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

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ABSTRACT

Background: Dysfunction of the gut microbiota is frequently reported as a manifestation of chronic diseases, 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 via a random-effects model were performed on alpha diversity, prespecified bacterial abundances including *Bifidobacterium* and *Lactobacillus* spp., and fecal SCFA concentrations comparing dietary fiber interventions 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% CI: 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 that 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 prespecified bacteria, or other SCFA concentrations.

Conclusions: Dietary fiber intervention, particularly involving fructans and galacto-oligosaccharides, leads to higher fecal abundance of *Bifidobacterium* and *Lactobacillus* spp. but does not affect 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. This review was registered at PROSPERO as CRD42016053101. *Am J Clin Nutr* 2018;107:965–983.

Keywords: diet, dietary fiber, gastrointestinal microbiome, gastrointestinal microbiota, gut microbiota, prebiotic

INTRODUCTION

The gut microbiota is a highly diverse and metabolically active community, consisting of $\sim 3.9 \times 10^{13}$ 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 via 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

The authors reported no funding received for this study.

Supplemental Tables 1–7 and Supplemental Figures 1–7 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn.

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Abbreviations used: FISH, fluorescence in situ hybridization; GI, gastrointestinal; HMO, human milk oligosaccharide; MD, mean difference; OTU, operational taxonomic unit; qPCR, quantitative polymerase chain reaction; RCT, randomized controlled trial; SCFA, short-chain fatty acid; SMD, standardized mean difference.

Received August 15, 2017. Accepted for publication February 14, 2018.

First published online May 11, 2018; doi: https://doi.org/10.1093/ajcn/nqy041.

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 relevance to health owing to its beneficial properties such as its immunomodulatory effects (24, 25).

Dietary fiber is defined as nondigestible carbohydrates of ≥3 monomeric units found inherently in foods, and also includes isolated or synthetic fibers with demonstrated physiologic 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). Fibers 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 of this systematic review.

METHODS

This systematic review was conducted in line with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (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 prespecified and documented in a protocol that was published in the PROSPERO as CRD42016053101: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016053101.

Literature search

A literature search was performed in the electronic databases MEDLINE, EMBASE, CENTRAL, and CINAHL (from inception to 4 October 2017), through the use of 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 multistep 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 Search Portal and clinicaltrials.gov to identify ongoing trials. Two review authors (DS and HMS) screened articles in a blinded, standardized manner, with disagreements in judgment resolved by consensus or a third reviewer (KLC).

Study selection

Search results were merged into the reference management software Endnote (X7; Thomson Reuters) and de-duplicated before screening with the use of 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 when 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 y 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 celiac disease, inflammatory bowel disease, irritable bowel syndrome, and other functional GI disorders, were excluded. Studies including mixed population groups in which the healthy subgroup 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 nonparametric richness estimator); Shannon diversity index (a metric combining richness and evenness, with equal weighting given to abundant and rare species); and Simpson diversity index (a metric of richness and evenness, in which 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 (individual and total) were included as an exploratory outcome.

Data extraction and management

Two reviewers (DS and HMS) independently extracted the data from eligible studies. Data extracted included: study design (duration, location, details of "run-in" and "washout" 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 prespecified primary, secondary, and exploratory outcome data, the mean, SD, SE, or 95% CIs that were reported at end of intervention were extracted for analysis. When studies used multiple intervention groups of different fiber doses, data for the highest intervention dose were extracted. When studies used multiple intervention groups of different fibers at the same dose compared with a single control group, data were extracted from each intervention group and pooled together. A weighted average of the intervention groups and the study variance were then calculated (44).

Risk of bias was independently assessed by 2 reviewers (DS and HMS) 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 whether 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 as the difference between the end of intervention values for the intervention and comparator groups. Data reported as median and IQR 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 CIs when 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). When end of intervention endpoint data were unable to be obtained, the results were described in text only.

Meta-analysis was performed when outcomes were reported in ≥2 studies with the use of Revman (version 5.3; Cochrane Collaboration). The mean difference (MD) was used to calculate effect sizes when outcome data were presented in the same units (Shannon diversity index, total number of observed OTUs). When outcome data were reported in different units, effect sizes were calculated with the use of 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 with the use of the I^2 statistic, in which significant heterogeneity was defined as $I^2 \geq 50\%$.

Predefined subgroup analyses were undertaken for primary and secondary outcomes that were reported in ≥2 studies in each subgroup. Predefined 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 groups of <5 g/d, 5–10 g/d, and >10 g/d), trial design (parallel and crossover), and microbial analysis method (e.g., culture, sequencing). Fructans and galacto-oligosaccharides were classified as "accepted prebiotic" fibers, whereas "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. 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).

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. When 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, in which each study was sequentially omitted and the remaining data reassessed. 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 in which ≥10 studies were included in meta-analysis (48) and reporting bias was 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 3 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 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 washout 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 (7 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., whole-grain 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 and treatment periods ranged from 5 d to 3 mo, with a median length of 3 wk.

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

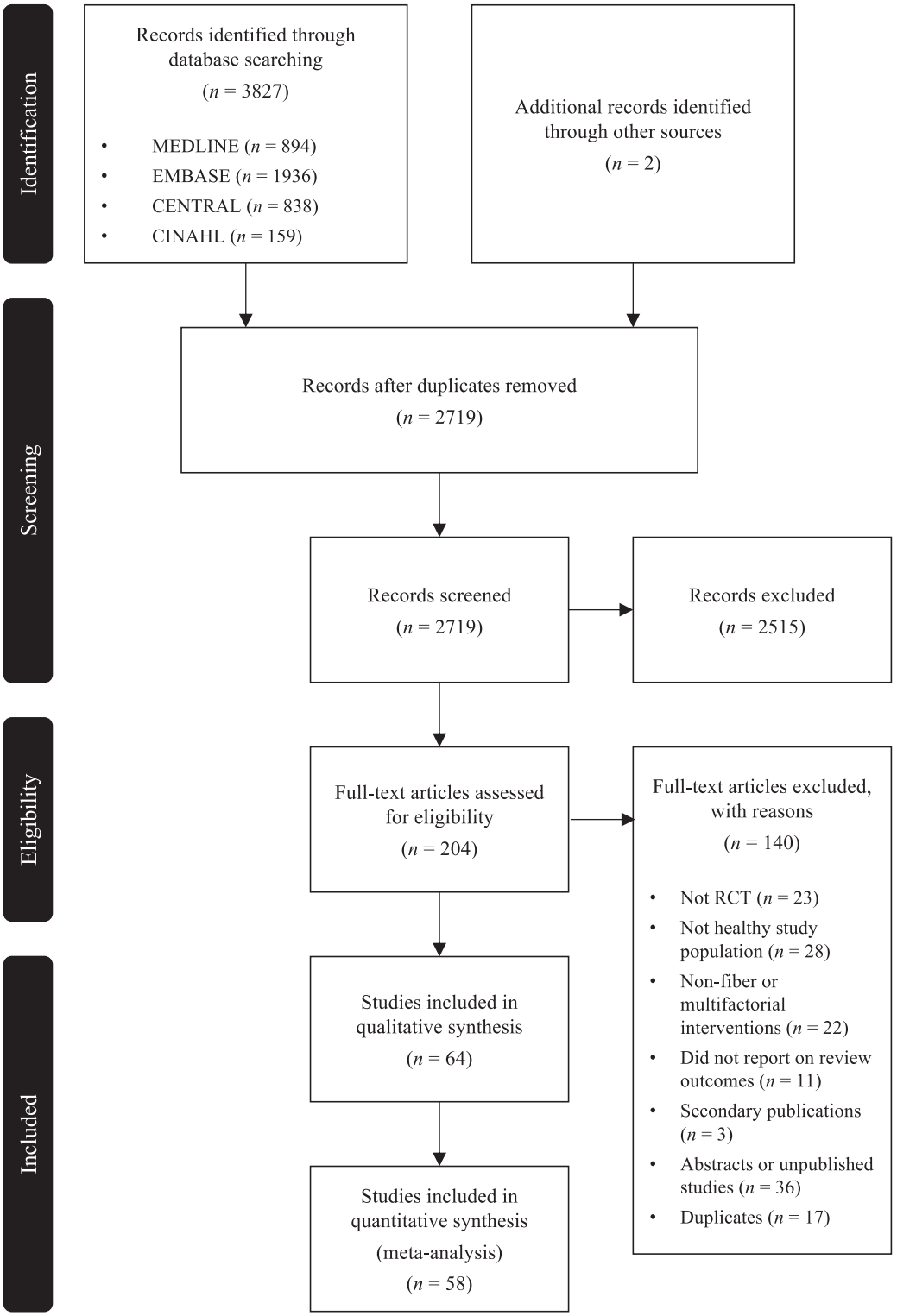

FIGURE 1 Flow diagram of studies evaluated in the systematic review. RCT, randomized controlled trial.

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 6 primary studies (61, 67, 83, 84, 88, 93) and one secondary publication (49).

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 58 studies were suitable for meta-analysis; results from the following studies were unable to be statistically pooled and are presented

TABLE 1
Statistical analysis for the outcomes reported in ≥2 randomized controlled trials and included in the meta-analysis[1]

			Results		Heterogeneity		
Outcomes	No. of studies in meta-analysis (references)	n[2]	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 (−0.25, 0.12)	0.48	10.73	0.06	53
Total number of observed OTUs	3 (72, 75, 84)	53	MD: −4.37 (−42.92, 34.19)	0.82	0.07	0.97	0
Bifidobacterium spp.	51 (52–58, 60, 61, 63–68, 70, 71, 73–76, 82, 84–94, 96–112, 114)	1629	SMD: 0.64 (0.42, 0.86)	<0.00001	327.93	<0.00001	85
Lactobacillus spp.[3]	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 (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 (−0.12, 0.39)	0.29	37.53	0.0002	68
Roseburia spp.	4 (68, 79, 84, 97)	189	SMD: 0.33 (−0.14, 0.80)	0.17	10.16	0.02	70
Eubacterium rectale	2 (84, 101)	30	SMD: −0.26 (−1.20, 0.67)	0.58	3.94	0.05	75
Ruminococcus bromii	3 (81, 84, 101)	76	SMD: 0.15 (−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 (−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 (−0.08, 0.63)	0.13	119.36	<0.00001	86
Propionate	19 (52, 53, 63, 66, 71, 74, 77, 80, 82, 84, 86, 90, 91, 93, 94, 96, 103, 112, 115)	677	SMD: 0.01 (−0.20, 0.22)	0.95	46.23	0.0003	61
Butyrate	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 (0.00, 0.47)	0.05	64.21	<0.00001	70

[1]Data were meta-analyzed through the use of a random-effects model and presented as MDs or SMDs as appropriate. Statistical heterogeneity was assessed via the chi-square test and quantified with the use of the I^2 statistic. MD, mean difference; OTU, operational taxonomic unit; SCFA, short-chain fatty acid; SMD, standardized mean difference.
[2]Number of participants in meta-analysis.
[3]Results from outlier study excluded from this meta-analysis.

narratively under their respective subheadings (59, 62, 69, 77–79, 83, 93, 95, 97, 101, 113, 115). The characteristics of included studies, separated into fiber supplementation studies and food interventions, are presented in **Tables 2** and **3**, respectively.

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 through the use of Shannon diversity index. Of these, 6 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 2 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 (−38,010; 95% CI: −64,473, −11,546; $P = 0.007$) as well as Simpson's inverse index (−17,515; 95% CI: −30,992, −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 that it was significantly higher in the intervention group receiving polydextrose compared with placebo after 21 d ($P = 0.014$) (88). A trial involving 15 g/d arabinoxylan supplementation reported variable intervention effects when α-diversity was evaluated with 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 3 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 2 studies, although there were 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 whole-grain and refined-grain diets found no difference in α-diversity at end of intervention between the 2 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 *A. 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 and 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 predefined dosages (≤5 g/d fiber SMD: 0.51; 95% CI: 0.18, 0.84; $P = 0.003$, $I^2 = 70\%$; 5–10 g/d SMD: 0.48; 95% CI: 0.13, 0.83; $P = 0.007$, $I^2 = 87\%$; >10 g/d SMD: 0.85; 95% CI: 0.45, 1.25; $P < 0.00001$, $I^2 = 85\%$). No differences were found in subgroup analyses of trial design or microbiota analysis method (Supplemental Table 6).

Eight trials were not included in the meta-analysis. In the supplement trials of accepted prebiotics, a significantly higher *Bifidobacterium* spp. abundance was reported after supplementation involving inulin (115) and human milk oligosaccharides (HMO) (62) compared with placebo at the end of intervention, whereas a significant within-group increase from baseline was detected after 10 g/d inulin supplementation (95). In the candidate prebiotic trial of resistant starch supplementation, *Bifidobacterium* spp. abundance was significantly higher in the intervention group compared with placebo at end of intervention (77). In the supplement studies of general fiber, *Bifidobacterium* spp. abundance was higher after xylo-oligosaccharide supplementation compared with placebo (69) whereas manno-oligosaccharides had no effect on *Bifidobacterium* spp. compared with placebo (113). The third supplement trial of general fiber (resistant maltodextrin) reported no change in *Bifidobacterium* spp. abundance within groups using FISH, although a significant increase from baseline was reported for the intervention group on qPCR analysis (83). Finally, a food study comparing intakes of whole grains with refined-grain products found no significant difference in *Bifidobacterium* spp. abundance at the end of the intervention period (78).

Lactobacillus spp. abundance was measured in 28 studies involving 867 participants. Data from 24 studies (730 participants)

TABLE 2
Characteristics of randomized controlled trials of fiber supplementation comparing dietary fiber with placebo or low-fiber comparators in healthy adults[1]

Study (reference)	Participants	Interventions				RCT design				
	n; age;[2] % F	Fiber, daily dose, g	Prebiotic	Comparator, daily dose, g	Compliance[3]	Design	Duration, d	Run in	Washout	Analysis
Abell 2008 (81)	46; 25–66; 65	RS, 22	C	RS, 1	Y	Crossover	28	Y	Y	qPCR
Alfa 2017 (77)	84; 32–96; 42	RS2, 21	C	Corn starch, 21	Y	Parallel	72	Y	N	Illumina
Alles 1999 (52)	27.4; 40.4; 45	TOS, 15	A	Glucose & lactose mix, 15	Y	Parallel	21	Y	N	Culture
Baer 2014 (83)	14; 47; 9	Resistant maltodextrin, 50	C	Maltodextrin, 50	Y	Crossover	21	N	Y	454 pyrosequencing; DGGE; FISH; qPCR
Beards 2010 (53)	30; 33;[4] 66[4]	PDX; RS, 45.6	C	Maltilol, 45.6	N	Parallel	44	N	N	FISH
Blædel 2016 (115)	21; 23–45; 100	Inulin, 15	A	Placebo	Y	Crossover	21	N	Y	Illumina
Boler 2011 (84); Hooda 2012 (49)[5]	21; 21–28; 0	PDX;[6] Soluble maize fiber, 21	C	Placebo	N	Crossover	21	N	N	qPCR; pyrosequencing[4]
Bouhnik 1996 (54)	10; 22–39; 50	SC-FOS, 12.5	A	Saccharose, 10	N	Parallel	12	Y	Y	Culture
Bouhnik 1999 (58)	8; 29.6; 55	SC-FOS, 20	A	Saccharose, 20	N	Parallel	7	N	N	Culture
Bouhnik 2004 (57)	64; 30;[4] 55[4]	SC-FOS;[6] GOS;[6] Isomalto-OS; Inulin;[6] RS; Soybean-OS, 10	A	Sucrose & maltodextrin mix, 10	N	Parallel	7	Y	N	Culture
Bouhnik 2006 (56)	40; 29; 55	SC-FOS (Actilight), 10	A	Sucrose & maltodextrin mix, 10	N	Parallel	7	Y	N	Culture
Bouhnik 2007 (55)	39; 33.9; NR	Inulin, 5	A	Sucrose & maltodextrin mix, 5	N	Parallel	28	Y	Y	Culture
Brahe 2015 (59)	35; 59.6;[4] 100	Flaxseed mucilage, 10	G	Placebo	Y	Parallel	42	N	N	Quantitative metagenomics
Calame 2008 (60)	16; 30.9; NR	Arabic gum, 40	G	Placebo	Y	Parallel	28	N	N	qPCR
Clarke 2016 (86)	30; 27; 57	Beta 2-1 fructan, 15	A	Maltodextrin, 15	Y	Crossover	28	N	Y	qPCR
Cloetens 2010 (87)	20; 24; 70	AXOS, 10	C	Maltodextrin, 20	N	Crossover	21	N	Y	qPCR
Costabile 2010 (90)	31; 25; 56	Very long chain inulin, 10	A	Maltodextrin, 10	N	Crossover	21	N	Y	FISH
Costabile 2012 (88)	31; 33; 52	PDX, 8	C	Maltodextrin, 8	N	Crossover	21	N	Y	DGGE; FISH
Damen 2012 (91)	27; 25; 63	AXOS, 2.14	C	Placebo	Y	Crossover	21	Y	Y	FISH
Depeint 2008 (92)	30; 36.3; 60	Beta-GOS, 7	A	Sucrose, 7	N	Crossover	7	Y	Y	FISH
Dewulf 2013 (61)	30; 47.5; 100	Inulin-type fructan (Synergy 1), 16	A	Maltodextrin, 16	N	Parallel	Reported as 3 mo	N	N	qPCR; phylogenetic microarray
Elison 2016 (62)	40; 22–57; 52	HMO:[7] 2'FL; LNnT; mixture (2:1 mixture of 2'FL + LNnT), 20	A	Glucose, 2	Y	Parallel	14	Y	N	Illumina
Fastinger 2008 (63)	25; 26.7; 50	Resistant maltodextrin, 15	C	Maltodextrin, 15	N	Parallel	21	Y	Y	qPCR
Fernando 2010 (93)	12; 25.6; 42	Raffinose, 5	G	Placebo	N	Crossover	21	N	N	qPCR; T-RFLP
Finegold 2014 (64)	16; 21–49;[4] 66[4]	XOS, 2.8	C	Maltodextrin, 2.8	N	Parallel	56	Y	Y	Pyrosequencing
François 2012 (94)	52; 42; 48	Wheat bran extract, 10	G	Placebo	N	Crossover	21	Y	Y	FISH

(*Continued*)

TABLE 2 (*Continued*)

Study (reference)	Participants *n*; age;[2] % F	Interventions				RCT design				
		Fiber, daily dose, g	Prebiotic	Comparator, daily dose, g	Compliance[3]	Design	Duration, d	Run in	Washout	Analysis
Fuller 2007 (95); Ramirez-Farias 2009 (50)[5]	12; 38.1; 75	Inulin, 10	A	Nil	Y	Crossover	16	N	N	qPCR
Gopal 2003 (65)	19; 20–60;[4] 44[4]	GOS, 2.4	A	Placebo	Y	Parallel	28	Y	Y	Culture
Holscher 2015 (97)	29; 27; 52	Agave inulin, 7.5	A	Placebo	N	Crossover	21	Y	Y	Illumina
Jie 2000 (66)	30; 29.9; 45	PDX, 12	C	Nil	N	Parallel	28	Y	N	Culture
Kleessen 2007 (67)	45; 23.5; 55	Inulin:[7] Chicory inulin; Jerusalem artichoke inulin, 15.4	A	Placebo	N	Parallel	21	Y	N	Culture; FISH
Lecerf 2012 (68)	59; 20.1; 57	XOS;[6] Inulin-XOS mix, 6.64	C	Wheat dextrin, 6.64	N	Parallel	28	N	N	qPCR
Lin 2016 (69)	20; 24.2; 80	XOS, 1.2	C	Placebo	N	Parallel	42	Y	Y	Culture
Lomax 2012 (70)	43; 55; 74	Beta 2-1 fructan, 8	A	Maltodextrin, 8	Y	Parallel	28	Y	N	FISH
Maki 2012 (99)	55; 35.1;[4] 54[4]	AXOS, 2.4	C	Placebo	N	Crossover	21	N	Y	FISH
Maneerat 2013 (100)	35; 67.4;[4] 53[4]	GOS, 8	A	Maltodextrin, 8	N	Crossover	21	N	Y	FISH
Martínez 2010 (101)	10; 23–38; 50	RS:[7] RS2; RS4, 33.2	C	Native wheat starch, 33.2	N	Crossover	21	Y	Y	Pyrosequencing
Pallav 2014 (72)	14; 31.4;[4] 65	Polysaccharidepeptide (I'm-Yunity), 3.6	G	Nil	N	Parallel	14	N	N	Pyrosequencing
Pasman 2006 (73)	29; 34.1; 0	Nutriose FB (dextrin), 45	A	Maltodextrin, 22.5	Y	Parallel	35	Y	N	Culture
Petry 2012 (102)	32; 18–40; 100	Inulin, 20	A	Maltodextrin, 20	N	Crossover	28	N	Y	qPCR
Ramnani 2010 (74)	66; 32.9; 50	Inulin, 5	A	Placebo	Y	Parallel	21	Y	Y	FISH
Ramnani 2015 (103)	38; 35.1;[4] 50	Agave inulin, 5	A	Maltodextrin, 5	Y	Crossover	21	Y	Y	FISH
Salden 2017 (80)	27; 48; 48	Arabinoxylans, 15	G	Maltodextrin, 15	Y	Parallel	42	N	N	Illumina
Slavin 2011 (105)	10; 27–49;[4] 0	Chicory inulin, 20	A	Placebo	Y	Crossover	21	N	N	Culture
Ten Bruggencate 2006 (107)	29; 22.7; 0	FOS, 20	A	Sucrose, 6	Y	Crossover	14	N	Y	qPCR
Tuohy 2001 (108)	NR; NR; 55	Mix (FOS & PHGG), 10	Mix	Placebo	Y	Crossover	21	N	N	FISH
Vulevic 2008 (109)	41; 69.3;[4] 64[4]	GOS (Bimuno), 5.5	A	Maltodextrin, 5.5	Y	Crossover	70	N	Y	FISH
Vulevic 2015 (110)	40; 70.4; 62	GOS (Bimuno), 5.5	A	Maltodextrin, 5.5	Y	Crossover	70	N	Y	FISH
Walton 2010 (113)	31; 21; 58	MOS, 5	C	Placebo	Y	Crossover	21	N	Y	FISH
Walton 2012 (111)	37; 58.9;[4] 57[4]	GOS, 8	A	Placebo	N	Crossover	21	Y	Y	qPCR
Walton 2012 (112)	40; 31.4;[4] 60[4]	AXOS, 2.2	C	Placebo	Y	Crossover	21	Y	Y	FISH
Wu 2011 (76)	15; 40.6; 93	Konjac glucomannan, 4.5	G	Nil	N	Parallel	28	N	N	FISH

[1]A, accepted prebiotic fiber; AXOS, arabinoxylan-oligosaccharide; C, candidate prebiotic fiber; DGGE, denaturing gradient gel electrophoresis; FISH, fluorescent in situ hybridization; FOS, fructo-oligosaccharide; G, general fiber; GOS, galacto-oligosaccharide; HMO, human milk oligosaccharide; LNnT, lacto-N-neotetraose; 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; T-RFLP, Terminal restriction fragment length polymorphism; XOS, xylo-oligosaccharide; 2′FL, 2′-O-fucosyllactose.

[2]Age expressed as mean y; age range provided when means were not obtainable.

[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.

[6]Refers to analyzed intervention arm with the highest prebiotic classification (accepted prebiotic fiber > candidate prebiotic fiber > general fiber) selected for fiber type subgroup analysis.

[7]Refers to intervention fibers that have been pooled together for meta-analyses.

TABLE 3
Characteristics of randomized controlled trials of food interventions comparing dietary fiber with low-fiber comparators in healthy adults[1]

		Interventions					RCT design				
Study (reference)	Participants *n*; age;[2] % F	Intervention	Comparator	Daily fiber difference, g	Study diet[3]	Compliance[4]	Design	Duration, d	Run in	Washout	Analysis
Ampatzoglou 2015 (82)	33; 48.8; 64	WG diet	RG diet	10	N	Y	Crossover	14	Y	Y	FISH
Carvalho-Wells 2010 (85)	32; 31.6; 66	WG cereal	Non-WG cereal	6.5	N	N	Crossover	21	Y	Y	FISH
Cooper 2017 (78)	46; 25.8; 46	WG market basket	RG market basket	5	N	Y	Parallel	42	N	N	Illumina
Costabile 2008 (89)	31; 25; 52	WG cereal	Wheat bran cereal	7.4	N	N	Crossover	21	Y	Y	FISH
Gråsten 2007 (96)	14; 59.7;[5] 100	Rye bread	White wheat bread	19	N	Y	Crossover	56	Y	Y	Culture
Jenkins 1999 (98)	24; 33; 50	Wheat bran	Wheat flour	19	N	Y	Crossover	14	N	Y	Culture
Karl 2017 (79); Vanegas 2017 (51)[6]	81; 40–65;[5] 60	WG diet	RG diet	8	Y	Y	Parallel	42	Y	N	Illumina
Nemoto 2011 (71)	36; 22–67; 63	Fermented brown rice	"Non-functional food"	4.62	N	Y	Parallel	14	N	N	Culture
Ross 2011 (104)	17; 35; 65	WG diet	RG diet	13	Y	Y	Crossover	14	Y	Y	qPCR
Smith 2006 (106)	18; 42.8; 0	Lupin kernel fiber diet	Control diet	22	Y	N	Crossover	28	N	Y	FISH
Tap 2015 (75)	19; 19–25; 53	High-fiber diet	Low-fiber diet	30	Y	Y	Crossover	5	N	Y	454 pyrosequencing
Zeng 2015 (114)	77; 63.4; 70	Whole cereal legume diet	Control diet	14.5	Y	Y	Parallel	90	N	N	Culture

[1]FISH, fluorescent in situ hybridization; qPCR, quantitative polymerase chain reaction; RG, refined grain; WG, whole grain.
[2]Age expressed as mean y; age range provided when means were not obtainable.
[3]Whether the participant's entire diet was provided by the study.
[4]Compliance to intervention; assessed by primary study.
[5]Refers to randomized population rather than actual population.
[6]Secondary publication reporting additional outcomes from the primary study.

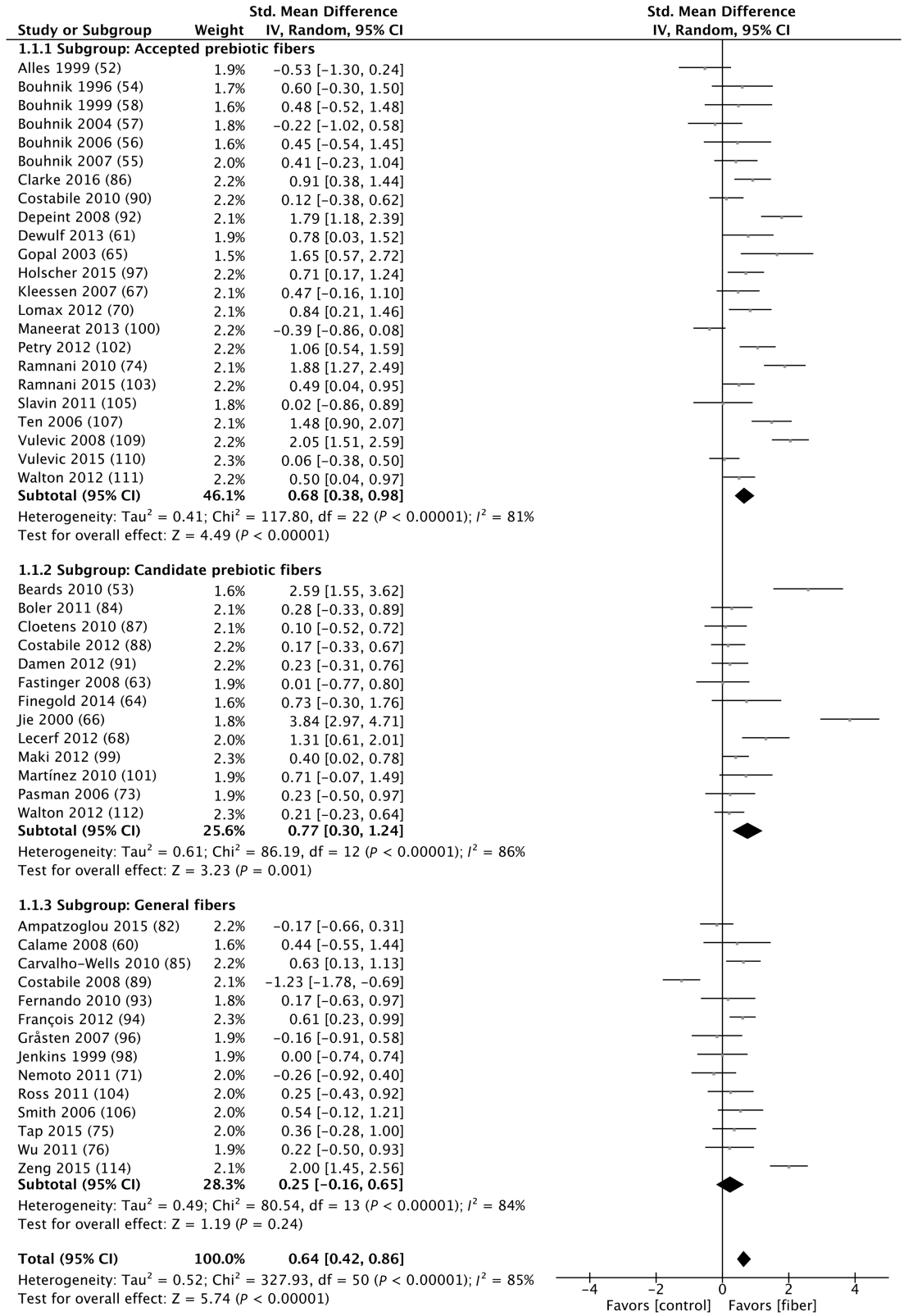

FIGURE 2 Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low-fiber comparators. Studies are subgrouped by fiber type, with the overall effect included at the bottom. Data are presented as means and SDs of *Bifidobacterium* spp. abundance at end of intervention. Effects of trials are presented as weights (percentages) and standardized mean differences (95% CIs). IV, inverse variance; Std., standardized.

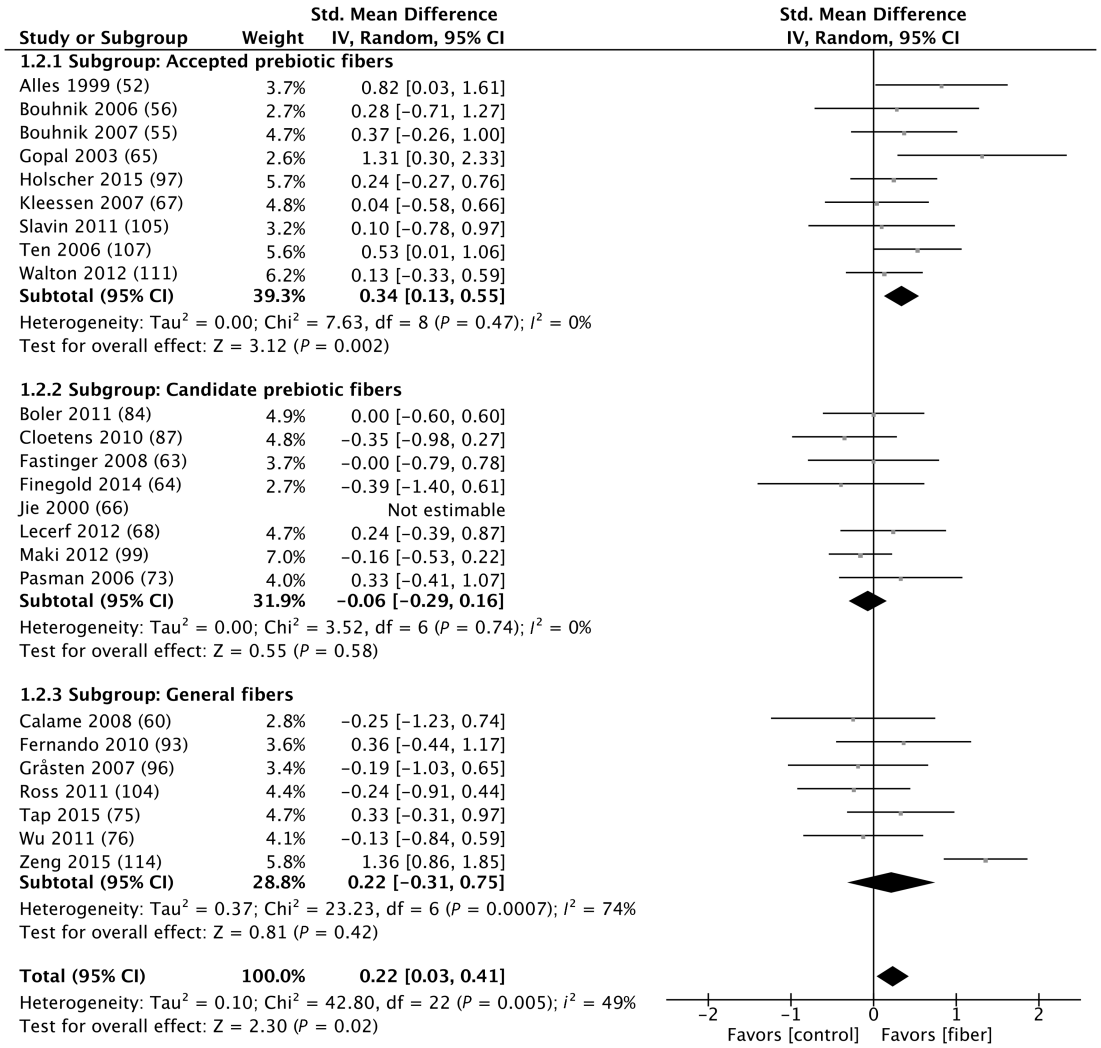

FIGURE 3 Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low-fiber comparators. Studies are subgrouped by fiber type, with the overall effect included at the bottom. Data are presented as means and SDs of *Lactobacillus* spp. abundance at end of intervention. Effects of trials are presented as weights (percentages) and standardized mean differences (95% CIs). IV, inverse variance; Std., standardized.

were reported in a form suitable for meta-analysis (52, 55, 56, 60, 63–68, 73, 75, 76, 84, 87, 93, 96, 97, 99, 104, 105, 107, 111, 114). Dietary fiber led to a significantly greater *Lactobacillus* spp. abundance compared with placebo/low-fiber comparators (SMD: 0.37; 95% CI: 0.07, 0.68; $P = 0.02$). However, heterogeneity was considerable ($I^2 = 80\%$), and was skewed by results from a single outlier study (66) (4.70; 95% CI: 3.69, 5.70). A sensitivity analysis excluding this study produced a more homogeneous study population ($I^2 = 49\%$), with a modest impact on the result (SMD: 0.22; 95% CI: 0.03, 0.41; $P = 0.02$) (**Figure 3**). The outlier study (66) was excluded from subsequent subgroup analyses.

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

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

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

There were 4 studies that could not be pooled into the meta-analysis. A prebiotic supplementation trial of HMOs reported no difference in *Lactobacillus* spp. abundance between intervention and control groups (62). There was also no significant

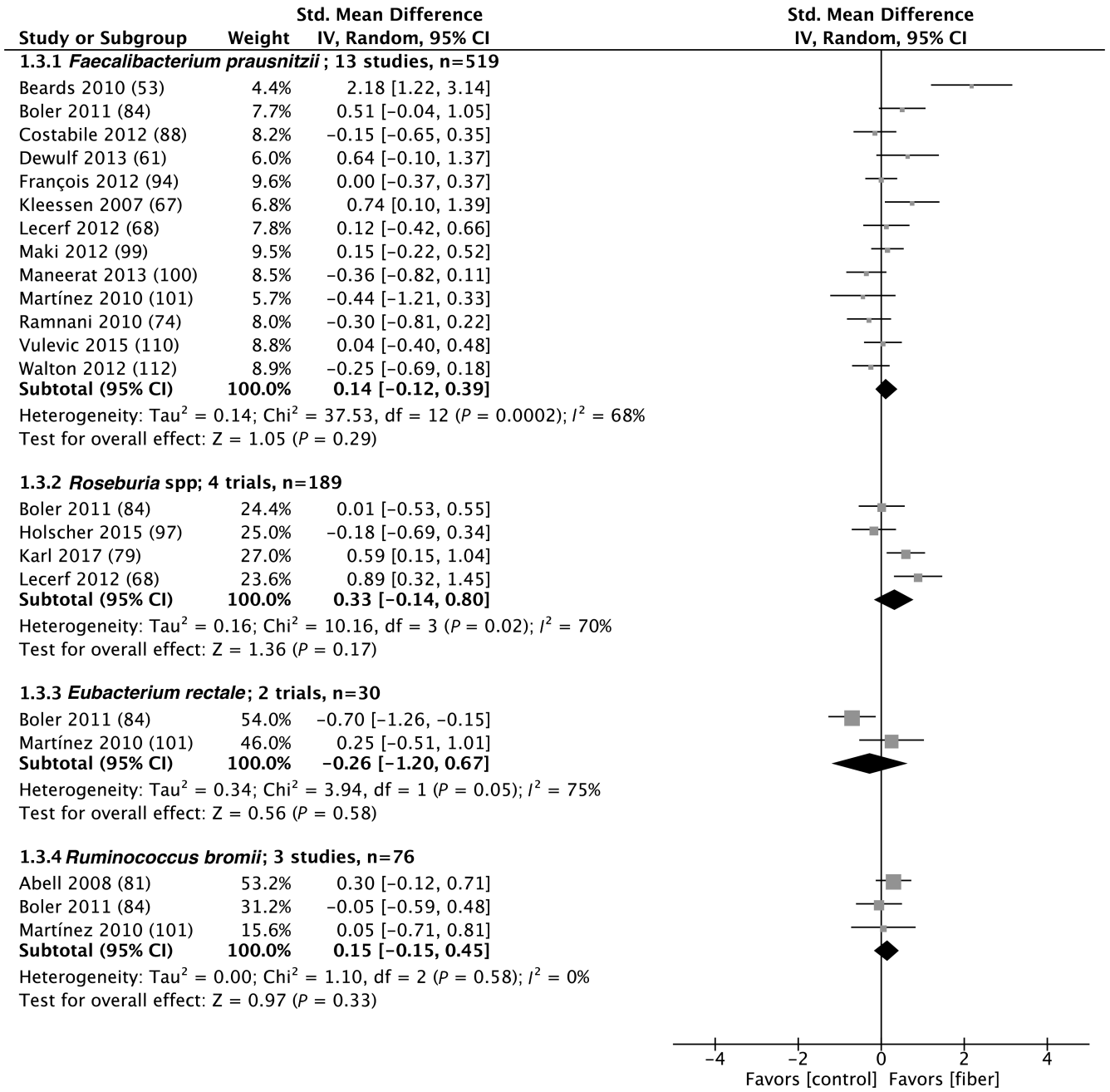

FIGURE 4 Forest plot of randomized controlled trials in healthy adults comparing dietary fiber with placebo/low-fiber comparators. Data are presented as means and SDs of *Faecalibacterium prausnitzii*, *Roseburia* spp., *Eubacterium rectale*, and *Ruminococcus bromii* abundance at end of intervention. Effects of trials are presented as weights (percentages) and standardized mean differences (95% CIs). IV, inverse variance; Std., standardized.

difference in *Lactobacillus* spp. reported in a whole-grain food intervention study compared with controls (78). Of the 2 remaining studies, there was higher *Lactobacillus* spp. abundance after xylo-oligosaccharide supplementation compared with placebo (69), and significant within-group increases in *Lactobacillus* spp. abundance were demonstrated after 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 and 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 prespecified 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 1 study reporting a decrease in abundance after supplementation

of flaxseed mucilage (59) and the other reporting an increase in abundance after 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 2 prebiotic fiber supplement trials (50, 62). A third trial found the relative abundance of *Roseburia* spp. was lower after 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 1 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 3 studies including 42 participants. Two studies (30 participants) were suitable for meta-analysis (84, 101). Dietary fiber did not affect *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 3 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 SCFAs

A total of 25 studies involving 870 participants reported between-group differences in fecal SCFA concentrations after 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 concentrations were determined through gas-liquid chromatography in all but 1 study (90) in which HPLC 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 after 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 after 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 concentrations after 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), 1 study as molar ratio (84), and 1 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 concentration when expressed as wet compared with dry weight of feces. There were no differences in effect based on analysis method for fecal propionate concentration, 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, in which α-diversity was reported with the use of Shannon diversity index (MD: −0.10; 95% CI: −0.19, −0.01; $P = 0.03$), whereas 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 3 crossover trials included in this analysis. One study did not include a washout period (84), and washout periods lasted 14 (75) and 21 d (88) in the other 2. 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 with the use of 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); 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; and for 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 4 d to 3 wk 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 washout 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 that dietary fiber interventions involving accepted prebiotic fibers led to higher abundance of *Bifidobacterium* and *Lactobacillus* spp. These results support the selectivity criteria of the prebiotic concept, in which 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 2 genera, with significant effects demonstrated for *Bifidobacterium* but not *Lactobacillus* spp. This may represent differences in substrate preferences between the 2 genera, in which *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 affect 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 effects of food and supplement interventions showed food interventions had no effect on *Bifidobacterium* and *Lactobacillus* spp. 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; and 4 studies, 127 participants, respectively). It must also be noted that most of the trials using 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 (<5 g, 5–10 g, >10 g) with no discernible gradient in effectiveness, suggesting <5 g of dietary fiber is sufficient. This may represent a potential limit to the amount of fiber that can be fermented by *Bifidobacterium* spp. 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. ($I^2 = 49\%$). Although 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* spp. Another plausible explanation is the differences in nutrient requirements of these taxa as discussed previously. Furthermore, "responder and nonresponder" effects for *Bifidobacterium* spp. abundance, which have been shown previously (97, 123, 124), may be affected 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 washout 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 that 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 after 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 and *Bifidobacterium* or *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 relevance 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 2 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 via the same diversity indexes. 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 relation 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. whereas candidate prebiotic fibers had an effect on *Bifidobacterium* spp. abundance but not *Lactobacillus* spp. 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 concentrations of other fecal SCFAs were not significantly different compared with controls after 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 more taxa than those considered here, including the eukaryote (e.g., fungi) members of the gut microbiota. In addition, longer-duration studies are needed to better assess the chronic effect of fiber on microbiota diversity.

We 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.

The authors' responsibilities were as follows—HMS and KLC: initiated the study; DS, KW, HMS, MR, and KLC: developed the protocol; DS and HMS: performed eligibility screening and data extraction; DS and JTK: analyzed the data and performed the statistical analysis; DS, KW, MR, MM, JTK, ERS, HMS, and KLC: interpreted the data; DS: wrote the initial manuscript; KW, MR, MM, GH, JTK, ERS, HMS, and KLC: critically revised the manuscript; and authors: read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

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