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

So, Daniel; Whelan, Kevin; Rossi, Megan; Morrison, Mark; Holtmann, Gerald; Kelly, Jaimon T.; Shanahan, Erin R.; Staudacher, Heidi M.; Campbell, Katrina L.

Published in:
American Journal of Clinical Nutrition

DOI:
10.1093/ajcn/nqy041

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

Review authors

Daniel So, APD

Kevin Whelan, PhD

Megan Rossi, APD, PhD

Mark Morrison, PhD

Gerald Holtmann, PhD

Jaimon T. Kelly, APD, PhD Candidate

Erin R Shanahan, PhD

Heidi M Staudacher, APD, PhD

Katrina L. Campbell, AdvAPD, PhD

Affiliations

1. Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia (DS; JK; KC)
2. King's College, London, Department of Nutritional Sciences, United Kingdom (MR; KW)
3. The University of Queensland Diamantina Institute, The University of Queensland, Translational Research Institute, Brisbane, Australia (ES; MM)
4. Faculty of Medicine, University of Queensland, Brisbane, Australia (MM, GH, HS)
5. Department of Gastroenterology & Hepatology, Princess Alexandra Hospital, Brisbane, Australia (GH, ES)
6. Department of Nutrition and Dietetics, Princess Alexandra Hospital, Brisbane, Australia (KC)

Authors last names

So, Whelan, Rossi, Morrison, Holtmann, Kelly, Shanahan, Staudacher, Campbell

Disclaimers

None.

Corresponding author

Katrina L Campbell, kcampbel@bond.edu.au

Faculty of Health Science and Medicine, Bond University

14 University Drive, Robina, Queensland, 4226, Australia

Phone: (07) 559 53573

Sources of support

This work has received no specific funding.

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

ABSTRACT

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

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

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

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

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

KEYWORDS

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

BACKGROUND

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

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

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

where it is available to the microbial community. Dietary fiber encompasses an array of heterogeneous compounds whose physicochemical properties vary based on their particle size, chemical structure, solubility, viscosity and fermentability (29, 30). Fiber with fermentable characteristics are substrates for the microbial population in the colon, stimulating growth of specific organisms and leading to production of various metabolites including SCFA (19, 29, 31). Indeed, some fibers can be further classified as 'prebiotic' (e.g. fructans) if they have been shown to be selectively utilized by host microorganisms conferring a health benefit (32).

The current body of evidence regarding the effect of dietary fiber on the gut microbiota is informed via specific prebiotic fiber interventions (33, 34), whole-diet interventions (35-37) and cross-sectional associations (38, 39). However, these investigations are limited in that prebiotic fibers represent only a subset of total dietary fiber, and confounding factors such as disease states and intake of other fermentable substrates, are unaccounted for in whole diet studies and cross-sectional studies (40). Therefore, there is a gap in knowledge regarding the precise impact of dietary fiber intervention on the gut microbiota in healthy subjects, and this is the focus on the systematic review.

METHODS

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

Literature search

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

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

Study selection

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

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

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

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

Data extraction and management

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

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

Statistical analysis

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

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

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

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

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

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

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

RESULTS

Study characteristics

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

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

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

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

Dietary fiber and gut microbiota diversity (α-diversity)

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

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

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

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

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

Dietary fiber and bacterial abundances

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

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

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

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

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

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

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

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

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

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

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

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

Dietary fiber and short-chain fatty acids

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

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

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

acetate following fiber intervention compared with placebo/low fiber comparators [SMD: 0.28 (95% CI: -0.08, 0.63), $P = 0.13$] with substantial heterogeneity between studies ($I^2 = 86$). The effect of fiber intervention on fecal propionate concentration was reported in 19 studies of 677 participants (52, 53, 63, 66, 71, 74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112, 115). No differences were found between fecal propionate and comparators [SMD: -0.01 (95% CI: -0.20, 0.22), $P = 0.95$], with moderate heterogeneity detected ($I^2 = 61\%$). The effect of fiber intervention on fecal butyrate concentration was reported in 20 studies of 712 participants (52, 53, 59, 63, 66, 71, 74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112, 115). Fecal butyrate was significantly higher following fiber intervention compared with placebo/low fiber comparators [SMD: 0.24 (95% CI: 0.00, 0.47), $P = 0.05$], although considerable heterogeneity was present ($I^2 = 70\%$).

Of the studies evaluating differences in fecal SCFA concentration following fiber intervention compared with placebo/low fiber comparators, 13 studies expressed mean SCFA concentrations per wet weight of feces (52, 53, 66, 67, 71, 73, 74, 77, 82, 90, 91, 96, 115), 10 studies as dry weight of feces (55, 59, 63, 64, 68, 80, 93, 94, 103, 112), one study as molar ratio (84), and one study as a combination of wet weight of feces and molar ratio (86). Additional subgroup analyses were performed to compare differences in fecal SCFA concentrations when expressed as wet weight compared with dry weight (**Supplemental Table 7**). Fiber intervention led to significantly higher fecal concentrations of total SCFA, acetate and butyrate compared with comparators when expressed per wet weight of feces. However, there were no significant differences when mean SCFA concentrations were expressed per dry weight of feces. Study heterogeneity was considerably greater for fecal acetate and butyrate, but not total fecal SCFA concentrations when expressed as wet compared with dry wet of feces. There were no differences in effect based on analysis method for fecal

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

Differences in intervention effects based on trial design

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

Risk of bias

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

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

Reporting bias

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

DISCUSSION

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Author contributions

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

Competing interests

None declared.

Acknowledgements

The authors wish to thank David Honeyman for assisting with the development of the search strategy. Many thanks to the authors of included studies who provided outcome data necessary for the extraction of data of the variables included in the meta-analyses.

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

			Results		Heterogeneity		
Outcomes	**No. of studies in meta-analysis (references)**	***n*[1]**	**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
***Bifidobacterium* 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
***Lactobacillus* 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
Faecalibacterium prausnitzii	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
***Roseburia* spp.**	4 (68, 79, 84, 97)	189	SMD: 0.33 (95% CI: -0.14; 0.80)	0.17	10.16	0.02	70
Eubacterium rectale	2 (84, 101)	30	SMD: -0.26 (95% CI: -1.20; 0.67)	0.58	3.94	0.05	75
Ruminococcus bromii	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

			Results		Heterogeneity		
Outcomes	**No. of studies in meta-analysis (references)**	***n*[1]**	**Meta-analysis overall estimate (95% CI)**	***P***	**Chi-square test**	***P***	**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 I^2 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

	Participants	Interventions				RCT Design				
Study	**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	Maltilol, 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%	**PDX**[5]; 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

	Participants	Interventions				RCT Design			
Study	**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
Calame 2008 (60)	16; 30.9; NR	Arabic gum, 40 g	G	Placebo	Y	Parallel	28	N	N	qPCR
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

	Participants	Interventions				RCT Design				
Study	**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%	**HMO[6]:** 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

Participants		Interventions				RCT Design				
Study	**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%	**Inulin[6]:** Chicory inulin; Jerusalem artichoke inulin, 15.4 g	A	Placebo	N	Parallel	21	Y	N	Culture; FISH
Lecerf 2012 (68)	59; 20.1; 57%	**XOS**[5]; 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%	**RS**[6]: 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

	Participants	Interventions				RCT Design				
Study	**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 Bruggencate 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

	Participants	Interventions					RCT Design			
Study	**n; age[1]; % F**	**Intervention**	**Comparator**	**Daily fiber difference**	**Study diet[2]**	**Compl-iance[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

	Participants	Interventions					RCT Design				
Study	**n; age[1]; % F**	**Intervention**	**Comparator**	**Daily fiber difference**	**Study diet[2]**	**Compl-iance[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
Zeng 2015 (114)	77; 63.4; 70%	Whole cereal legume diet	Control diet	14.5 g	Y	Y	Parallel	90	N	N	Culture

[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.

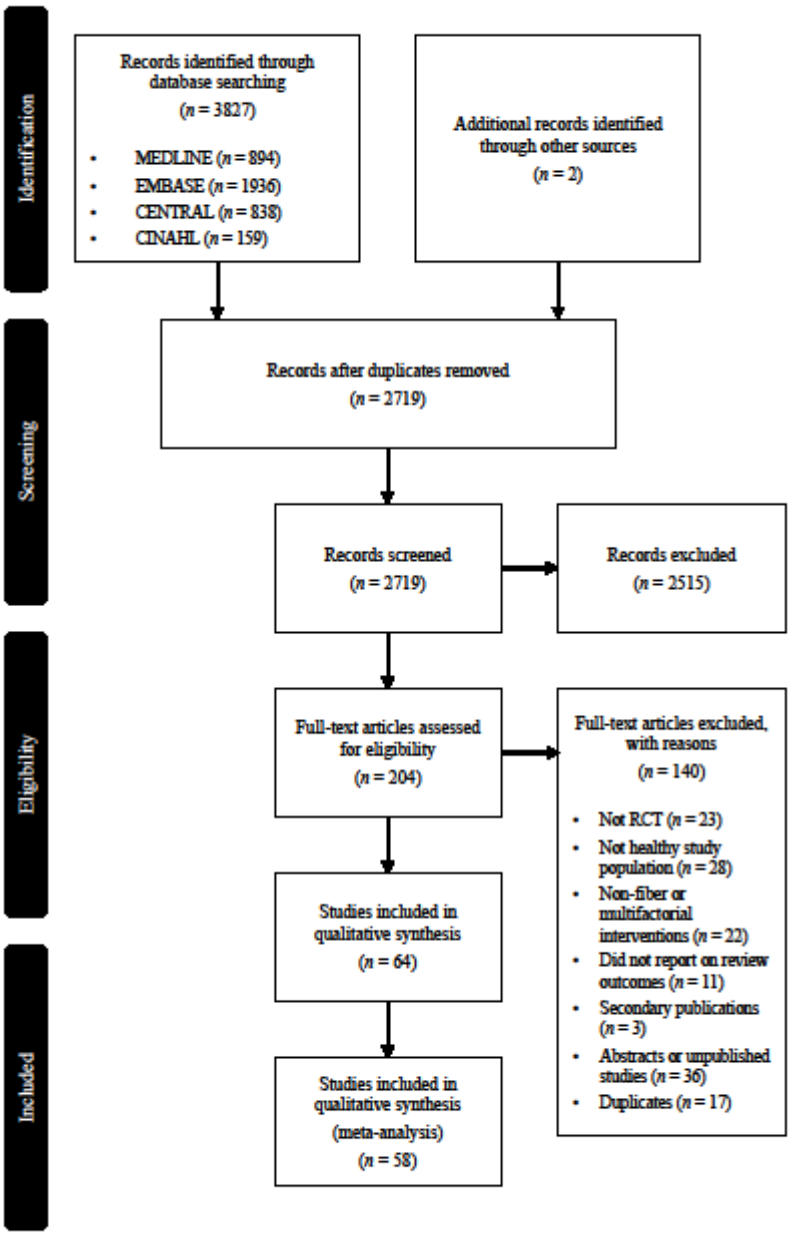


Figure 1: Flow diagram of studies evaluated in the systematic review.

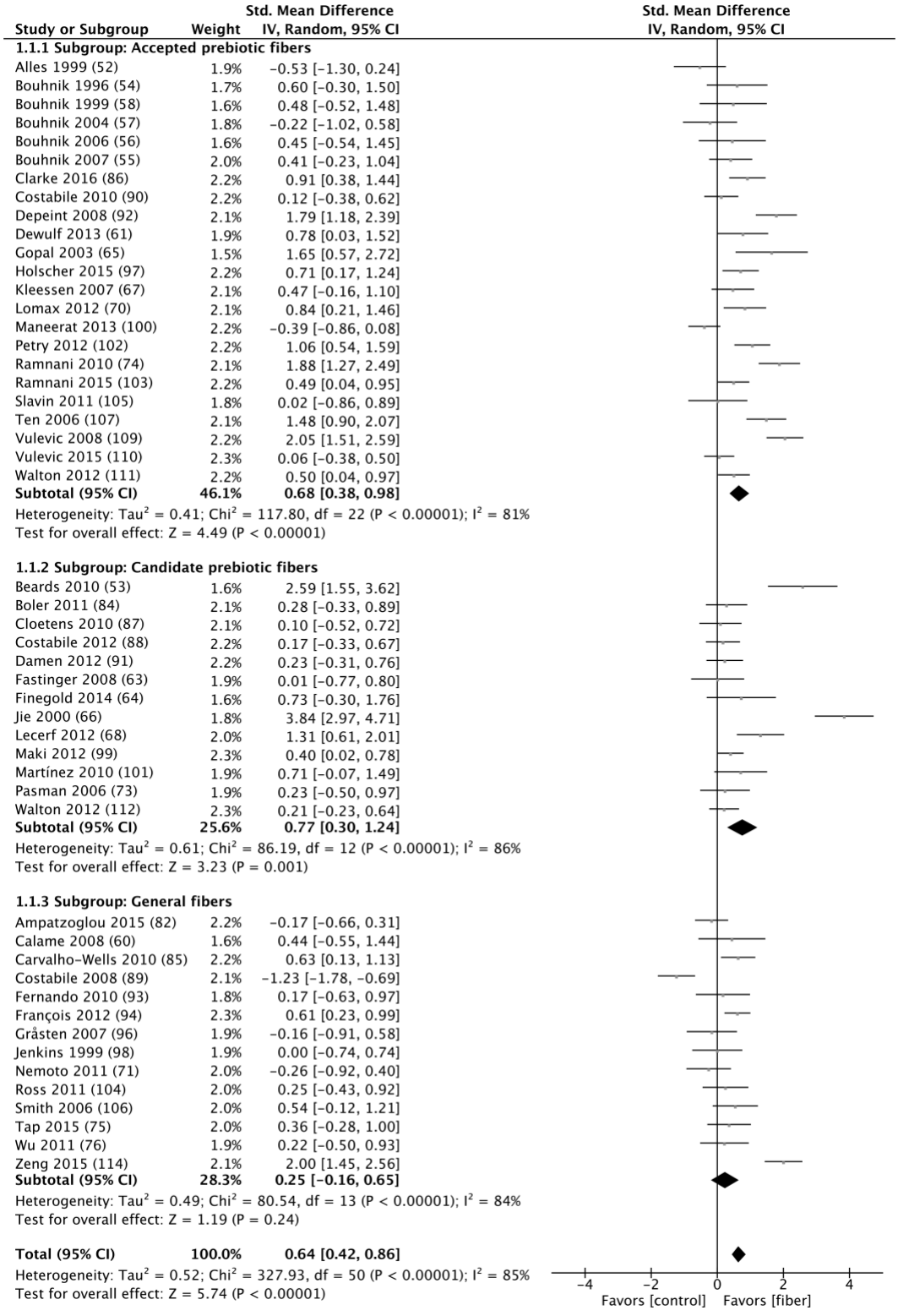


Figure 2: Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low fiber comparators. Studies are sub-grouped by fiber type, with the overall effect included at the bottom. Data are presented as means and SDs of *Bifidobacterium* spp. abundance at end of 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.

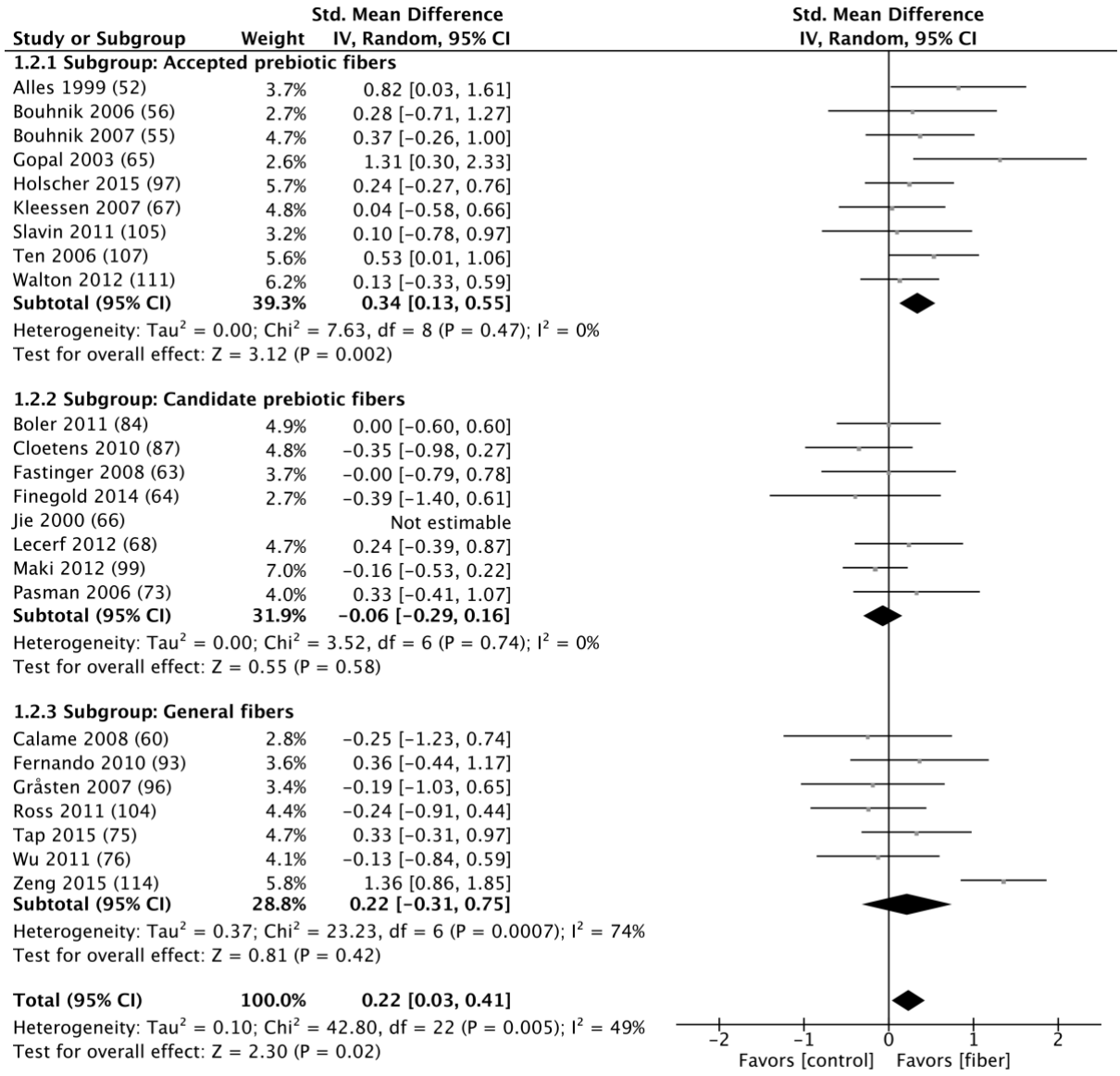


Figure 3: Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low fiber comparators. Studies are sub-grouped by fiber type, with the overall effect included at the bottom. Data are presented as means and SDs of *Lactobacillus* spp. abundance at end of intervention 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.

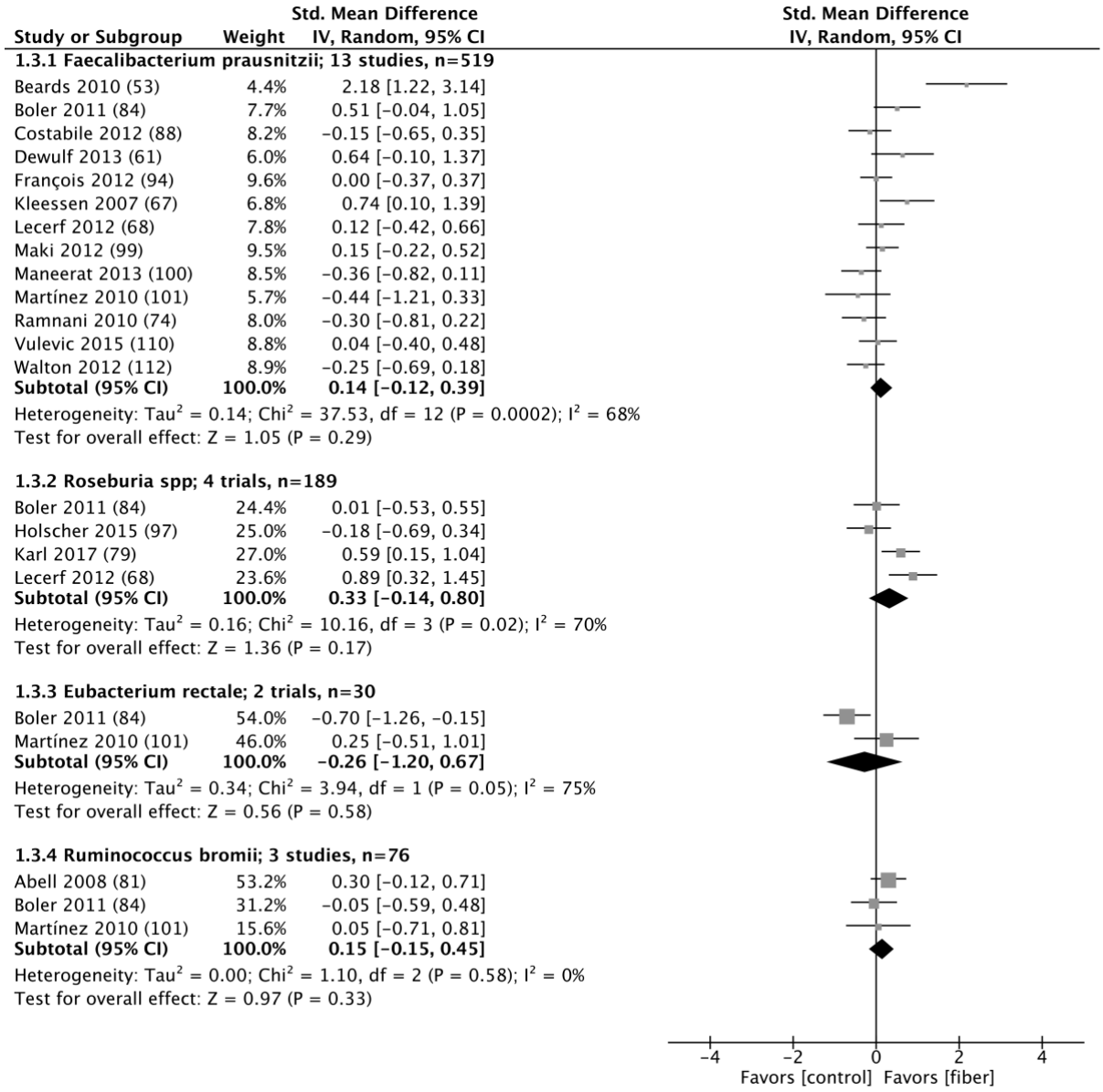


Figure 4: Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low fiber comparators. The means and SDs of Faecalibacterium prausnitzii, Roseburia spp., Eubacterium rectale and Ruminococcus bromii abundance at end of intervention are reported for trials. 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

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

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 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

Supplemental Table 3: Search algorithm: CENTRAL

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

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-oigosaccharide* 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*

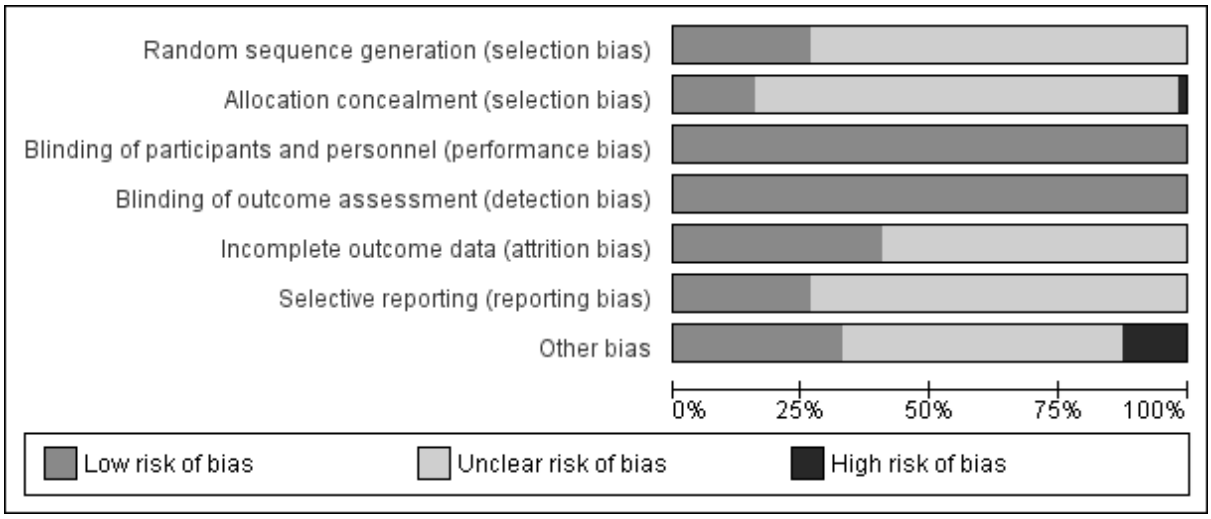
Study Citation	Reason for exclusion
Nil author 2013 (1)	Not RCT
Alfa 2017 (2)	Duplicate
Azcarate-Peril 2013 (3)	Not healthy study population
Azcarate-Peril 2016 (4)	Not healthy study population
Azcarate-Peril 2017 (5)	Not healthy study population
Azpiroz 2016 (6)	Not healthy study population
Baer 2009 (7)	Abstracts or unpublished studies
Benus 2010 (8)	Non-fiber or multifactorial intervention
Brahe 2014 (9)	Duplicate
Brejnholt 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

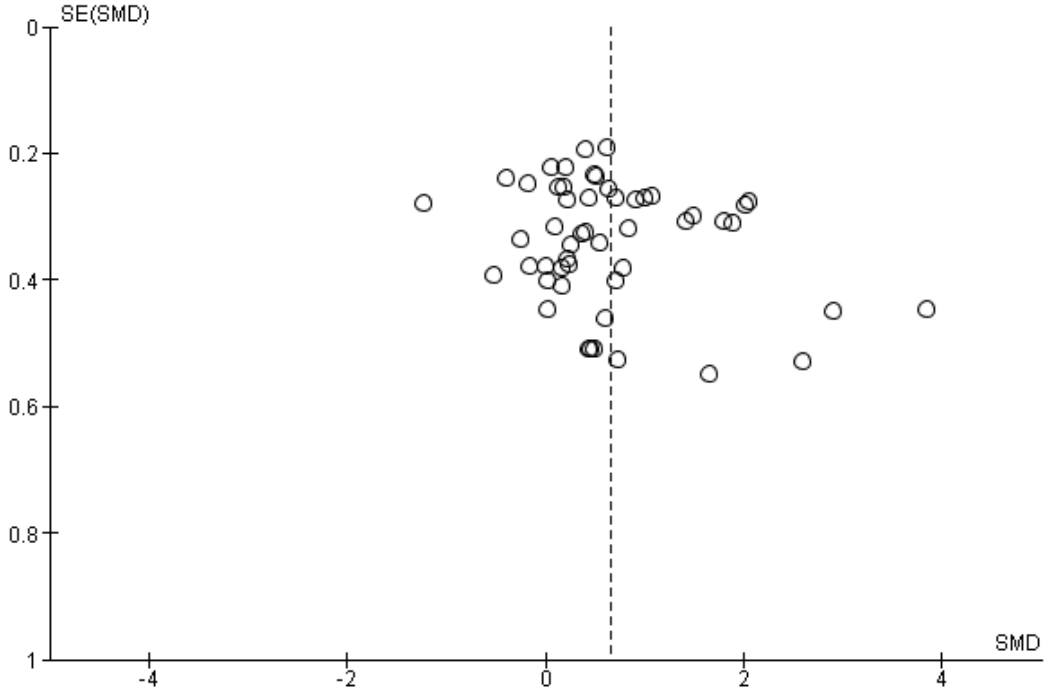
* Citation numbers do not correspond to citations in main manuscript, and are provided at the end of this document.

Risk of Bias

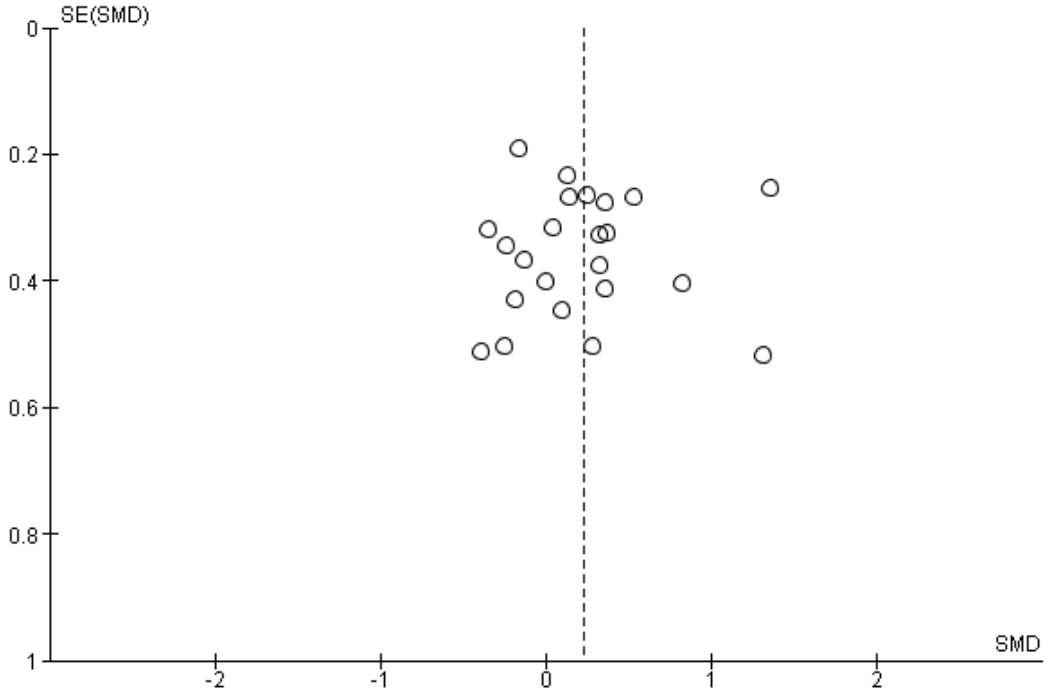


Supplemental Figure 1: Risk of bias across the included studies showing the summary percentage in each domain

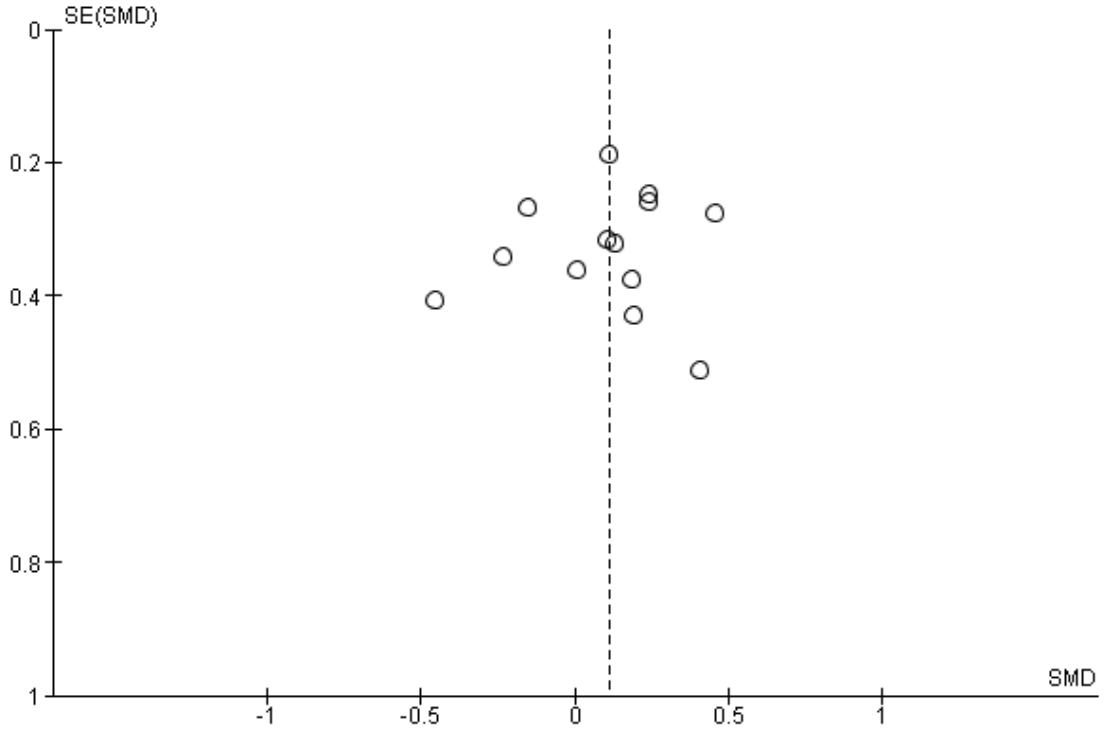
Reporting Bias



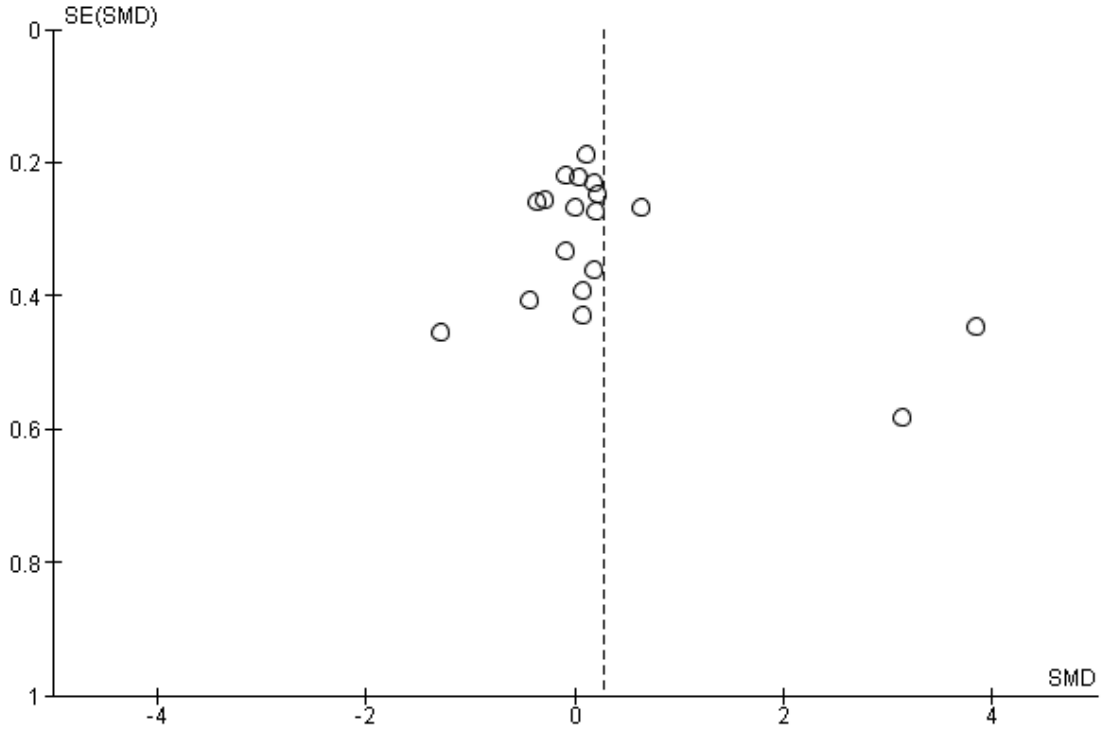
Supplemental Figure 2: Funnel plot for the effect of dietary fiber on *Bifidobacterium* spp. abundance



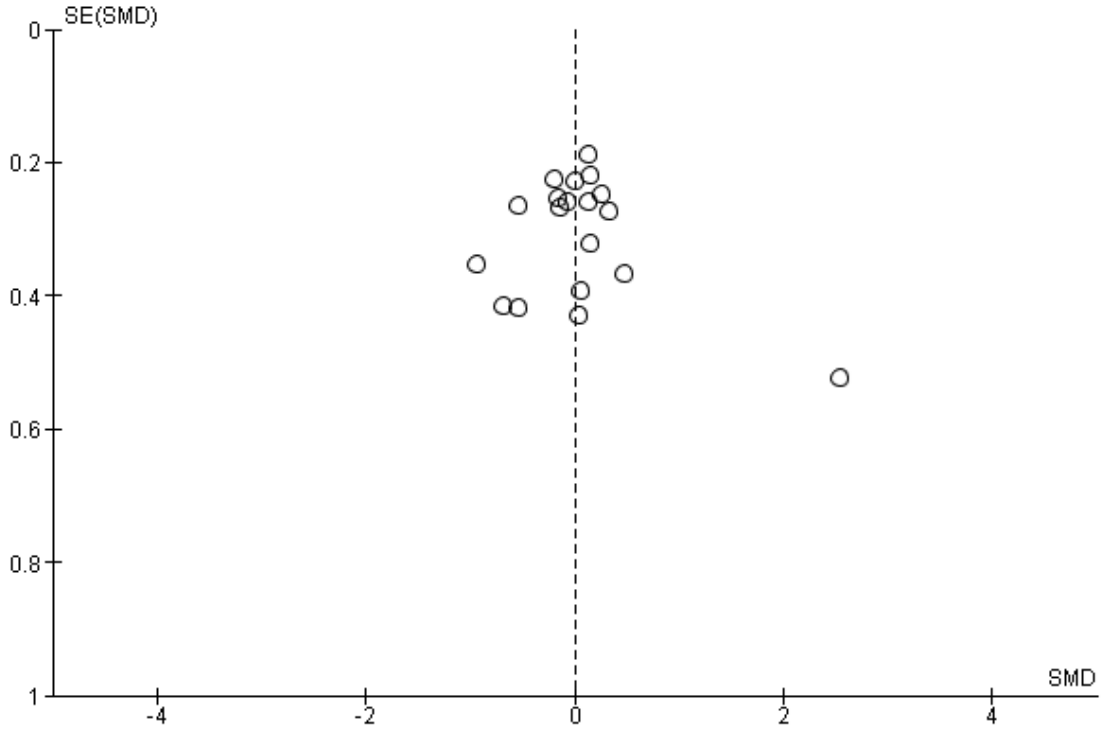
Supplemental Figure 3: Funnel plot for the effect of dietary fiber on *Lactobacillus* spp. abundance



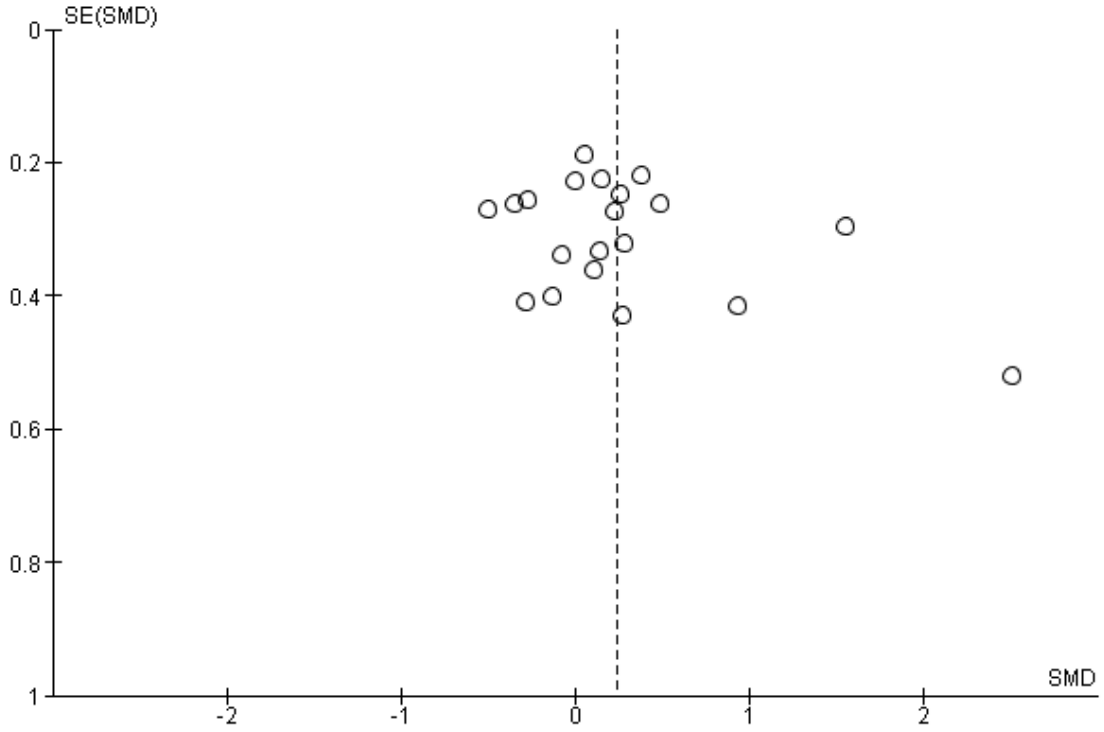
Supplemental Figure 4: Funnel plot for the effect of dietary fiber on total fecal SCFA



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

					Result		Heterogeneity		
Outcome	**Subgroup analysis**	**Subgroup difference (I^2)**	**Subgroups**	**Studies in subgroup (*n*)**	**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%
Bifidobacterium 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%
	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%
Lactobacillus spp.	Intervention type	0%	Food	4	SMD: 0.35 (95% CI: -0.46, 1.16)	0.40	18.73	0.00003	84%
			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	0.47	0%
			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%

					Result		Heterogeneity		
Outcome	**Subgroup analysis**	**Subgroup difference (I^2)**	**Subgroups**	**Studies in subgroup (*n*)**	**Meta-analysis overall estimate (95% CI)**	***P***	**Chi-squared test**	***P***	**I^2**
	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%
Faecalibacterium prausnitzii	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%
			>10g/d	4	SMD: 0.39 (95% CI: -0.09, 0.87)	0.11	6.24	0.10	52%
	Trial design	53.6%	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%
Roseburia 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

					Result		Heterogeneity		
Outcome	**Subgroup analysis**	**Subgroup difference (I^2)**	**Subgroups**	**Studies in subgroup (*n*)**	**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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