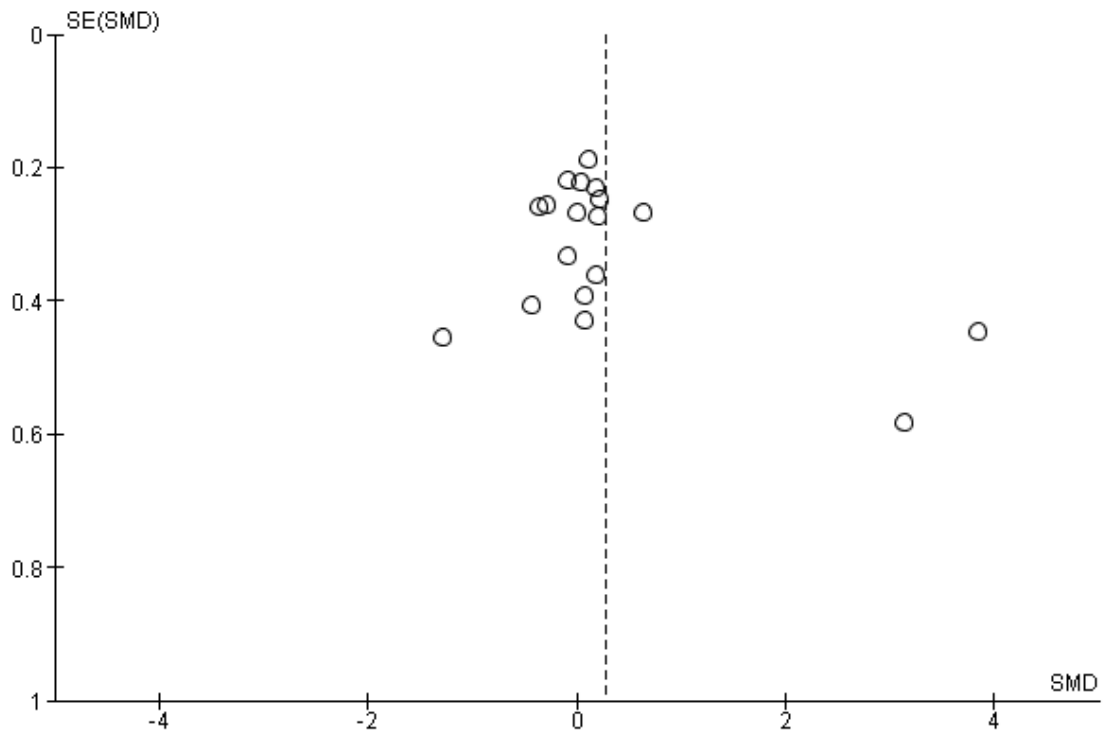
Supplemental Figure 2: Funnel plot for the effect of dietary fiber on *Bifidobacterium* spp. abundance



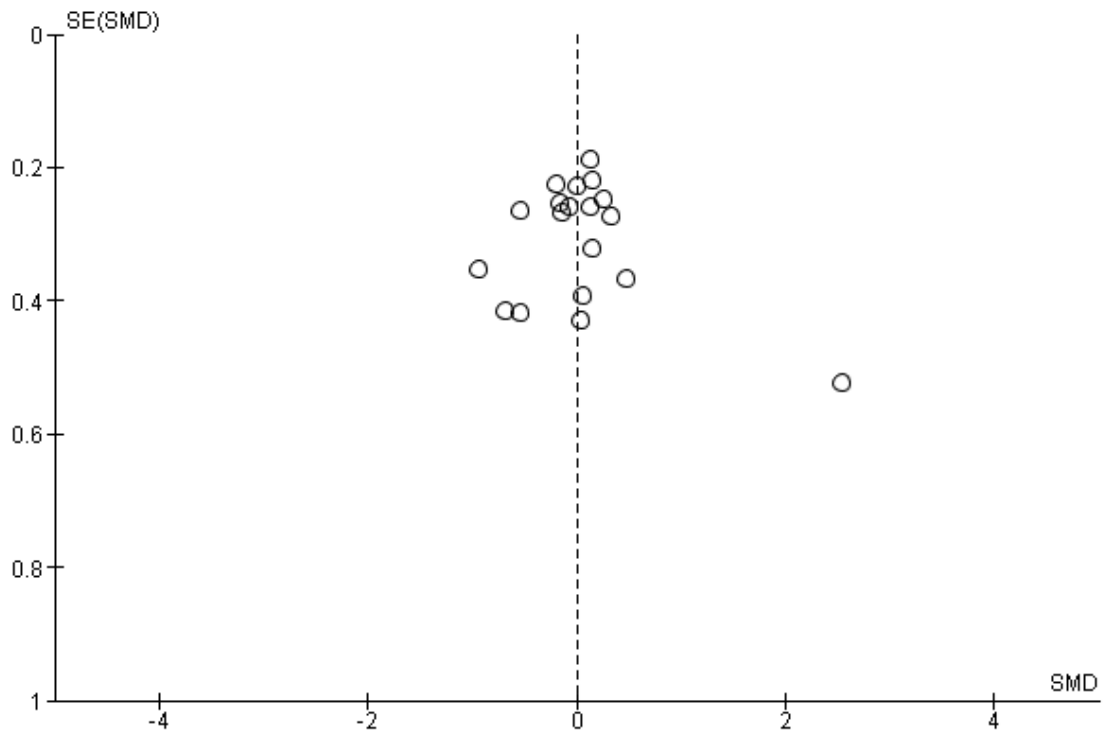
Supplemental Figure 3: Funnel plot for the effect of dietary fiber on *Lactobacillus* spp. abundance



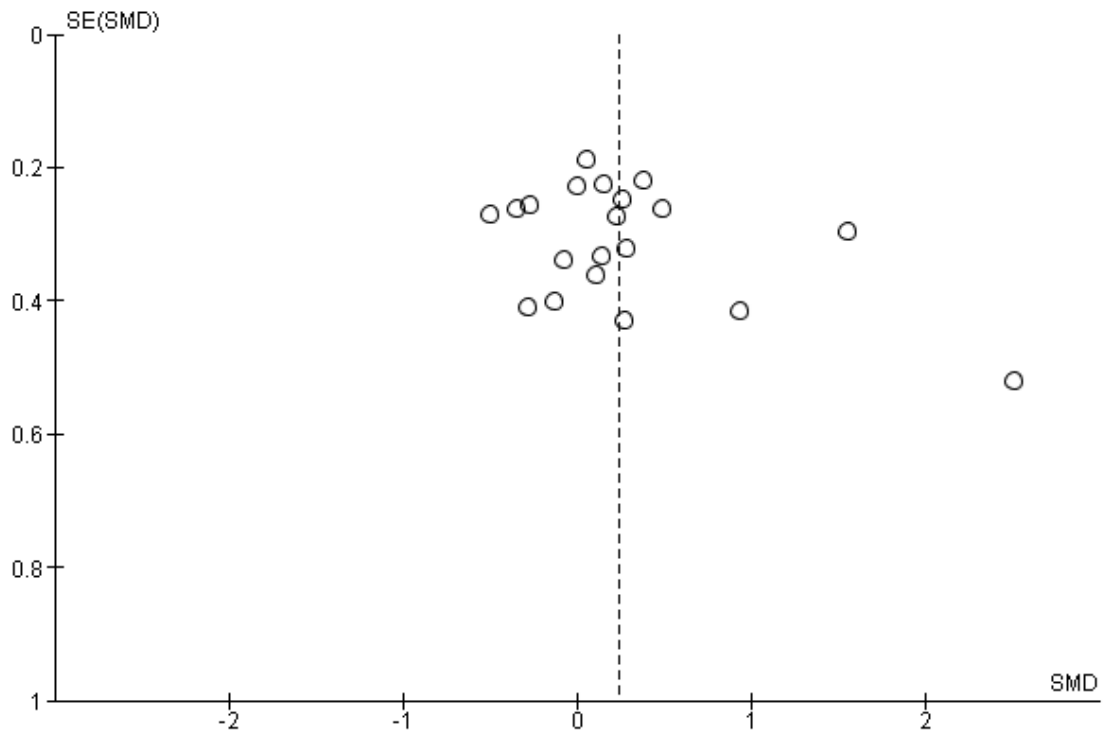
Supplemental Figure 4: Funnel plot for the effect of dietary fiber on total fecal SCFA



Supplemental Figure 5: Funnel plot for the effect of dietary fiber on fecal acetate



Supplemental Figure 6: Funnel plot for the effect of dietary fiber on fecal propionate



Supplemental Figure 7: Funnel plot for the effect of dietary fiber on fecal butyrate

Supplemental Table 6: Outcomes of pre-defined subgroup analyses undertaken

Outcome	Subgroup analysis	Subgroup difference (I ²)	Subgroups	Studies in subgroup (n)	Result			Heterogeneity	
					Meta-analysis overall estimate (95% CI)	P	Chi-squared test	P	I ²
Shannon Diversity Index	Trial design	0%	Cross-over	3	MD: -0.10 (95% CI: -0.19, -0.01)	0.03	1.36	0.51	0%
			Parallel	3	MD: -0.03 (95% CI: -0.57, 0.51)	0.91	9.35	0.009	79%
<i>Bifidobacterium</i> spp.	Intervention type	68.6%	Food	10	SMD: 0.75 (95% CI: 0.52, 0.98)	<0.00001	234.35	<0.00001	83%
			Supplement	41	SMD: 0.20 (95% CI: -0.36, 0.76)	0.49	76.94	<0.00001	88%
	Fiber type	45.3%	Accepted prebiotic	23	SMD: 0.68 (95% CI: 0.38, 0.98)	<0.00001	117.8	<0.00001	81%
			Candidate prebiotic	13	SMD: 0.77 (95% CI: 0.30, 1.24)	0.001	86.19	<0.00001	86%
			General fiber	14	SMD: 0.25 (95% CI: -0.16, 0.65)	0.24	80.54	<0.00001	84%
				11	SMD: 0.51 (95% CI: 0.18, 0.84)	0.003	33.52	0.0002	70%
	Dose response	8.8%	≤5g/d	11	SMD: 0.51 (95% CI: 0.18, 0.84)	0.003	33.52	0.0002	70%
			5-10g/d	18	SMD: 0.48 (95% CI: 0.13, 0.84)	0.007	133.22	<0.00001	87%
			>10g/d	22	SMD: 0.85 (95% CI: 0.45, 1.25)	<0.00001	143.72	<0.00001	85%
	Trial design	77%	Cross-over	30	SMD: 0.44 (95% CI: 0.21, 0.66)	<0.00001	149.67	<0.00001	81%
			Parallel	21	SMD: 0.98 (95% CI: 0.52, 1.44)	<0.00001	148.63	<0.00001	87%
	Analysis method	0%	Culture	13	SMD: 0.70 (95% CI: 0.07, 1.33)	0.03	99.72	<0.00001	88%
			qPCR	11	SMD: 0.62 (95% CI: 0.29, 0.94)	0.0002	30.28	0.0008	67%
			FISH	19	SMD: 0.71 (95% CI: 0.31, 1.10)	0.0004	187.79	<0.00001	90%
Sequencing			4	SMD: 0.61 (95% CI: 0.27, 0.95)	0.0005	0.83	0.84	0%	
Food			4	SMD: 0.35 (95% CI: -0.46, 1.16)	0.40	18.73	0.00003	84%	
<i>Lactobacillus</i> spp.	Intervention type	0%	Supplement	19	SMD: 0.16 (95% CI: 0.01, 0.31)	0.04	19.27	0.38	7%
			Fiber type	69.1%	Accepted prebiotic	9	SMD: 0.34 (95% CI: 0.13, 0.55)	0.002	7.63
			Candidate prebiotic	7	SMD: -0.06 (95% CI: -0.29, 0.16)	0.58	3.52	0.74	0%
			General fiber	7	SMD: 0.22 (95% CI: -0.31, 0.75)	0.42	23.23	0.0007	74%
	Dose	0%	≤5g/d	6	SMD: 0.16 (95% CI: -0.24, 0.56)	0.44	9.67	0.09	48%

Outcome	Subgroup analysis	Subgroup difference (I ²)	Subgroups	Studies in subgroup (n)	Result		Heterogeneity		
					Meta-analysis overall estimate (95% CI)	P	Chi-squared test	P	I ²
<i>Faecalibacterium prausnitzii</i>	response		5-10g/d	5	SMD: 0.14 (95% CI: -0.12, 0.39)	0.29	3.23	0.52	0%
			>10g/d	12	SMD: 0.29 (95% CI: -0.01, 0.59)	0.06	26.08	0.006	58%
	Trial design	57.7%	Cross-over	11	SMD: 0.08 (95% CI: -0.09, 0.25)	0.38	9.04	0.53	0%
			Parallel	12	SMD: 0.37 (95% CI: 0.04, 0.70)	0.03	26.8	0.005	59%
	Analysis method	55.1%	Culture	7	SMD: 0.61 (95% CI: 0.13, 1.08)	0.01	15.99	0.01	62%
			qPCR	9	SMD: 0.13 (95% CI: -0.07, 0.33)	0.21	7.36	0.50	0%
			FISH	2	SMD: -0.15 (95% CI: -0.48, 0.18)	0.37	0.01	0.94	0%
			Sequencing	3	SMD: 0.18 (95% CI: -0.19, 0.56)	0.33	1.53	0.46	0%
	Dose response	38.0%	≤5g/d	3	SMD: -0.10 (95% CI: -0.39, 0.19)	0.51	2.71	0.26	26%
			5-10g/d	6	SMD: -0.05 (95% CI: -0.23, 0.13)	0.57	2.55	0.77	0%
	Trial design	53.6%	>10g/d	4	SMD: 0.39 (95% CI: -0.09, 0.87)	0.11	6.24	0.10	52%
			Cross-over	8	SMD: 0.06 (95% CI: -0.18, 0.29)	0.63	12.71	0.08	45%
Parallel			5	SMD: 0.60 (95% CI: -0.09, 1.29)	0.009	22.6	0.0002	82%	
<i>Roseburia</i> spp.	Trial design	89.2%	Cross-over	2	SMD: -0.09 (95% CI: -0.46, 0.29)	0.65	0.25	0.62	0%
			Parallel	2	SMD: 0.71 (95% CI: 0.36, 1.06)	<0.00001	0.64	0.42	0%

Supplemental Table 7: Outcomes of post hoc subgroup analyses undertaken

Outcome	Subgroup analysis	Subgroup difference (I ²)	Subgroups	Studies in subgroup (n)	Result		Heterogeneity		
					Meta-analysis overall estimate (95% CI)	P	Chi-squared test	P	I ²
Total SCFA	Reporting method	44.5%	Dry weight of feces	6	SMD: 0.02 (95% CI: -0.23, 0.26)	0.89	2.81	0.73	0%
			Wet weight of feces	6	SMD: 0.25 (95% CI: 0.01, 0.49)	0.04	0.80	0.98	0%
Acetate	Reporting method	77.3%	Dry weight of feces	6	SMD: -0.08 (95% CI: -0.40, 0.25)	0.65	10.26	0.07	51%
			Wet weight of feces	10	SMD: 0.69 (95% CI: 0.05, 1.33)	0.03	98.97	<0.00001	91%
Propionate	Reporting method	0%	Dry weight of feces	6	SMD: -0.07 (95% CI: -0.33, 0.20)	0.61	7.15	0.21	30%
			Wet weight of feces	11	SMD: 0.09 (95% CI: -0.26, 0.44)	0.61	38.22	<0.00001	74%
Butyrate	Reporting method	74.1%	Dry weight of feces	7	SMD: 0.02 (95% CI: -0.18, 0.22)	0.81	1.26	0.97	0%
			Wet weight of feces	11	SMD: 0.47 (95% CI: 0.07, 0.87)	0.02	49.36	<0.00001	80%

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