

## The association between the maternal diet and the maternal and infant gut microbiome: a systematic review

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### Abstract

During pregnancy, changes occur to influence the maternal gut microbiome, and potentially the fetal microbiome. Diet has been shown to impact the gut microbiome. Little research has been conducted examining diet during pregnancy with respect to the gut microbiome. To meet inclusion criteria, dietary analyses must have been conducted as part of the primary aim. The primary outcome was the composition of the gut microbiome (infant or maternal), as assessed using culture-independent sequencing techniques. This review identified seven studies for inclusion, five examining the maternal gut microbiome and two examining the fetal gut microbiome. Microbial data were attained through analysis of stool samples by 16S ribosomal RNA gene-based microbiota assessment. Studies found an association between the maternal diet and gut microbiome. High-fat diets (% fat of total energy), fat-soluble vitamins (mg/d) and fibre (g/d) were the most significant nutrients associated with the gut microbiota composition of both neonates and mothers. High-fat diets were significantly associated with a reduction in microbial diversity. High-fat diets may reduce microbial diversity, while fibre intake may be positively associated with microbial diversity. The results of this review must be interpreted with caution. The number of studies was low, and the risk of observational bias and heterogeneity across the studies must be considered. However, these results show promise for dietary intervention and microbial manipulation in order to favour an increase of health-associated taxa in the gut of the mother and her offspring.

**Key words:** Pregnancy; Diet; Nutrition; Gut microbiome; Maternal microbiome; Infant microbiome

Advancements in the past decade in next-generation sequencing and associated bioinformatics analyses have facilitated a more in-depth study of the human gut 'microbiome'; a word coined to describe the overall community of micro-organisms in the gastrointestinal tract<sup>(1)</sup>. Links between the microbiome and many physiological conditions of the associated host have been made<sup>(2–4)</sup>. The various components contributing and modulating the microbiome are yet to be truly defined; however, environmental factors such as lifestyle and diet have come to the fore<sup>(5,6)</sup>.

Diet and dietary patterns have been shown to rapidly alter microbial diversity and in turn influence host physiology<sup>(7,8)</sup>.

In non-pregnant cohorts, the dietary macronutrients fat and fibre have most commonly been demonstrated to be able to cause a shift in microbial diversity, with fibre consumption associated with beneficial effects<sup>(9–11)</sup>.

With respect to dietary patterns, the Mediterranean diet, the Western diet, low-fat and high-fibre diets have been examined in greatest detail, with some research showing Western diet to influence the gut microbiome more considerably than BMI<sup>(8,12)</sup>. Diets high in fibre have been shown to have the ability to increase the relevant abundance of SCFA-producing bacteria<sup>(13)</sup>. This is in contrast to diets rich in animal fats, high in saturated fat

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and protein, which have been shown to have a negative impact<sup>(14)</sup>. The blueprint for the optimal gut microbiome is still unknown, but the negative association of decreased diversity is commonly observed. Decreased diversity is linked to a phenomenon called dysbiosis (a disruption of normal gut microbiota); diversity is involved in the survival and adaptability of any ecosystem, the microbiome being no exception<sup>(15)</sup>. Furthermore, diets such as the Western diet are associated with decreased microbial diversity<sup>(12,16)</sup>.

Diversity is the method used to assess the gut microbiome.  $\alpha$  Diversity (also described as the intra-personal variation) is the individual's diversity in the microbiota. It has been suggested that a higher  $\alpha$  diversity correlates with a healthier microbiome<sup>(17,18)</sup>. As for many ecosystems, a high species diversity is linked with greater resistance to dysbiosis (disruption of microbiota composition from outside normal ranges) and an overall health within the host<sup>(19)</sup>.

$\beta$  Diversity on the other hand describes the interpersonal variation of microbial composition and can be based on collapsing all microbial data to a single coordinate point and measuring the distance (using various metrics, e.g. Bray-Curtis, unweighted and weighted UniFrac, Euclidean) between this point and another, usually another participant, person or collection site.

In pregnancy, the gut microbiome is thought to be dynamic with a change seen in first trimester diversity compared with that of the third trimester<sup>(20)</sup>. Mode of delivery, pre-term birth, breastfeeding and maternal diet have been identified as important factors that directly influence the composition of the neonatal gut microbiota<sup>(21)</sup>. Likewise, the presence of furry pets in the home has been shown to influence the composition of the gut microbiota of newborns<sup>(22)</sup>.

There is limited literature examining the association between maternal macronutrient and micronutrient intake and infant and maternal gut microbiome. Without this knowledge, it is impossible to develop a therapeutic use of dietary manipulation to modulate the microbiome and in turn lead to improvements in infant and maternal health.

The aim of this systematic review was to summarise current evidence relating to the association between maternal diet in pregnancy and both the maternal and neonatal gut microbiome.

## Methods

### Protocol and registration

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement for reporting on systematic reviews was followed<sup>(23)</sup>. A search checklist of items to include methods, strategy, study selection process, a risk of bias tool and summary measures was used and reported.

### Eligibility criteria

To be included in the review, the studies had to be observational or cross-sectional in design, subjects needed to be pregnant women and/or infants within the first 6 weeks postpartum. The study needed to include a formal dietary analysis during pregnancy and use a culture-independent sampling technique

to assess the gut microbiome. Studies had to include details of ages, ethnicities and demographic characteristics of the women/infants. Studies that evaluated the effect of dietary supplementation or probiotic use only, without formal dietary assessment, were excluded, as book chapters, online abstracts and conference proceedings were not included. Articles had to be published in English, and no time restrictions was imposed.

### Outcomes

The main outcomes examined in this review were the maternal or neonatal gut microbiome composition and diversity, as assessed by culture-independent sequencing techniques. These outcomes are expressed as microbial diversity in terms of both  $\alpha$  (intra-individual variation) and  $\beta$  (inter-individual variation) diversity and relative abundance of specific microbes. Indices such as Shannon's index, whole-tree phylogenetic diversity and Simpson's index, which measure diversity within microbial communities or UniFrac distances, Bayesian models or principal component analysis, which measure diversity between microbial communities were included.

### Information sources

The following five electronic databases were searched; MEDLINE (PubMed), Cochrane Library, Web of Science, CINAHL and Ovid. The last search was conducted on 7 October 2019.

### Search

Search terms are as follows: human; antenatal; pregnant; pregnancy; maternal; microbiome; microbial; microbiota; microbe; gut bacteria; gut microbiome; nutrient; diet; nutrition; dietary.

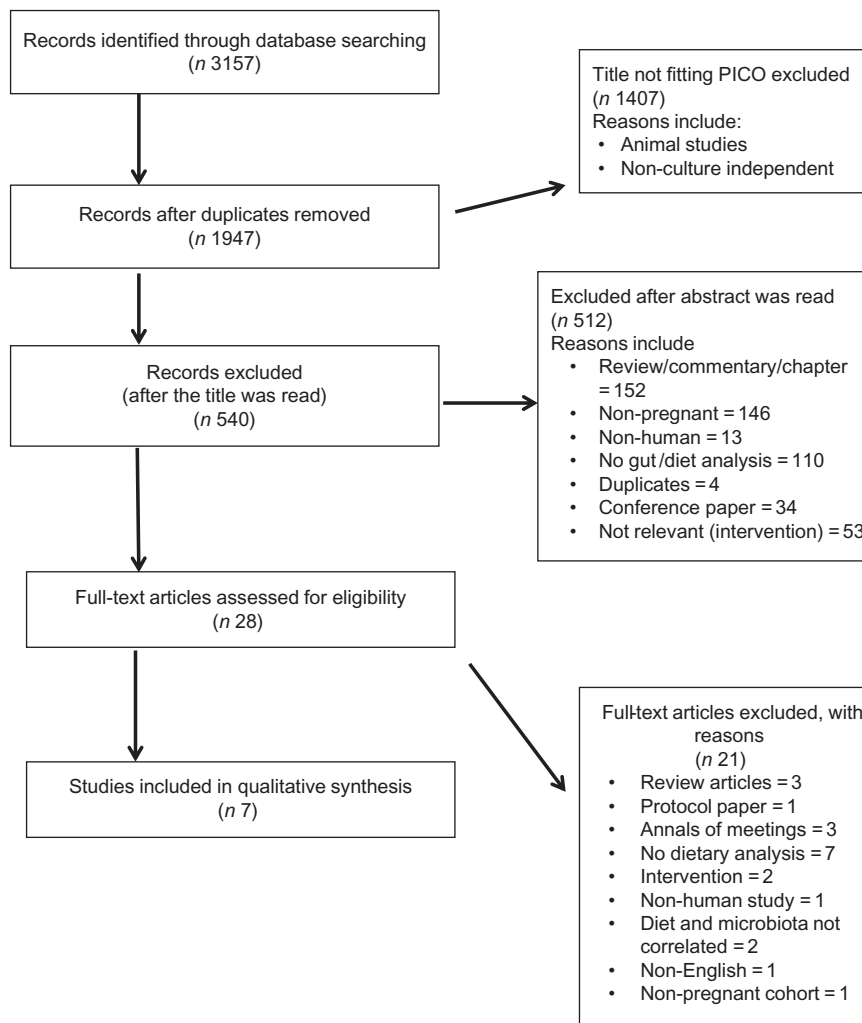
Search terms were identified by initial scoping searches and then adjusted depending on the electronic database searched, to better match the key words and indexing terms of each database, and align with MeSH (Medical Subject Headings) terms.

### Study selection

**Summary measures.** It was not possible to carry out a summary analysis or meta-analysis for this systematic review due to heterogeneity across the included studies. This included differences in stage of pregnancy of participants, the stool sample analysed, the dietary assessment tool used and the method of microbiota analysis. An overall description of individual results is therefore provided in the Results section, separated into two sections: maternal gut microbiota and neonatal gut microbiota.

## Results

Identified articles were added to a reference manager software package (EndNote version 7.7.1), and duplicates removed. A new file was created minus the duplicates. Studies were then screened based on the study title. Papers were then excluded based on reading an abstract and its fitting of the defined population, comparison, intervention and outcome (PICO) terms.



**Fig. 1.** Flow diagram of study selection. Flow diagram depicting each stage of the study identification process. PICO, population, comparison, intervention and outcome.

Abstracts were reviewed independently by two researchers (S. E. M and E. C. O'B.), and two individual spreadsheets were created with researchers' final included abstracts. Full papers of said abstracts were reviewed independently by two researchers (S. E. M. and E. C. O'B.) and both parties selected final papers. Disagreements were resolved by a third party (F. M. M.). A flow chart created based on the PRISMA guidelines can be seen below (Fig. 1).

### Study characteristics

The study characteristics are described in Table 1.

### Risk of bias in individual studies

The seven studies were assessed for risk of bias using the 2016 ROBINS-I ('Risk Of Bias In Non-randomised Studies – of Interventions') assessment tool<sup>(31)</sup>. The ROBINS-I consists of an assessment and a scoring algorithm that ranks studies with little, moderate or severe bias, on contact with the Cochrane Group; this was agreed to be the most suitable risk of bias tool. Three researchers (S. E. M., E. C. O'B. and D. F. B.) independently assessed the included articles.

### Risk of bias assessment

All studies were subject to a varying level of bias due to the observational nature of the analysis and potential confounders. Four studies were found to be at serious risk of bias in at least one domain, with three studies at moderate risk of bias (Table 2). No study was judged to be at a critical risk of bias in any domain. Therefore, the seven studies were included in this review<sup>(24-30)</sup>.

### Maternal diet and the maternal gut microbiota

The association between maternal diet and the maternal gut microbiome composition in pregnancy was investigated in five studies. All five studies reported that the maternal gut microbiome in pregnancy is influenced by maternal diet to varying degrees. In addition, specific macronutrients are associated with distinct bacterial compositions and relative abundances and can modulate, either positively or negatively, the diversity of the gut microbiome.

Three studies identified an association between dietary fat intake and gut microbiome composition<sup>(25,26,28)</sup>. Two of these studies reported a negative correlation between  $\alpha$  diversity and intakes of cholesterol<sup>(25)</sup>, total fat and SFA<sup>(26)</sup>. The third

**Table 1.** Summary of results

Authors	Year of publication	Title	<i>n</i>	Study cohort	Country
Chu <i>et al.</i> <sup>(24)</sup>	2016	The early infant gut microbiome varies in association with a maternal high-fat diet	136	Part of a larger, population-based study that examines the development of the neonatal microbiome across multiple body sites	USA
Mandal <i>et al.</i> <sup>(25)</sup>	2016	Fat and vitamin intakes during pregnancy have stronger relations with a pro-inflammatory maternal microbiota than does carbohydrate intakes	60	Norwegian NoMIC cohort; a cohort which oversampled preterm deliveries, 35% of babies in cohort were born preterm (NoMIC)	Norway
Röytiö <i>et al.</i> <sup>(26)</sup>	2017	Dietary intake of fat and fibre according to reference values relates to higher gut microbiota richness in overweight pregnant women	88	Part of a larger RCT with pregnant obese women taking probiotic and/or fish oil supplement	Finland
Lundgren <i>et al.</i> <sup>(27)</sup>	2018	Maternal diet during pregnancy is related to the infant stool microbiome in a delivery-mode-dependent manner	145	Participants gathered from New Hampshire Birth Cohort Study	USA
Barrett <i>et al.</i> <sup>(28)</sup>	2018	A vegetarian diet is a major determinant of gut microbiota composition in early pregnancy	Total: 27 Vegetarian: 9 Control: 18	SPRING study cohort: probiotic supplementation for pregnant women with overweight and obesity	Australia
Gomez-Arango <i>et al.</i> <sup>(29)</sup>	2018	Low dietary fibre intake increases <i>Collinsella</i> abundance in the gut microbiota of overweight and obese pregnant women	Total: 126 Ow: 53 Ob: 73	SPRING study cohort: probiotic supplementation for pregnant women with overweight and obesity	Australia
Laitinen <i>et al.</i> <sup>(30)</sup>	2019	Overall dietary quality relates to gut microbiota diversity and abundance	84	Part of a larger RCT with pregnant obese women taking probiotic and/or fish oil supplement	Finland

Population characteristics							
	Mean age (years)	Mean pre-pregnancy BMI (kg/m <sup>2</sup> )	Pre-term birth rate (%)	Smoking status (%)	Gestational age at time point	Third-level education (%)	GDM rate (%)
Chu <i>et al.</i>	30.0 (SD 5.9)	27.8 (SD 5.9)	11.5	Not reported	Third trimester	Not reported	30%
Mandal <i>et al.</i>	Not reported	22.9 (SD 3.5)	35	15	Second trimester; 22 weeks; Stool collected day 4 postpartum	46	N/A
Röytiö <i>et al.</i>	30.1 (SD 4.7)	30.2 (SD 4.6); overweight/obesity	Not reported	Not reported	First trimester; 13.3 weeks	50	N/A
Lundgren <i>et al.</i>	31.9	25.6	Not reported	4.8	24–28 weeks	70	11
Barrett <i>et al.</i>	V: 33 (29–34); C: 34 (32–37)	V: 28.3 (26.5–35.5); C: 28.4 (26.5–35.3)	Not reported	Not reported	First trimester; 16 weeks	Not reported	V: 11.1; C: 11.1
Gomez-Arango <i>et al.</i>	Ow: 32 (29–34); Ob: 30.5 (28–34)	Ow: 27.9 (27–29.1); Ob: 34.3 (31.8–41.3); overweight/obesity	Not reported	Not reported	First trimester; 16 weeks	Not reported	0
Laitinen <i>et al.</i>	30.1 (SD 4.7)	30.3 (SD 4.6); overweight/obesity	Not reported	Not reported	First trimester; 13.3 weeks	50	N/A

Data collection		
	Dietary data	Microbiome data
Chu <i>et al.</i>	DSQ: captured dietary habits over past month	Infant stool: 16S rRNA sequencing on samples collected at delivery and 6 weeks postpartum
Mandal <i>et al.</i>	FFQ	Maternal stool: 16S rRNA sequencing on samples collected at day 4 postpartum
Röytiö <i>et al.</i>	3-d food diary: recorded the week before study visit	Maternal stool: 16S rRNA sequencing on samples collected at <18 weeks gestation
Lundgren <i>et al.</i>	FFQ: Alternative Mediterranean Score calculated	Infant stool: 16S rRNA sequencing on samples collected at 6 weeks postpartum
Barrett <i>et al.</i>	FFQ: captured dietary information from start of pregnancy	Maternal stool: 16S rRNA sequencing on samples collected at <16 weeks gestation
Gomez-Arango <i>et al.</i>	FFQ: captured dietary information from start of pregnancy	Maternal stool: 16S rRNA sequencing on samples collected at <16 weeks gestation
Laitinen <i>et al.</i>	IDQ	Maternal stool: 16S rRNA sequencing on samples collected at <18 weeks gestation

Table 1. (Continued)

Analysis performed			
	Measures used	Correction for multiple testing	Effect of correction factor
Chu <i>et al.</i>	PcoA unweighted UniFrac distances, LefSe	None used	N/A
Mandal <i>et al.</i>	Shannon, whole-tree PD PcoA weighted and unweighted UniFrac	Not used for reported compositional analysis. Benjamini–Hochberg correction performed for subsequent analysis of reported compositional findings.	N/A
Röytiö <i>et al.</i>	Shannon, observed OTU, Chao 1, PD	Benjamini–Hochberg correction	High-fibre/low-fat intake associated with lower relative abundance of Bacteroidaceae remained significant. Other associations did not remain significant
Lundgren <i>et al.</i>	PERMANOVA, PcoA generalized UniFrac distances	Benjamini–Hochberg correction	Associations remained significant
Barrett <i>et al.</i>	Chao 1, Shannon, ACE, Simpson Bray–Curtis dissimilarity, Canonical correspondence, PERMANOVA, LefSe	None used	N/A
Gomez-Arango <i>et al.</i>	Chao 1, Shannon PcoA, LefSe, Bray–Curtis dissimilarity	None used	N/A
Laitinen <i>et al.</i>	Chao 1, observed OTU, PD, Shannon	Adjusted FDR of <0.1	Associations did not remain significant after correction
Outcomes			
	Influence of maternal diet	Impact on relative abundance of bacteria	
Chu <i>et al.</i>	A high-fat maternal diet is associated with distinct changes in the neonatal gut microbiome	High-fat maternal diet associated with lower relative abundance of <i>Bacteroides</i>	
Mandal <i>et al.</i>	Vitamin D, retinol and cholesterol negatively associated with maternal gut diversity	Vitamin D, retinol and cholesterol associated with relative increased abundance of Proteobacteria	
Röytiö <i>et al.</i>	Adherence to recommended reference intakes of dietary fibre and fat associated with increased maternal gut diversity	Inverse relationship was observed with vitamin E and protein intake. High-fibre/low-fat intake associated with lower relative abundance of Bacteroidaceae	
Lundgren <i>et al.</i>	The influence of maternal diet on infant gut microbiome differs by delivery mode. Vaginally born: higher fruit consumption associated with higher odds of cluster 2 profile. C-section: high dairy consumption associated with high odds of cluster B profile	Vaginally born microbiome clusters: (1) <i>Bifidobacterium</i> ; (2) <i>Streptococcus</i> and <i>Clostridium</i> ; (3) <i>Bacteroides</i> C-section born microbiome clusters: (A) <i>Bifidobacterium</i> ; (B) high <i>Clostridium</i> , low <i>Streptococcus</i> , low <i>Ruminococcus</i> ; (C) Enterobacteriaceae family	
Barrett <i>et al.</i>	Vegetarian diet did not influence $\alpha$ diversity compared with omnivorous diet	Vegetarian diet associated with increased relative abundance of <i>Roseburia</i> and Lachnospiraceae and decreased relative abundance of <i>Collinsella</i>	
Gomez-Arango <i>et al.</i>	When corrected for TEI, $\beta$ diversity differed by dietary fibre intake	After adjustment for TEI, high dietary fibre was associated with increase relative abundance of <i>Holdemania</i> , <i>Coproccoccus</i> , <i>Roseburia</i> and others of similar phyla Low dietary fibre was associated with <i>Collinsella</i> , <i>Sutterella</i> , <i>Bilophila</i> and others	
Laitinen <i>et al.</i>	Highest IDQ quartile was associated with greater gut microbiome diversity compared with lower IDQ quartile	Higher IDQ score associated with increased relative abundance of <i>Coproccoccus</i> and <i>F. prausnitzii</i> and lower abundance of <i>Sutterella</i>	

NoMIC, Norwegian microflora study; RCT, randomised controlled trial; SPRING, Study of Probiotics IN Gestational diabetes; Ow, overweight; Ob, obese; GDM, gestational diabetes mellitus; N/A, not applicable; V, vegetarian; C, control; DSQ, Dietary Screener Questionnaire; rRNA, ribosomal RNA; IDQ, Index of Dietary Quality; PcoA, principal component analysis; LefSe, linear discriminant analysis effect size; PD, phylogenetic diversity; OTU, operational taxonomic unit; PERMANOVA, permutational multivariate ANOVA; ACE, abundance-based coverage estimator; FDR, false discovery rate; C-section; Caesarean section; TEI, total energy intake.



**Table 2.** ROBINS-I (Risk Of Bias In Non-randomised Studies – of Interventions) risk of bias results

Domain	Chu <i>et al.</i> <sup>(9)</sup>	Mandal <i>et al.</i> <sup>(25)</sup>	Röytiö <i>et al.</i> <sup>(26)</sup>	Lundgren <i>et al.</i> <sup>(27)</sup>	Barrett <i>et al.</i> <sup>(28)</sup>	Gomez-Arango <i>et al.</i> <sup>(29)</sup>	Laitinen <i>et al.</i> <sup>(30)</sup>
Bias due to confounding	Moderate	Serious	Moderate	Serious	Moderate	Moderate	Serious
Bias in selection of participants into the study	Serious	Moderate	Low	Moderate	Moderate	Low	Low
Bias in classification of intervention	Low	Moderate	Low	Serious	Moderate	Low	Low
Bias due to deviations from intended interventions	Low	Low	Low	Low	Low	Low	Low
Bias due to missing data	Low	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Bias in measurement of outcomes	Serious	Low	Low	Serious	Moderate	Low	Moderate
Bias in selection of the reported results	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Overall	Serious	Serious	Moderate	Serious	Moderate	Moderate	Serious

study<sup>(28)</sup> reported a difference in  $\beta$  diversity, although  $\alpha$  diversity did not differ. Furthermore, microbial composition differed by type of fat. Intakes of cholesterol and MUFA were associated with relative increases in Proteobacteria composition<sup>(25)</sup>. In contrast, SFA intake was linked to relative decreases in this phylum and also negatively associated with the genus *Roseburia* ( $\rho = -0.4$ ,  $P = 0.038$ )<sup>(28)</sup>. The study by Barrett *et al.*<sup>(28)</sup> compared the effect of a vegetarian diet *v.* omnivorous diet in early pregnancy on the maternal microbiome composition. Barrett *et al.*<sup>(28)</sup> reported that women on the vegetarian diet had a higher intake of PUFA, of which, linoleic acid positively correlated with *Holdemania* ( $\rho = 0.51$ ,  $P = 0.006$ ) and *Roseburia* ( $\rho = 0.40$ ,  $P = 0.04$ ) abundance, but negatively with *Collinsella* ( $\rho = -0.50$ ,  $P = 0.009$ ).

Four studies reported results on dietary carbohydrate intake and gut microbiome composition<sup>(26,28–30)</sup>. Each of these studies reported that higher dietary fibre intakes were positively associated with increased gut microbiota diversity and richness. Moreover, similar associations between dietary fibre intake and relative abundance of specific bacteria were reported in three of these papers<sup>(28–30)</sup>. Higher fibre intakes were positively associated with increased relative abundances of *Holdemania*, *Roseburia*, *Lachnospira* and *Coproccoccus*. In contrast, dietary fibre intake was negatively associated with relative *Collinsella* (Actinobacteria) and *Sutterella* (Proteobacteria) abundances.

The study by Mandal *et al.*<sup>(25)</sup> reported increased dietary intakes of fat-soluble vitamins, such as vitamin D and retinol are inversely correlated with  $\alpha$  diversity. Vitamin D showed the strongest associations for both measures. For Shannon's diversity, only vitamin D was significantly associated ( $-5.1\%$  change in diversity per unit increase in vitamin D intake,  $P < 0.001$ ). The authors report that associations between dietary components and  $\beta$  diversity did not show any effects (UniFrac (weighted and unweighted; data not shown)). Furthermore, multiple regression modelling was used to assess associations between microbial composition and one standard deviation of nutrient intake for several dietary components. Vitamin D was associated with relative increases in Actinobacteria and Proteobacteria. Retinol was also associated with relative increases in Proteobacteria composition. Conversely, protein and vitamin E correlated with relative decreases in Proteobacteria.

Protein intake was collected and examined by all studies; however, significant findings were not seen<sup>(24–28,31)</sup>.

### Maternal diet and the neonatal gut microbiome

Two studies investigated the effect of maternal diet in pregnancy on the neonatal gut microbiome. Both studies reported that maternal diet in pregnancy is associated with distinct changes in the neonatal gut microbiome.

Chu *et al.*<sup>(24)</sup> identified an association between maternal dietary fat intake and distinct changes in the neonatal gut microbiota, at birth and 4–6 weeks of age. Participants were grouped by extremes of dietary fat intake (1 SD greater or less than the cohort mean), to produce a high-fat maternal diet group ( $n$  13, 43.1 % fat intake) and low-fat group ( $n$  13, 24.4 % fat intake). Significant differences in neonatal microbiome clusters were detected between groups (principal component analysis unweighted UniFrac:  $P = 0.04$ ). There was an inverse association between high-fat maternal diet and relative abundance of *Bacteroides* in neonatal stool at delivery, persisting at 6 weeks, whereas *Enterococcus* abundance was higher in the high-fat group at delivery only.

The study by Lundgren *et al.*<sup>(27)</sup> found that associations between maternal diet and the gut microbiome composition of infant stool samples differed by mode of delivery. Three distinct genera clusters were identified in vaginally born infants (cluster 1: *Bifidobacterium*; cluster 2: *Streptococcus* and *Clostridium* and cluster 3: *Bacteroides*). Through multinomial logistic regression, the odds of falling within cluster 2 were 2.73 times higher with each additional fruit serving per d. Furthermore, maternal fruit intake was negatively associated with the *Bifidobacterium* group. The clusters differed in infants delivered by Caesarean section (cluster 1: *Bifidobacterium*; cluster 2: high *Clostridium*, low *Streptococcus* and low *Ruminococcus*; cluster 3: high Enterobacteriaceae, *Ruminococcus* and Lachnospiraceae). In this sub-group, the analysis found a 2.36 increase in odds of being in a high *Clostridium*-low *Streptococcus* cluster with every increase of dairy portion. Maternal fish intake was positively associated with the *Streptococcus* genus in both groups of infants. In addition, red meat consumption was positively associated with the *Bifidobacterium* genus for the Caesarean section group. Likewise, the association between maternal alternative Mediterranean diet score differed slightly by mode of delivery, with positive associations existing with the Enterobacteriaceae family and the genus *Streptococcus* in the vaginally born group. In the Caesarean section group, a negative association was observed. Taking premature infants out of the analysis did not change results.

## Discussion

### Main findings in this study

Pregnancy is a unique time point during which improvement to the health of the woman can also benefit the immediate and long-term health of the child. Manipulating the gut microbiome during pregnancy may be beneficial to the health of both mother and baby<sup>(21)</sup>. Indeed, each of the studies included in this review demonstrates the important influence of maternal diet in pregnancy in modulating the gut microbiome of mother and infant, both beneficially and detrimentally. They provide evidence that diet quality, determined by factors including amount of fibre, fat, fat-soluble vitamins, fruit and vegetables, and fish and meat consumed, is associated with distinct gut microbiota profiles and diversity of the gut microbiota. Interestingly, the findings from Lundgren *et al.*<sup>(27)</sup> demonstrate that the influence of maternal diet on gut microbiota profiles differ by delivery mode.

The findings from this review align with those of the prevailing literature. Recent studies have shown the influence of diet and the gut–brain axis in the prenatal period, with the gut microbiome potentially playing a role in neurodevelopment<sup>(32)</sup>. In addition, diet has been shown to change the composition and metabolism of gut microbes<sup>(33)</sup>. Fibre and to a lesser degree fat have been identified as important modulators of the human gut microbiome<sup>(6,11)</sup>. It is estimated that approximately 20–60 g of undigested carbohydrate reaches the large intestine (the area with the highest density of gut microbes) daily<sup>(34)</sup>. This is larger than the amount of fat and protein that reach the colon, which are both readily digested in the upper gastrointestinal tract<sup>(10)</sup>, and thus are more likely to impact on the small intestinal microbiota. In high-fat diets (>35 % of total energy intake), a greater proportion of fat will reach the colon and it is hypothesised that this causes reduction of bacteria usually used for carbohydrate degradation, causing a shift in the microbiome as a whole<sup>(35)</sup>. In contrast, high-fibre diets (>25 g/d<sup>(36)</sup>) are associated with greater relative abundances of SCFA-producing bacteria (such as *Holdemania* and *Roseburia*) and relative depletion of lactate producers (such as *Collinsella*), with the former considered directly associated with beneficial metabolic profiles<sup>(37)</sup>.

In addition, probiotics have emerged as another promising means by which to manipulate the maternal gut microbiota with a view to improve health and clinical outcomes<sup>(11)</sup>. However, the research behind their use in pregnancy has not shown clear reduction of adverse outcomes such as preterm birth or secondary outcomes such as gestational diabetes or reduction in glucose level<sup>(38,39)</sup>. Jarde *et al.*<sup>(39)</sup> conducted a systematic review with nineteen studies which found no definitive link between probiotic supplementation and improved clinical sequelae. Likewise, Lindsay *et al.*<sup>(38)</sup> examined the effect of probiotic supplementation on several important clinical outcomes including birth weight and fasting glucose, with no reported difference in those parameters. Further clarity is required regarding the clinical benefits of probiotic supplementation use during pregnancy. Hence, dietary manipulation of the maternal (and neonatal) gut microbiota may offer more readily available opportunities in the immediate term for improving the health of mother and child.

Environmental determinants have been demonstrated as important mediators of the human gut microbiota, including the shared home environment. Factors such as having other children at home, or having furry pet animals, have been shown to directly influence the composition of the maternal and neonatal gut microbiota<sup>(6,40)</sup>. None of the studies in this review explored these variables.

Significant heterogeneity pervades multiple domains of the studies included in this review. Consequently, the findings of this review should be interpreted with caution and considered in the context of the wider literature. Four of the five studies focusing on maternal gut outcomes studied a cohort of women with overweight and obesity. Although this could be considered a representative sample in the context of rising overweight and obesity rates, a comprehensive well-designed study examining normal-weight and overweight/obese women in pregnancy, nutrients and the microbiome must be conducted first for comparison. BMI was self-reported by participants in the study by Lundgren *et al.*<sup>(27)</sup>. It has been shown that self-reported BMI underestimates actual BMI in pregnancy<sup>(41)</sup>.

In addition, the method of dietary assessment varied considerably across the studies. Five studies assess diet by FFQ, one by 3-d food diaries, and one by Index of Diet Quality. Roytio *et al.*<sup>(26)</sup> used 3-d food diaries as well as providing participants with oral and written instruction and a portion picture booklet. This would allow for a more accurate correlation between diet and the microbiome. Of the five studies that employed FFQ, there were differences in the period of time assessed (from 4 to 16 weeks) and the time point in pregnancy it was administered (two in first trimester, two in second trimester and one in third). As pregnancy progresses, diet may vary considerably due to increased early satiety, reflux and constipation. There is also potential for misclassification of food groups using FFQ. In the Willett FFQ used in Lundgren *et al.*<sup>(27)</sup>, fruit and fruit juices are both in the fruit food group. Fruit juices contain high amounts of free sugar and lower amounts of fibre, and therefore the effect on the gut microbiota could be considerably different<sup>(42)</sup>. Likewise, differences in the temperature at which collected stool samples were stored and the time point at which they were collected across the studies could influence the comparability of the results.

A major strength of this systematic review is the techniques used in the search strategy and the analysis of bias. The PRISMA guidelines recommended by the Cochrane Group were used<sup>(23)</sup>.

Another strength of this review is that all seven studies used culture-independent analytical techniques. The use of culture-specific sampling technique is now seen as a major risk of bias in the microbiological research. The benefit of culture-independent analytical techniques is that all microbial species present in the microbiome can be identified and therefore analysed<sup>(1)</sup>.

### Future directions of studies

The examination of detailed dietary data in pregnancy and its influence on the microbiome must be conducted in detail in a cohort representative of a normal obstetric population. Without this, findings from subgroups are difficult to interpret. Dietary

analysis should be conducted in a systematic manner. Food diaries most accurately capture intake within the last week and therefore may be most appropriate compared with FFQ that capture intake in the last few months. With this said, there is emerging evidence to suggest that long-term food patterns have a stronger role in the metabolism and composition of the human gut microbiome than short-term dietary changes<sup>(16)</sup>. Therefore, perhaps both FFQ and food diaries methodologies should be used for each analysis.

## Conclusion

In summary, this review demonstrates the important influence of maternal diet in pregnancy in modulating the gut microbiome of mother and infant, both beneficially and detrimentally. The findings provide evidence that diet quality, determined by factors including amount of fibre, fat, fat-soluble vitamins, fruit and vegetables, and fish and meat consumed, is associated with distinct gut microbiota profiles and diversity of the gut microbiota. However, confidence in the quality of this evidence is limited due to methodological limitations within the studies, and variability between studies. Pregnancy is a unique time point during which benefits to the health of the mother can also benefit that of the child. Hence, further high-quality research is required in this area to elucidate the relationship between diet quality and the gut microbiota of mother and child.

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