REVIEW

A Systematic Review of Dietary Influences on Fecal Microbiota Composition and Function among Healthy Humans 1–20 Years of Age

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ABSTRACT

Diet is a key modulator of fecal microbiota composition and function. However, the influence of diet on the microbiota from toddlerhood to adolescence and young adulthood is less well studied than for infancy and adulthood. We aimed to complete a qualitative systematic review of the impacts of diet on the fecal microbiota of healthy humans 1–20 y of age. English-language articles, published after 2008, indexed in the PubMed/MEDLINE, Cochrane, Web of Science, and Scopus databases were searched using keywords and Medical Subject Headings terms. Quality assessment of included studies was conducted using the Quality Criteria Checklist derived from the Nutrition Evidence Library of the Academy of Nutrition and Dietetics. A total of 973 articles were identified through database searching and 3 additional articles were included via cross-reference. Subsequent to de-duplication, 723 articles were screened by title and abstract, of which 709 were excluded based on inclusion criteria established a priori. The remaining 14 studies were independently screened by 2 reviewers for final inclusion. Included studies were published between 2010 and 2019 and included 8 comparative cross-sectional studies, 4 cross-sectional studies, 1 randomized crossover study, and 1 substudy of a randomized 2-period crossover trial. Associations of a diet rich in indigestible plant polysaccharides with *Prevotella*, or with an enterotype dominated by this genus, often comprised of the species *Prevotella copri*, were observed. In addition, associations of a high-fat and -sugar diet with *Bacteroides*, or with an enterotype dominated by this genus, were observed predominantly in comparative cross-sectional and cross-sectional studies spanning the ages of 1–15 y. This review identified a gap in the literature for ages 16–20 y. In addition, randomized controlled trials for dietary intervention are needed to move from association-based observations to causal relations between diet and microbiota composition and function.This systematic review was registered at www.crd.york.ac.uk/prospero as CRD42020129824. *Adv Nutr* 2021;12:1734–1750.

Keywords: diet, dietary patterns, fecal microbiome, toddler, adolescent

Introduction

Diet influences microbial colonization of the gastrointestinal tract, affecting health throughout the lifespan (1–4). Food components, such as nondigestible carbohydrates, specific amino acids, and fats (and nonfood compounds such as bile acids and enzymes), resist digestion in the small intestine and reach the colon, where they serve as substrates for microbial fermentation (5). The fermentation process produces volatile fatty acids: SCFAs—butyrate, propionate, and acetate—from carbohydrates, and branched-chain fatty acids (BCFAs)—valerate, isovalerate, and isobutyrate—from protein (5–8). SCFAs are suggested to protect against obesity and type 2 diabetes, whereas BCFAs regulate electrolyte absorption and secretion in colonocytes (9).

Dietary patterns have been utilized to assess the influence of diet on the fecal microbiota, such as through categorization of the Western-type diet, characterized by processed foods, animal proteins and fats, dairy, refined carbohydrates (10), and low dietary fiber (11), and associated with Maillard Reaction Products (MRPs) (12, 13). The MRPs are formed during the heating of food when reducing sugars chemically react with free amino groups in amino acids or proteins

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Abbreviations used: ASA24, Automated Self-Administered 24-h Dietary Recall; BCFA, branched-chain fatty acid; BD, brown diet; CT, Central; F:B, Firmicutes to Bacteroidetes; KEGG, Kyoto Encyclopedia of Genes and Genomes; MRP, Maillard Reaction Product; NE, Northeastern; OTU, operational taxonomic unit; PICOS, Participants, Intervention (or Exposure), Comparator, Outcome, Study Design; QCC, Quality Criteria Checklist; RCT, randomized controlled trial; WD, white diet.

TABLE 1 PICOS criteria for inclusion and exclusion of studies examining impacts of diet on the fecal microbiota in humans 1–20 y of age

Criteria	Definition
Participants	Healthy humans 1–20 y old. Studies in species other than human were excluded.
Intervention (or Exposure)	Diet: dietary intake, dietary patterns, nutrient and food group intakes.
Comparator	Not applicable.
Outcome	The impact of diet (dietary intake, dietary patterns, nutrient and food group intakes) on the fecal microbiota (composition, diversity, metagenomics, DNA pathways or function, metabolites, and metabolomics).
Study Design	Randomized controlled trials, cross-sectional, longitudinal, or case studies. Narrative reviews, systematic reviews, and meta-analyses were excluded. Studies were limited to English language published in 2008 or thereafter.

(12, 13). Furthermore, the Western-type diet is associated with an increased incidence of metabolic disease in developed nations (14). In contrast, diets high in fruits, vegetables, nuts, seeds, legumes, and whole grains and low in animal fats and sugary foods are protective against metabolic disorders and cardiovascular disease (15–17). These diets are supportive of health-promoting microbiota and metabolomic profiles, as evidenced by associations with greater abundance of *Lachnospira*, *Prevotella*, and *Roseburia* and increased concentrations of fecal SCFAs (18).

Although research in this area has focused on adults (i.e., those >20 y of age), emerging evidence is revealing similar connections in ages preceding adulthood (19). Of recent interest is the investigation of dietary factors, including dietary patterns, in childhood and their impacts on the fecal microbiota (20). Understanding how diet influences early-life and childhood fecal microbiota development may improve our ability to intervene in cases of unfavorable microbiota conditions linked to poor immune and metabolic function (21–23). Although narrative-based and systematic reviews have examined diet and the fecal microbiota, most have focused on early-life feeding (i.e., human milk and formula feeding) (24, 25), disease states (i.e., autism spectrum disorder and obesity) (26–28), and the lifespan (i.e., infancy to elderly living) (29, 30). The goal of this review was to form a qualitative synthesis of literature examining impacts of diet on the fecal microbiota in healthy humans 1–20 y of age, because this represents a stage of life when the child transitions to a more complex diet and greater autonomy in food choices (31, 32) and represents the age range commonly observed by pediatricians in US clinical practice (33).

Methods

Systematic review procedures were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) 2015 statement (34). The review was registered in the PROSPERO database as CRD42020129824.

Eligibility criteria

The eligibility criteria were outlined using the Participants, Intervention (or Exposure), Comparator, Outcome, Study Design (PICOS) format (**Table 1**).

Search strategy and selection of studies

The PICOS statement was formulated a priori to systematically search 4 databases: PubMed/MEDLINE, Scopus, Web of Science, and Cochrane Library. Keyword searches were performed in each of the 4 databases and included combinations of the keywords as follows: *1*) "diet," "diets," "dietary pattern," "dietary patterns"; *2*) "gastrointestinal microbiome," "fecal microbiome," "fecal microbiota"; and *3*) "infant," "child, preschool," "child," "children," "adolescent," and "young adult." Based on Medical Subject Headings terms in PubMed, the age ranges and corresponding terms were defined as follows: infant (1–23 mo), child, preschool (2–5 y), child (6–12 y), adolescent (13–18 y), and young adult (19–24 y).

Inclusion criteria for full-text review were as follows: *1*) the study included humans aged 1–20 y; *2*) the participants were healthy; *3*) the selected intervention or exposure was diet; *4*) the primary outcome was the impact of diet on the fecal microbiota, metagenome, and metabolites; *5*) the study design was a randomized controlled trial (RCT), cross-sectional, longitudinal, or a case study; *6*) the study was published in English; and *7*) the study was published in 2008 or thereafter, when advanced sequencing technologies were more widely used (35). Studies that failed to meet the inclusion criteria were excluded.

Process of study selection

Two of the authors (AMD and MA-L) independently identified and reviewed articles by title and abstract. Subsequent to screening by title and abstract, the remaining eligible articles were screened via full-text versions. Where AMD and MA-L had disagreements over inclusion of an article, the decision for inclusion was resolved by the coauthors SMD and NAK. All authors came to agreement on which studies to include in this review based on the aforementioned inclusion and exclusion criteria.

Data extraction

Citations were compiled into Mendeley Desktop and duplicates were identified and merged. Full texts of articles were accessed for full-text screening. Data were extracted by AMD and MA-L using a data extraction form wherein author, title, journal, year, and abstract were recorded.

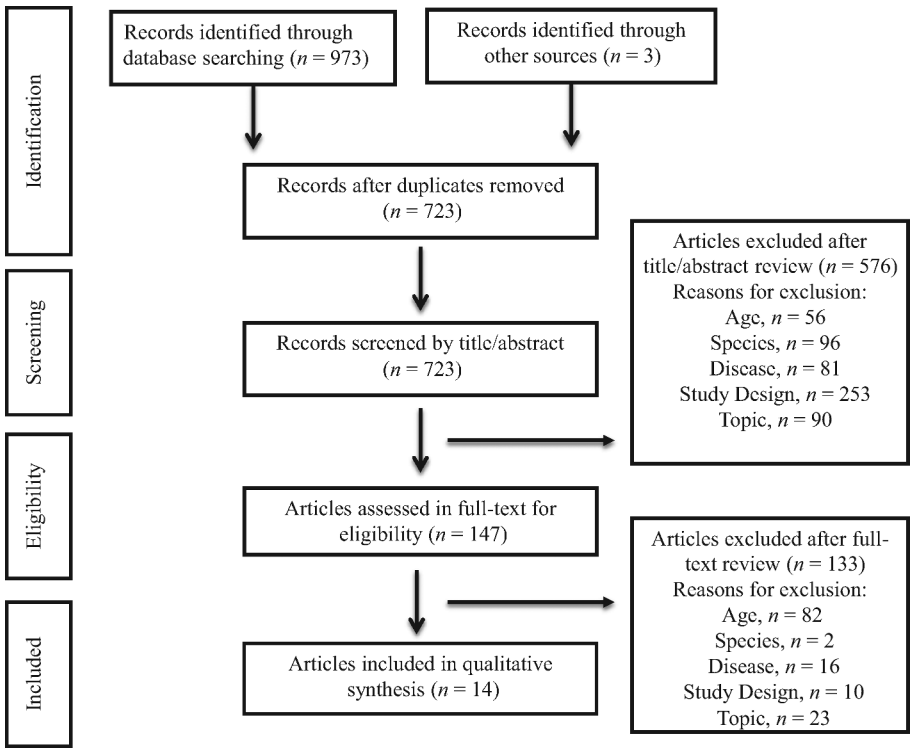

FIGURE 1 Flowchart of study selection.

Quality assessment of studies

Quality assessment included country of study, participant characteristics, study design, method of microbiota assessment, intervention protocol, and principal outcomes. The assessment was conducted by AMD and MA-L via the Quality Criteria Checklist (QCC) for primary research. This tool was developed by the Academy of Nutrition and Dietetics and has been used in prior reviews (36). The QCC is comprised of 4 relevance questions and 10 validity questions designed for interpretation of research quality. Each validity question has subcomponents for further interpretation. A final tally of the answered questions allows the study to be denoted with a "positive," "negative," or "neutral" designation.

Results

The initial screening of databases was conducted in July 2019. In total, 973 citations were extracted from database searching and 3 via cross-reference, giving a total of 723 after de-duplication. Of these 723, 709 articles were excluded for various reasons: age (outside of ages 1–20 y), species (other than human), disease (studies conducted in populations with disease), study design (reviews or meta-analyses), and topic (not within the scope of impacts of diet on human fecal microbiota) (**Figure 1**). Six articles initially had split decisions for inclusion by the 2 main reviewers (AMD and MA-L), 1 was included after review by SMD or NAK. In total, 14 studies were included for qualitative synthesis in the final review: 8 comparative cross-sectional studies, 4 cross-sectional studies, 1 randomized crossover study, and 1 substudy of a randomized 2-period crossover trial, as denoted in **Table 2**. **Table 3** shows the quality assessment ratings of the included studies. AMD rated 2 of the studies neutral and the remaining 12 as positive. MA-L rated 4 of the studies neutral, 1 negative, and the remaining 9 as positive.

Observational studies

Infancy, toddlerhood, preschool years, and early childhood (1–6 y of age).

Three studies were included: 2 (37, 38) received 2 positive ratings for quality assessment and 1 (31) received 2 neutral ratings from the 2 reviewers, respectively (Table 3). Fecal microbiota of 1–4 y-olds, median age 2.7 y ($n = 28$), were compared with that of adults 21–60 y old ($n = 23$), and significant differences were observed for 5 phyla and 26 genera, suggesting transition of the fecal microbiota to an adult-like state may extend into the preschool years (37). Specifically, Clostridium cluster IV, Bacteroidetes, and 7 of 8 genera within the phylum Bacteroidetes were significantly more abundant in adults than in children. In contrast, *Bifidobacterium* relative abundance was significantly greater in children (11%) than in adults (3%). However, the abundance of *Bifidobacterium* decreased with age (i.e., *Bifidobacterium* species relative abundance was 32.1- and 5.0-fold higher at 1–2 y than 2–3 y and 3–4 y, respectively) (37). A primary limitation of the study was its method of dietary assessment, because it assumed children attending daycares adhered to local state and federal nutritional rules and regulations, which were assumed to be reflective of a Western-type diet,

TABLE 2 Characteristics of studies examining impacts of diet on the fecal microbiota in humans 1–20 y of age[1]

Country of study, age range, and participants/groups	Study design	Method of diet assessment	Method of microbiota assessment	Intervention protocol	Outcomes	Authors
USA (North Carolina); 1–4 y; $n = 28$ (adults 21–60 y, $n = 23$)	Comparative cross-sectional	Children attended daycares adhering to nutritional requirements defined by local state and federal rules and regulations.	Microarray targeting V1–V6 16S rRNA and qPCR	N/A	• 5 phylum-like microbial groups and 26 genus-like microbial groups differed between children and adults. • *Bifidobacterium* was 5 times higher in children than in adults, whereas Clostridium cluster XIVa did not differ. • Fecal microbiota diversity was greater in adults than in children. • Suggests development of fecal microbiota to an adult-like state extends into 1–4 y of life.	Ringel-Kulka et al. (37)
Australia; 2–3 y; $n = 37$	Cross-sectional	Australian Child and Adolescent Eating Survey (FFQ) and 24-h recall.	V6–V8 16S rRNA by Illumina MiSeq	N/A	• Dairy serving intake negatively associated with diversity and richness, and Bacteroidetes, and positively with *Erysipelatoclostridium* spp. and the F:B ratio. • Dairy and vegetarian protein (soy, pulses, and nuts) explained 7%–10% of the variance in microbiome composition, whereas vegetables and fruit explained 8% of the variance in microbiome composition. • Yogurt intake positively associated with an OTU related to *Streptococcus salivarius* ssp. • Vegetable protein intake positively associated with *Lachnospira*. • Vegetable protein (potentially driven by soy) positively associated with *Bacteroides xylanisolvens*. • Fruit intake negatively associated with *Ruminococcus gnavus*.	Smith-Brown et al. (31)
Italy and Burkina Faso; 1–6 y; $n = 29$ (Burkina Faso $n = 14$, Italy $n = 15$)	Comparative cross-sectional	Italian parents completed a detailed medical, diet, and lifestyle survey. Burkina Faso parents provided an in-depth interview on children's diet and a 3-d dietary questionnaire.	V5–V6 16S rRNA by 454-pyrosequencing	N/A	• Burkina Faso children's diet was low in fat and animal protein and high in starch, fiber, and plant polysaccharides. • Italian children's diet was high in animal protein, sugar, starch, and fat and low in fiber. • Actinobacteria and Bacteroidetes were enhanced in children from Burkina Faso, whereas Firmicutes and Proteobacteria were greater in Italian children. • F:B ratio was ~6 times greater in Italian children. • Genera *Prevotella*, *Xylanibacter*, and *Treponema* were enhanced in Burkina Faso children.	De Filippo et al. (38)

(*Continued*)

TABLE 2 (*Continued*)

Country of study, age range, and participants/groups	Study design	Method of diet assessment	Method of microbiota assessment	Intervention protocol	Outcomes	Authors
USA (Florida); 3–6 y; $n = 28$ child–parent pairs (1 withdrew during first intervention, $n = 28$ upon study completion; adults' age: 35 ± 0.06 y[a])	Randomized, crossover	Parents completed daily and weekly questionnaires via Qualtrics, in addition to 3 nonconsecutive, unannounced 24-h dietary recalls (ASA24).	V1–V3 16S rRNA by Illumina MiSeq	0.5 oz (14 g) [or 1.5 oz (42 g) for adults] almonds or an equivalent of almond butter daily for 3 wk followed by 4-wk washout periods. Control: precrossover ($n = 14$), postcrossover ($n = 14$); Intervention: precrossover ($n = 15$), postcrossover ($n = 14$)	• With intervention, changes in microbiome were greater in children than in adults. • Children in almond intervention increased total HEI scores (53.7 ± 2.6[b] to 61.4 ± 2.2[b]). • HEI component scores for total protein foods, seafood and plant proteins, and fatty acids increased. • No significant differences in immune status (salivary IgA, LPS-stimulated cytokines, serum antioxidant potential, and triglycerides) between control and almond intervention. • No effect of intervention on number of stools per week. • Main effects of week by intervention were not significant for GSRS syndromes, with the exception of children showing significantly lower constipation in the final week of intervention vs. the control period.	Burns et al. (39)
USA (Illinois); 4–8 y; $n = 22$	Cross-sectional	Nutrient intake assessed by 3-d food diaries. Youth and Adolescent (YAQ) FFQ utilized for dietary patterns.	V3–V4 16S rRNA by Illumina MiSeq	N/A	• Dietary Pattern 1 (fish, protein foods, refined carbohydrates, vegetables, fruit, juice and sweetened beverages, kid's meals, and snacks and sweets) linked to higher Bacteroidetes, *Bacteroides*, and *Ruminococcus* and lower *Bifidobacterium*, *Prevotella*, *Blautia*, and *Roseburia*. • Dietary Pattern 2 (grains, dairy, legumes, nuts, and seeds) associated with higher Cyanobacteria and *Phascolarctobacterium* and lower *Dorea* and *Eubacterium*.	Berding et al. (20)

(*Continued*)

TABLE 2 (*Continued*)

Country of study, age range, and participants/groups	Study design	Method of diet assessment	Method of microbiota assessment	Intervention protocol	Outcomes	Authors
Netherlands; 6–9 y; $n = 281$	Cross-sectional	Parent-report FFQ for children at 4–5 y of age.	Shotgun metagenomic sequencing by Illumina sequencing	N/A	• Three enterotypes were observed: *Bacteroides* ($n = 143$), *Prevotella* ($n = 74$), and *Bifidobacterium* ($n = 64$). • Plant-based protein positively correlated with the *Prevotella* enterotype but not with the *Bacteroides* and *Bifidobacterium* enterotypes. • Plant-based protein and dietary fiber intake negatively correlated to plasma insulin concentrations in the *Bacteroides* and *Prevotella* enterotypes, but not the *Bifidobacterium* enterotype. • Plant-based protein negatively correlated with relative abundances of *Streptococcus mitis*, *Bifidobacterium angulatum*, and *Bifidobacterium dentium*. • *Streptococcus parasanguinis* and *Streptococcus gordonii* positively correlated with animal-based protein intake. • *Collinsella intestinalis* negatively correlated with dietary fiber intake. • Enterotype differences observed in functional capacity for transformation of fermentation metabolites to compounds such as SCFAs. • β-Diversity was more similar within children than within adults. • *Bifidobacteria* was greater in children than in adults. • 6- to 9-y-olds possessed a more adult-like microbiota, suggesting ages 4–6 y may be pivotal in the transition to an adult-like microbiota.	Zhong et al. (40)
Netherlands; 6–10 y; $n = 472$	Cross-sectional	FFQ	qPCR on isolated DNA samples	N/A	• 78.2% of children presented *M. smithii*, and 8.3% of children presented *M. stadtmanae*. • Children who consumed organic milk and yogurt were >5 times and >4 times as likely, respectively, to present *M. smithii*.	van de Pol et al. (41)

(*Continued*)

TABLE 2 (*Continued*)

Country of study, age range, and participants/groups	Study design	Method of diet assessment	Method of microbiota assessment	Intervention protocol	Outcomes	Authors
Philippines: rural (Baybay) and urban (Ormoc City); 7–9 y; $n = 43$ (rural $n = 24$, urban $n = 19$)	Comparative cross-sectional	Parents/guardians were interviewed using a 137-item FFQ modified from the Singapore National Dietary Survey and adapted to dietary habits of Filipino children.	V6–V8 16S rRNA by 454 pyrosequencing	N/A	• Rural children consumed 71% of their total dietary intake from carbohydrates and lesser amounts of fat and protein. • Urban children ate more meats, confectionary such as sweetened pastries and biscuits, and more fat. • 87.5% of Baybay children displayed in the P-type cluster (defined by Prevotellaceae) and 78.9% of the Ormoc children were in the BB-type cluster (defined by Bacteroidaceae, Bifidobacteriaceae, Ruminococcaceae, and Lachnospiraceae). • Prevotellaceae was comprised only of the genus *Prevotella* and consisted primarily of the species *Prevotella copri*. • *Prevotella* negatively correlated with fat and positively with dietary carbohydrate, whereas *Bacteroides* associated with fat and protein. • The BB-type microbiota linked to genes involved in lipid, sugar, and amino acid metabolism. • The P-type microbiota linked to genes utilized in glycan biosynthesis and metabolism.	Nakayama et al. (42)
China and Malaysia; 7–12 y; $n = 201$ (Guangzhou Southern Han Chinese $n = 81$, Penang Southern Han Chinese $n = 21$, Kelantin Southern Han Chinese $n = 45$, Penang Malay $n = 21$, Kelantin Malay $n = 33$)	Comparative cross-sectional	Singapore Health Promotion Board validated FFQ.	qPCR, 16S rRNA sequencing via Illumina MiSeq	N/A	• Geography-related factors (i.e., diet) rather than ethnicity (i.e., Southern Chinese or Malay children) delineated differences in microbiota. • *Bifidobacterium* and *Collinsella* positively correlated with refined sugar–enriched foods; *Collinsella* positively associated with fruits and curry foods. • *Bacteroides*, *Faecalibacterium*, *Bifidobacterium*, and *Collinsella* negatively correlated with caffeinated drinks, curry, oily foods, and Southeast Asian vegetables.	Khine et al. (43)

(*Continued*)

TABLE 2 (*Continued*)

Country of study, age range, and participants/groups	Study design	Method of diet assessment	Method of microbiota assessment	Intervention protocol	Outcomes	Authors
Thailand; 8–11 y; $n = 60$ [Bangkok, central region (CT) of Thailand, $n = 31$; Khon Kaen, northeastern region (NE) of Thailand, $n = 29$]	Comparative cross-sectional	Self-administered FFQ.	qPCR, V6–V8 16S rRNA	N/A	• Children of NE Thailand consumed more carbohydrate-based foods as well as dietary fiber from vegetables and fruits than those living in CT Thailand. • Total bacteria, *Lactobacillus* group, *Clostridium coccoides- Eubacterium rectale* group, *Clostridium leptum* group, *Bifidobacterium* spp., *Bacteroidetes fragilis* group, *Prevotella* group, and Enterobacteriaceae greater in children of NE Thailand. • *Bifidobacterium* did not differ between the 2 groups. • Vegetables positively correlated with *Prevotella* group, *Clostridium coccoides-Eubacterium rectale* group, and total bacteria. • Fruits and vegetables positively correlated with *Lactobacillus* group. • Fish decreased *Clostridium leptum* group, whereas consumption of chicken increased *Clostridium leptum* group. • *Bifidobacterium* spp. negatively associated with fish and beef.	La-ongkham et al. (7)
Thailand, rural (Buriram) and urban (Bangkok); 9–10 y; $n = 45$ (rural $n = 28$, urban $n = 17$)	Comparative cross-sectional	7-D dietary records.	V1–V2 16S rRNA by Illumina MiSeq	N/A	• Bangkok children consumed more bread, meat, beverages, fat, and sugar and less rice and vegetables than Buriram children. • Buriram children possessed greater total α-diversity. • Bangkok children had higher proportions of the class Actinobacteria and orders Bacteroidales and Selenomadales, and Buriram children were highly colonized by the order Clostridiales. • Buriram children had greater concentrations of the SCFAs butyrate and propionate.	Kisuse et al. (44)

(*Continued*)

TABLE 2 (*Continued*)

Country of study, age range, and participants/groups	Study design	Method of diet assessment	Method of microbiota assessment	Intervention protocol	Outcomes	Authors
Bangladesh; 8–13 y; $n = 6$ USA; 10–14 y; $n = 4$	Comparative cross-sectional	NR	V1–V3 16S rRNA by 454 pyrosequencing	N/A	• Bangladeshi children consumed more rice, bread, and lentils, whereas American children consumed a Western diet including various sources of carbohydrates, vegetables, and animal proteins. • Bangladeshi children displayed greater microbial diversity and evenness. • Bangladeshi children had increased intraindividual variability with age. • The genus *Prevotella* dominated in Bangladeshi children, whereas *Bacteroides* was most prevalent in American children. • The genus *Prevotella* consisted primarily of the species *Prevotella copri*. • Taxa found in both American and Bangladeshi children: *Blautia*, *Leuconostoc*, *Streptococcus*, Clostridiaceae-associated *Clostridium*, Lachnospiraceae-associated *Clostridium*, unclassified Clostridiales, *Roseburia*, and *Faecalibacterium prausnitzii*. • *Bifidobacterium* was more abundant in and *Lactobacillus* exclusive to Bangladeshi children.	Lin et al. (45)
Spain; 12.4 ± 0.34[a]; $n = 20$ (Human experiment 1 of study; sample consisted only of males)	Randomized 2-period crossover trial	Daily records sheets.	qPCR	14-d experimental dietary intervention periods (7-d menu of WD low in MRPs or BD high in MRPs, each diet repeated once); 40-d washout period between trials	• Adolescents in the BD intervention had decreased presence of *Enterobacteria*, *Lactobacilli*, and *Escherichia/Shigella*. • No differences between the BD and WD diets were observed in total bacteria, *Bifidobacteria*, *Bacteroides*, *Eubacterium rectale/Clostridium coccoides* group, or *Clostridium leptum*. • MRP markers, HMF and CML, inversely correlated with fecal abundance of *Lactobacilli* and *Enterobacteria*. • HMF negatively correlated with *Escherichia/Shigella*. • Amadori compounds negatively correlated with *Bifidobacteria*.	Seiquer et al. (12)

(*Continued*)

TABLE 2 (*Continued*)

Country of study, age range, and participants/groups	Study design	Method of diet assessment	Method of microbiota assessment	Intervention protocol	Outcomes	Authors
Egypt (Giza); 13.3–14.5 y; $n = 28$ USA (Ohio); 10.1–15.7 y; $n = 14$ (Both samples consisted only of males)	Comparative cross-sectional	NR	V4 16S rRNA by Illumina MiSeq	N/A	• American teenagers consumed a Western-type diet high in fat and sugar. • Egyptian teenagers consumed a Mediterranean-style diet high in fruits, vegetables, nuts, seeds, legumes, and whole grains. • American children clustered to the *Bacteroides* enterotype and Egyptian children to the *Prevotella* enterotype. • Egyptian and American samples differed based on 12 genera: *Prevotella, Megasphaera, Eubacterium, Mitsuokella, Catenibacterium, Bacteroides, Faecalibacterium, Ruminococcus, Blautia, Coprococcus, Adlercreutzia,* and *Anaerostipes*. • Egyptian teenagers had greater SCFAs butyrate, propionate, and acetate; microbial polysaccharide degradation–encoding genes; and polysaccharide-degrading genera (*Megasphaera, Eubacterium, Mitsuokella*, and *Catenibacerium*). • American children were more abundant in starch-degrading genera (*Ruminococcus, Coprococcus*, and *Blautia*). • Functional metagenomics profiling observed Egyptian teenagers were more abundant in carbohydrate metabolism pathways and American teenagers were more abundant in protein degradation pathways.	Shankar et al. (46)

[1] Studies listed by chronology of age ranges examined. ASA24, Automated Self-Administered 24-h Dietary Recall; BD, brown diet; CML, carboxymethyl-lysine; F:B, Firmicutes to Bacteroidetes; GSRS, Gastrointestinal Symptom Response Scale; HEI, Healthy Eating Index; HMF, hydroxymethylfurfural; MRP, Maillard Reaction Product; NR, not reported; N/A, not applicable; OTU, operational taxonomic unit; rRNA, ribosomal RNA; WD, white diet.
[a] Values are means ± SEs.
[b] Values are means ± SEMs.

TABLE 3 Outline of quality assessment ratings for included studies examining impacts of diet on the fecal microbiota in humans 1–20 y of age[1]

Articles included in review	Quality ratings	
	Reviewer 1	Reviewer 2
La-ongkham et al. (7)	+	+
Seiquer et al. (12)	+	+
Berding et al. (20)	+	+
Smith-Brown et al. (31)	⊘	⊘
Ringel-Kulka et al. (37)	+	+
De Filippo et al. (38)	+	+
Zhong et al. (40)	+	+
Nakayama et al. (42)	+	+
Kisuse et al. (44)	+	+
van de Pol et al. (41)	+	+
Khine et al. (43)	⊘	⊘
Lin et al. (45)	+	−
Shankar et al. (46)	+	⊘
Burns et al. (39)	+	⊘

[1] +, positive quality rating; −, negative quality rating; ⊘, neutral quality rating.

but actually dietary intakes were not reported (37). However, analyses of diet were not reported. Another limitation is that the study did not parse out children's age for all of its analyses (i.e., 1–2 y compared with adults, 2–3 y compared with adults, and 3–4 y compared with adults), preventing further comparisons between infant and toddler fecal microbiota composition in relation to that of adults in this study.

With the introduction of solid foods, an increase in the abundance and variety of dietary glycans, protein, and additional nutrients influencing microbiota development was observed (47, 48). Among 2- to 3-y-olds ($n = 37$), Smith-Brown et al. (31) reported that the median daily servings of dairy, derived from FFQs (4.07) and 24-h recall (1.94), was significantly and negatively associated with fecal microbial α-diversity (Shannon Index) and richness (Chao1), respectively. In addition, median daily servings of dairy (4.07, FFQ data) was significantly and negatively correlated with the relative abundance of the phylum Bacteroidetes and was positively correlated with the Firmicutes-to-Bacteroidetes (F:B) ratio, which has been associated with a high-fat and high-sugar diet (49). Median daily servings of plant proteins, soy, pulses, and nuts (0.66, FFQ data) was significantly negatively correlated with the relative abundance of Firmicutes. Further, median daily servings of plant proteins (0.18 based on 24-h recall data) was significantly positively associated with an operational taxonomic unit (OTU) related to *Bacteroides xylanisolvens*. *Bacteroides* species are commonly able to break down starch; however, *B. xylanisolvens* cannot (50). Because soybeans contain small amounts of starch, but provide xylan and other polysaccharides, soy intake may drive the positive association between plant protein and *B. xylanisolvens*. Moreover, median daily servings of yogurt (0.57, FFQ data) was significantly positively associated with the abundance of an OTU related to *Streptococcus salivarius* ssp. *thermophilus*, and median daily servings of dairy (1.94, 24-h recall data) was also significantly positively associated with the relative abundance of OTUs related to *Lachnoclostridium* spp. and *Erysipelatoclostridium ramosum*. Median daily servings of vegetables (1.35, 24-h recall data) was significantly positively associated with *Lachnospira* relative abundance, whereas total median daily servings of fruit (3.05, FFQ data) and a specific fruit subgroup [i.e., apple or pear (0.43, FFQ data)] were significantly negatively associated with species related to *Ruminococcus gnavus*. This study was novel in its examination of toddlers, and although its findings were observational, the utilization of FFQs and 24-h recall for diet assessment allowed consideration of both long- and short-term dietary intake (31).

De Filippo et al. (38) compared 1- to 6-y-olds ($n = 29$) from Florence, Italy ($n = 15$) with children from Burkina Faso ($n = 14$). Using intake expressed in g/d of reported food items, children from Florence consumed a Western-type diet high in animal protein, sugar, starch, and fat and low in fiber. Children from Burkina Faso consumed a traditional-type diet low in fat and animal protein and high in starch, fiber, and indigestible plant polysaccharides. Among children from Burkina Faso, relative proportions of the phyla Actinobacteria (10.1%) and Bacteroidetes (57.7%) were significantly greater than in children from Florence (6.7% and 22.4%, respectively), whereas the relative abundances of Firmicutes and Proteobacteria were significantly increased in children from Florence (67.7% compared with 27.3%, and 6.7% compared with 0.8%, respectively). In addition, children from Burkina Faso exhibited bacteria from the genera *Prevotella*, *Xylanibacter*, and *Treponema* involved in utilization of energy from indigestible plant polysaccharides (38). Finally, children from Burkina Faso exhibited significantly greater microbial richness (Chao1), whereas children from Florence displayed a significantly greater F:B ratio. Although this study suggests that diet modulated fecal microbiota, it did not control for confounds between the 2 samples, such as the potentially vast differences in sanitation, hygiene, and living conditions between the children from Florence and Burkina Faso (23, 38).

Late preschool years and childhood (4–12 y of age). Seven studies were included: 6 (7, 20, 40–42, 44) received 2 positive ratings and 1 (43) received 2 neutral ratings. Berding et al. (20) conducted a cross-sectional study in 4- to 8-y-olds ($n = 22$) and reported dietary patterns to be associated with microbial taxa and composition. Dietary Pattern 1, defined by intake of fish, protein foods, refined carbohydrates, vegetables, fruit, juice and sweetened beverages, kid's meals, and snacks and sweets, was linked to a significantly higher relative abundance of Bacteroidetes, *Bacteroides*, and *Ruminococcus* and significantly lower relative abundance of *Bifidobacterium*, *Prevotella*, *Blautia*, and *Roseburia*. Dietary Pattern 2, defined by intake of grains, dairy, legumes, nuts, and seeds, was associated with significantly higher relative abundance of Cyanobacteria and *Phascolarctobacterium* and significantly lower relative abundance of *Dorea* and *Eubacterium* (20). The method of deriving dietary patterns

from FFQs allowed for novelty in finding associations between diet and fecal microbiota. However, parent self-report of their child's food intake is known to be susceptible to error and bias (51).

Zhong et al. (40) observed a more adult-like microbiota in 6- to 9-y-olds ($n = 281$), suggesting that the ages of 4–6 y may be critical in the transition to an adult-like microbiota. Three enterotypes, which are utilized to stratify fecal microbiota community types based on microbial composition (52), were observed: *Bacteroides* ($n = 143$), *Prevotella* ($n = 74$), and *Bifidobacterium* ($n = 64$). The species *Prevotella copri* in the *Prevotella* enterotype significantly negatively correlated with *Bacteroides uniformis* and *Bifidobacterium longum* of the *Bacteroides* and *Bifidobacterium* enterotypes, respectively. Plant-based protein intake (energy from total plant-based protein per day, mean ± SD: 5.71% ± 1.48%) was significantly correlated with the *Prevotella* enterotype, but not with the *Bacteroides* and *Bifidobacterium* enterotypes. Via Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis, children in the *Bacteroides* and *Prevotella* enterotypes displayed significantly enhanced abundances of genes encoding for proteins involved in the production of butyrate, which has been reported to affect plasma insulin concentrations (53). *Faecalibacterium prausnitzii, Eubacterium halii*, *Roseburia inulinivorans*, and *Odoribacter splanchnicus* accounted for the observance of these genes. Further, both *Bacteroides* and *Prevotella* enterotypes showed significant negative correlations of intakes of total dietary fiber per day (mean ± SD: 2.54 ± 0.53 g/MJ) and plant-based protein (energy from total plant-based protein per day, mean ± SD: 5.71% ± 1.48), respectively, with insulin concentrations. Moreover, the *Prevotella* enterotype displayed significantly higher abundances of genes encoding for succinate dehydrogenase complex, which is involved in the production of succinate, a metabolite of dietary fiber fermentation that favorably affects glucose concentrations and body weight regulation (54). *P. copri* was the primary contributor to this finding. No differences in the relative abundances of genes encoding for proteins involved in propionate production were observed between the 3 enterotypes. This is the only study in this review that utilized shotgun metagenomic sequencing, allowing for gene-level analyses of the fecal microbiota. However, whereas dietary assessment was derived from parent-report FFQ data for children at age 4–5 y, fecal sample collection took place in the same children when they were between the ages of 6 and 9 y. The temporal gap between the collection of dietary information and fecal sample collection leaves room for ambiguity in the results (40).

Nakayama et al. (42) compared 7- to 9-y-olds ($n = 43$) in the Philippines based on differences between traditional (rural) and Western-type (urban) dietary habits. Based on percentage of overall dietary intake, rural children ($n = 24$) consumed greater carbohydrates (71% compared with 60%) and lesser amounts of fat (18% compared with 27%) and protein (11% compared with 13%) than urban children ($n = 19$). The majority of rural children were grouped in the termed P-type cluster (defined by Prevotellaceae), whereas most urban children appeared in the termed BB-type cluster (defined by Bacteroidaceae, Bifidobacteriaceae, Ruminococcaceae, and Lachnospiraceae). The family Prevotellaceae was comprised only of the genus *Prevotella* and consisted primarily of the species *P. copri*. Furthermore, the BB-type cluster was associated with genes involved in lipid, sugar, and amino acid metabolism. In contrast, genes utilized in glycan biosynthesis and metabolism were linked to the P-type cluster. The P-type cluster was predicted to have higher relative abundance of 2 KEGG genes annotated as amylase, and the BB-type cluster was predicted to have higher relative abundance of 2 KEGG pathways annotated as primary and secondary bile acid synthesis. As for other studies in this review, the method of dietary assessment via FFQs is a well-known source of potential error and bias (51). In addition, the rural and urban children lived in 2 distinct geographical locations, and discrepancies in environmental factors outside of diet (i.e., livestock, water supply, and socioeconomic status) that may influence fecal microbiota were not measured and controlled for (23, 42).

Khine et al. (43) compared 7- to 12-y-olds ($n = 201$) among 3 Asian cities (Guangzhou, $n = 81$; Penang, $n = 42$; Kelantin, $n = 78$) based on location-related differences in diet. Although raw food item data were not reported in the study, the authors stated that food items were recorded as portions and times eaten per month and expressed as a fraction of total foods consumed for analyses. The relative abundance of the genus *Collinsella* was significantly positively correlated with refined sugar–enriched foods, fruit, and curry foods, whereas *Bifidobacterium* abundance was significantly positively correlated with refined sugar–enriched foods. *Bacteroides*, *Faecalibacterium*, *Bifidobacterium*, and *Collinsella* were significantly negatively correlated with caffeinated drinks, curry, oily foods, and vegetables, respectively. Through the novel examination of ethnicity in this study (i.e., Chinese or Malay), it was concluded that location-related differences in diet primarily affected fecal microbiota and not ethnicity (43).

La-ongkham et al. (7) compared 8- to 11-y-olds ($n = 60$) living in northeastern (NE) ($n = 29$) and central (CT) ($n = 31$) Thailand. Food items were reported as mean ± SD number of times the food was consumed each day. Children in CT Thailand consumed significantly more cow milk (1.52 ± 0.93 compared with 1.06 ± 1.03 times/d), rice (2.42 ± 0.90 compared with 1.68 ± 1.07 times/d), and breakfast cereal (0.35 ± 0.63 compared with 0.08 ± 0.37 times/d) than children in NE Thailand, who consumed significantly more chicken (1.32 ± 0.86 compared with 0.92 ± 0.88 times/d), beef (0.66 ± 0.75 compared with 0.32 ± 0.77 times/d), noodles (1.00 ± 0.82 compared with 0.37 ± 0.30 times/d), Khanomjeen (0.93 ± 0.74 compared with 0.16 ± 0.29 times/d), sweet potato (0.44 ± 0.72 compared with 0.06 ± 0.12 times/d), vegetables (1.69 ± 0.99 compared with 0.58 ± 0.54 times/d), and fruit (1.88 ± 1.02 compared with 0.49 ± 0.49 times/d). The prevalence of total bacteria (expressed as log copy numbers per g wet weight feces), as

well as specific bacterial groups (*Lactobacillus*, *Clostridium coccoides*, *Eubacterium rectale*, *Clostridium leptum*, *Bacteroidetes fragilis*, and *Prevotella*), was significantly higher in children from NE Thailand. Differences in *Bifidobacterium* were not observed between the 2 groups. However, for all subjects, the *Lactobacillus* group was significantly positively correlated with consumption of fruits (1.16 ± 1.05 times/d) and vegetables (1.12 ± 0.96 times/d). In addition, vegetable consumption (1.12 ± 0.96 times/d) was significantly positively correlated with total bacteria, *Clostridium coccoides-Eubacterium rectale*, and *Prevotella*, reflective of findings in adult samples showing high plant polysaccharide diets to associate with the *Prevotella* enterotype (55). In all subjects, the *Clostridium leptum* group was significantly positively associated with chicken consumption (1.12 ± 0.89 times/d) and negatively with fish (0.99 ± 1.04 times/d). Beef (0.49 ± 0.77 times/d) and fish (0.99 ± 1.04 times/d) were significantly negatively correlated with the *Bifidobacterium* group. The FFQ used in this study contained only 14 items (7), and therefore was not as comprehensive as those administered in other studies in this review [i.e., a 137-item FFQ was utilized by Nakayama et al. (42)].

Kisuse et al. (44) compared 9- to 10-y-olds ($n = 45$) based on differences in diet between urban and rural communities. Based on 7-d dietary records, mean ± SD consumption of food groups was estimated in kilocalories per day. Children from urban Bangkok ($n = 17$) consumed significantly more bread (65.2 ± 83.0 compared with 12.5 ± 33.5 kcal/d), meat (112.7 ± 63.5 compared with 29.6 ± 28.6 kcal/d), and beverages (180.9 ± 125.1 compared with 84.0 ± 98.4 kcal/d) and less rice (273.2 ± 96.5 compared with 362.6 ± 133.5 kcal/d) and combined vegetables and fruits (25.5 ± 27.0 compared with 103.9 ± 78.1 kcal/d) than children from rural Buriram ($n = 28$). Regarding nutrient intake, urban children also consumed significantly more fat (47.9 ± 17.1 compared with 35.4 ± 8.5 g/d) and sugar (37.4 ± 21.9 compared with 21.6 ± 18.6 g/d) and less β-carotene (382.5 ± 294.9 compared with 903.1 ± 752.1 μg/d) than rural children. Rural children had significantly greater total α-diversity (Chao1). Urban children had higher proportions of the class Actinobacteria and orders Bacteroidales and Selenomadales, and rural children were more highly colonized by the order Clostridiales, containing families such as Peptostreptococcaceae and unclassified Ruminococcaceae. In addition, rural children had significantly higher concentrations of the SCFAs butyrate and propionate, potentially indicative of a higher fermentable fiber intake associated with their greater vegetable consumption. Akin to other studies in this review (38, 42), this study did not control for differences in living conditions between urban and rural samples that may have confounded the findings.

van de Pol et al. (41) examined the impact of organic dairy on the presence of archaea in feces of 6- to 10-y-olds ($n = 472$) and detected *Methanobrevibacter smithii* in 78.2% and *Methanosphaera stadtmanae* in 8.3% of children, respectively. Children who consumed organic milk and yogurt were 5 and 4 times as likely, respectively, to display *M. smithii* as children who did not consume organic milk and yogurt. This was the only study identified in this systematic review that reported the influence of diet on archaea in fecal microbiota of children.

Middle and late adolescence (8–15 y of age).

Two studies were included: 1 (45) received a positive rating and a negative rating and 1 (46) received a positive rating and a neutral rating. Lin et al. (45) compared Bangladeshi ($n = 6$) children (ages 8–13 y) to American ($n = 4$) children (ages 10–14 y). Bangladeshi children consumed a diet rich in rice, bread, and lentils, whereas American children consumed a Western-type diet, including various sources of carbohydrates, vegetables, and animal proteins. Bangladeshi children had significantly greater phylogenetic diversity, OTU-based diversity (Shannon entropy), and number of observed OTUs. The composition of phyla differed between the groups: Bangladeshi children had greater abundances of Firmicutes, Tenericutes, and Proteobacteria, whereas American children had higher abundances of Bacteroidetes. At the genus level, *Prevotella* dominated in Bangladeshi children, whereas *Bacteroides* was most prevalent in American children. The *Prevotella* species *P. copri* (90%), *P. stercorea* (7%), and *P. ruminocola* (2%) were observed in Bangladeshi children. Dietary assessment and determination of how specific food group amounts were estimated were not clearly reported in the methods section of this study (45), which makes the findings more difficult to interpret.

Shankar et al. (46) compared the fecal microbiota of American ($n = 14$) and Egyptian ($n = 28$) teenagers between the ages of 10 y and 15.7 y. American teenagers consumed a Western-type diet high in fat and sugar and clustered to the *Bacteroides* enterotype. Egyptian teenagers consumed a Mediterranean-type diet high in fruits, vegetables, nuts, seeds, legumes, and whole grains and clustered to the *Prevotella* enterotype. Egyptian teenagers showed significantly enhanced SCFAs, microbial polysaccharide degradation–encoding genes, and polysaccharide-degrading genera (*Megasphaera, Eubacterium, Mitsuokella,* and *Catenibacterium*). American children were significantly more abundant in starch-degrading genera (*Ruminococcus, Coprococcus*, and *Blautia*), a mucin-degrading genus (*Akkermansia*), and a clostridial genus (*Faecalibacterium*) and higher in a bile-degrading microbe (*Bilophila*) associated with high-fat diets. Similarly to the work by Lin et al. (45), information on methods of dietary assessment and whether specific food group amounts were estimated were not clearly reported in this study (46).

Dietary intervention studies

Preschool years (2–5 y of age).

One study (39) was included and received a positive rating and a neutral rating. In a randomized crossover trial of child–parent pairs ($n = 28$), Burns et al. (39) assigned 4-y-old children to intervention (0.5 oz or 14 g almonds daily or an equivalent amount of almond butter) or control (no almonds) for 3 wk. Among adults (~35 y of age), the amount

of almond or almond equivalent was 1.5 oz or 42 g. In children, changes were observed at the genus level: *Lactococcus*, *Clostridium*, *Dorea*, *Oscillospira*, and *Actinomyces* decreased significantly, whereas *Bacteroides*, *Lachnospira*, *Varibaculum*, *Blautia*, *Peptoniphilus*, and *Corynebacterium* increased significantly in the intervention participants. However, no additional changes were observed at the phylum level or in overall microbial diversity. Although the almond intervention showed slight effects on the microbiota, the observed effects of the intervention on the microbiota were more pronounced among children than among adults. However, the authors note that the Automated Self-Administered 24-h Dietary Recall (ASA24), at the time of submission of the current article, had not been validated for parent report of child intake. In addition, children attended school or daycare, making reports of food intake during these periods of time ambiguous (39). The primary strength of this study is that it is 1 of only 2 dietary interventions included in this review.

Late childhood and early adolescence (12–13 y of age). One study (12) was included and received 2 positive ratings. In a randomized 2-period crossover trial, Seiquer et al. (12) examined the impact of MRPs on fecal microbiota. The MRPs, such as those found in bread crusts (56), pancakes, and fast foods undergoing frying and reheating (57), are often found in Western diets consumed by adolescents (13), and microbes may use MRPs as a nitrogen and carbon source (56, 58). Seiquer et al. examined 20 males (mean ± SE age: 12.4 ± 0.34 y) consuming either a white diet (WD) low in MRPs or a brown diet (BD) high in MRPs. Adolescents in the BD intervention, which included foods such as fried chicken and potatoes, rather than boiled chicken and potatoes, had significantly lower relative abundance of *Enterobacteria, Lactobacilli*, and *Escherichia/Shigella*. No significant differences were observed for total bacteria, *Bifidobacterium*, *Bacteroides*, *Eubacterium rectale/Clostridium coccoides* group, or *Clostridium leptum* between the BD and the WD diet (12). The presence of specific MRP markers, hydroxymethylfurfural and carboxymethyl-lysine, was significantly inversely correlated with fecal abundance of *Lactobacilli*, a bacteria associated with health benefits (59), and *Enterobacteria*. Significant inverse correlations between *Escherichia/Shigella* relative abundance and hydroxymethylfurfural were observed, suggestive of potential antimicrobial effects (60). This study is novel to this review in that it is 1 of only 2 interventions included, and it is the only study focused on examination of MRPs' influences on the fecal microbiota.

Discussion

Evidence herein supports that diet influences the fecal microbiota in humans 1–15 y of age. Five studies (7, 38, 40, 42, 45), collectively examining the ages of 1–13 y, suggest that children who consume a diet rich in indigestible plant polysaccharides associate with *Prevotella* or with an enterotype dominated by this genus. In 3 of these studies (40, 42, 45) spanning the ages of 6–13 y, *P. copri* was a primary contributor. Two studies (40, 42) reported associations between the *Prevotella* genus or an enterotype dominated by this genus and increased abundances of genes encoding for fiber degradation (40, 42). The *Prevotella* enterotype associated with significantly higher abundances of genes encoding for succinate dehydrogenase complex involved in succinate production, with *P. copri* as a primary contributor in 1 study (40), and genes involved in glycan biosynthesis and metabolism were linked to the P-type microbiota primarily driven by the family Prevotellaceae (42). The trends revealed in this review support previous research showing associations between a Mediterranean-type diet and health benefits to the fecal microbiota, marked by both the presence of *Prevotella* and increased concentrations of fecal SCFAs associated with reduction of disease risk (18).

In contrast, *Bacteroides* was most prevalent in American 10- to 14-y-olds consuming a Western-type diet high in animal proteins and various refined carbohydrates (45). Furthermore, in 7- to 9-y-olds, *Bacteroides* was significantly positively correlated with fat and protein consumption, and the BB-type microbiota (defined by Bacteroidaceae, Bifidobacteriaceae, Ruminococcaceae, and Lachnospiraceae) was associated with consumption of high amounts of meats, sweetened confectionaries, and fats. Moreover, the BB-type microbiota associated with genes involved in lipid, sugar, and amino acid metabolism (42). American teenagers consuming a Western-type diet displayed significantly greater abundance of starch-degrading genera (*Ruminococcus, Coprococcus*, and *Blautia*) and enhanced abundances in protein degradation pathways, whereas Egyptian teenagers consuming a Mediterranean-style diet possessed significantly greater polysaccharide-degrading genera (*Megasphaera, Eubacterium, Mitsuokella*, and *Catenibacterium*), microbial polysaccharide degradation–encoding genes, and increased concentrations of the SCFAs butyrate, propionate, and acetate (46). In light of the emphasis on dietary patterns in the 2015 (61) and 2020 (62) Dietary Guidelines for Americans, this review has substantiated utilization of dietary patterns for assessment of nutritional impacts on health via modulation of the fecal microbiota. In addition, this review reveals a series of positive and negative relations between microbes and Mediterranean- and Western-type diets (**Table 4**).

Furthermore, this review highlights microbes implicated in associations between diet and potential health consequences in children. For example, *Lachnospira* was significantly positively related to vegetable intake (31), and *Lachnospira* has been shown to be reduced in children who later develop risk of asthma (63). Furthermore, total fruit intake and specific fruits, apple and pear, were significantly negatively associated with species related to *R. gnavus* (31). Although considerations between *R. gnavus*, diet (fruit intake), and disease (inflammatory bowel disease) (64) have been made in adults, these relations are not well understood (31). Moreover, Shankar et al. (46) suggested that *Akkermansia* and *Faecalibacterium*, which were associated with the Western-type diet in American teenagers and are purported to confer anti-inflammatory effects (65, 66), may

TABLE 4 Associations between diet types and microbiome composition in healthy children aged 1–15 y derived from included studies examining impacts of diet on the fecal microbiota in humans 1–20 y of age

Diet type	Associated microbes	
	Positive	**Negative**
Mediterranean-type: higher in fruits, vegetables, nuts, seeds, and legumes	• Firmicutes, Tenericutes, and Proteobacteria • Clostridiales • Peptostreptococcaceae and Prevotellaceae • *Prevotella* or enterotype dominated by this bacterium • *Lachnospira*, *Lactobacillus*, *Megasphaera*, *Eubacterium*, *Mitsuokella*, and *Catenibacterium* • *Bacteroides xylanisolvens*, *Prevotella copri*, *Prevotella stercorea*, and *Prevotella ruminocola*	• Firmicutes • *Dorea* and *Eubacterium* • *Collinsella* • *Ruminococcus gnavus*
Western-type: higher in sugar, fat, and animal protein	• Bacteroidetes and Actinobacteria • Bacteroidaceae, Bifidobacteriaceae, Ruminococcaceae, and Lachnospiraceae • *Bacteroides* or an enterotype dominated by this bacterium • *Ruminococcus*, *Coprococcus*, *Blautia*, *Akkermansia*, *Faecalibacterium*, and *Bilophila* • *Bacteroidales* and *Selenomadales*	• *Bifidobacterium*, *Prevotella*, *Blautia*, and *Roseburia*

reflect an adaptive response among American teenagers potentially experiencing high amounts of inflammation.

Regarding the detection of methanogenic archaea in human fecal matter, van de Pol et al. (41) observed a significantly greater relative abundance of *M. smithii* in their sample of 6- to 10-y-olds. Whereas *M. smithii* and *M. stadtmanae* have the capacity for methane production, only *M. smithii* has the ability to produce methane from formate (67). This may contribute to *M. smithii*'s greater presence in feces than *M. stadtmanae*, because hydrogen reduction as a part of methane formation in the luminal space provides for greater fermentation potential (67). The Integrated Microbial Next Generation Sequencing database (68) reported methanogenic archaea in soil, and the uptake of soil by cows, particularly organically raised cows allotted greater range outdoors (69), may be a route for archaea to make their way into the rumen of cows and subsequently into dairy products. This may have contributed to the observation that children who consumed organic milk and yogurt were more likely to possess *M. smithii* in their fecal matter (41). However, a limitation of this study is that the authors could not distinguish between their detecting the presence of cell-free DNA originating from lysed archaea as opposed to living archaea. Further, a causal relation between the children consuming organic milk and yogurt and the increased likelihood of detecting archaea in their feces cannot be made.

Although limitations exist for the use of quality assessment tools in systematic reviews and meta-analyses (70), deploying the QCC provided the authors with a standardized methodology for assessment and discussion of the included studies. Moreover, limitations of the included observations are that they were made primarily in cross-sectional studies and only in the age range of 1–15 y. Owing to the lack of literature on the effect of dietary intake on fecal microbiota composition between the ages 16 and 20 y, one may only theorize about if the trends observed in 1- to 15-y-olds would persist in 16- to 20-y-olds. However, because similar observations to those in the included 1–15 y age range have also been reported in adults [i.e., the link between a Mediterranean-type diet and the genus *Prevotella* (18)], we expect that these associations would also be seen in those aged 16–20 y. Further, prospective observational studies, which would allow inference of how evolving dietary changes with age affect the fecal microbiota of a single sample across time, were not included. Furthermore, across the included studies different methods of dietary assessment were utilized. Whereas 7 of the included studies (7, 20, 31, 40, 42, 41, 43) examined long-term dietary intake via FFQs, 4 studies assessed short-term food intake through daily records sheets (12), 3-d dietary questionnaires (38), 24-h diet recalls (45), and 7-d food records (44). The differences in dietary assessment methods across studies make it difficult to draw conclusions as to which specific microbes are affected by short- as opposed to long-term dietary intake.

Although past research has examined under- and over-reporting among dietary assessment tools (i.e., ASA24, 4-d food records, and FFQs) via comparison to recovery biomarkers (71), future research should consider the need for a study designed to identify the most accurate methods of dietary assessment in relation to the fecal microbiota. In addition, samples from rural and urban environments were frequently compared without controlling for additional environmental factors influential to the fecal microbiota, such as exposure to livestock, access to medical care, water supply, or socioeconomic status (23), and without consideration for adequacy of fiber intake among their samples, with recommendations ranging, depending on the

organization, from 5 to 35 g/d for children 1–13 y old (71, 72). Lastly, future research should address the need for uniform methods of dietary assessment, larger sample sizes, literature in the ages of 16–20 y, and RCTs with intervention and control diets to drive insight into mechanistic-causal impacts of diet on the fecal microbiota in healthy humans.

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