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

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List of Abbreviations:

BMI: Body Mass Index

FFQ: Food Frequency Questionnaire

IDQ: Index of Diet Quality

GDM: Gestational Diabetes Mellitus

PCoA: Principal Component Analysis

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

ROBINS-1: Risk Of Bias In Non-randomised Studies - of Interventions

SCFA: Short Chain Fatty Acids

OTU: Operational Taxonomic Unit

LefSe: Linear Discriminant Analysis Effect Size

PD: Phylogenetic Diversity

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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 rRNA 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/day) and fibre (g/day) 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.

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Introduction

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 microorganisms in the gastrointestinal tract [1]. Links between the microbiome and many physiological conditions of the associated host have been made [2; 3; 4]. 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 [5; 6].

Diet and dietary patterns have been shown to rapidly alter microbial diversity and in turn influence host physiology [7; 8]. 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 [9; 10; 11].

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 a Western diet to influence the gut microbiome more considerably than BMI [8; 12]. Diets high in fibre have been shown to have the ability to increase the relevant abundance of SCFA-producing bacteria [13]. This is in contrast to diets rich in animal fats, high in saturated fat and protein, which have been shown to have a negative impact [14]. 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 [15]. Furthermore, diets such as the Western diet are associated with decreased microbial diversity [12; 16].

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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 [17; 18]. 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 [19].

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 co-ordinate point and measuring the distance (using various metrics e.g., Bray-Curtis, un-weighted 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 to that of the third trimester [20]. 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[21]. Likewise, the presence of furry pets in the home has been shown to influence the composition of the gut microbiota of newborns[22].

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

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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

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement for reporting on systematic review was followed[23]. Search checklist of items to include, methods, strategy, study selection process, a risk of bias tool and summary measures were 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 post-partum. 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 were book chapters, online abstracts and conference proceedings were not included. Articles had to be published in English and no time restrictions was imposed

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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 PCoA which measure diversity between microbial communities.

Information Sources:

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

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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; 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 it's fitting of the defined PICO terms. Abstracts were reviewed independently by two researchers (S.M and E.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.M and E.O.B) and both parties selected final papers. Disagreements were resolved by a third party (F.McA). A flow chart created based on the PRISMA guidelines can be seen below (Figure 1).

< Figure 1: Flow diagram of study selection >

Study characteristics

The study characteristics are described in Table 2.

Risk of bias in individual studies

The seven studies were assessed for risk of bias using the 2016 ROBINS-1 ("Risk Of Bias In Non-randomised Studies - of Interventions") assessment tool[24]. The ROBINS-1 consists of an assessment and a scoring algorithm

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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.M, E.O.B, and DB) independently assessed 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 1 domain, with three studies at moderate risk of bias (Table 1). No study was judged to be at a critical risk of bias in any domain. Therefore, the seven studies were included in this review [25; 26; 27; 28; 29; 30; 31].

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 [26; 27; 29]. Two of these studies reported a negative correlation between alpha diversity and intakes of cholesterol[26], total fat and saturated fatty acid[27] (SFA). The third study[29] reported a difference in beta diversity, although alpha diversity did not differ. Furthermore, microbial composition differed by type of fat. Intakes of cholesterol and

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monounsaturated fatty acids (MUFA) were associated with relative increases in Proteobacteria composition[26]. 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)[29]. The study by Barrett et al compared the effect of a vegetarian diet vs omnivorous diet in early pregnancy on the maternal microbiome composition. Barrett et al reported that women on the vegetarian diet had a higher intake of polyunsaturated fatty acids (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 [27; 29; 30; 31]. 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 3 of these papers [29; 30; 31]. Higher fibre intakes were positively associated with increased relative abundances of Holdemania, Roseburia, and Lachnospira and Coprococcus. In contrast, dietary fibre intake was negatively associated with relative Collinsella (Actinobacteria) and Sutteralla (Proteobacteria) abundances.

The study by Mandal et al, 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

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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 [24-29].

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 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 (one 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 (PcoA unweighted UniFrac: p=0.04). There was an inverse

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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. 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 day. Furthermore, maternal fruit intake was negatively associated with the Bifidobacterium group. The clusters differed in infants delivered by c-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 for the c-section group. Likewise, the association between Maternal alternative Mediterranean diet (aMED) score differed slightly by mode of delivery, with positive associations existing with Enterobacteriaceae family and the genus Streptococcus in the vaginally-born group. In the c-section group a negative association was observed. Taking pre-mature infants out of the analysis did not change results.

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<Table 1>

<Table 2>

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[21]. Indeed, each of the studies included in this review demonstrate 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 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[32] In addition, diet has been shown to change the composition and metabolism of gut microbes[33]. Fibre and to a lesser degree fat have been identified as important modulators of the human gut microbiome [6; 11]. It is estimated that approximately 20-60g of undigested carbohydrate

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reaches the large intestine (the area with the highest density of gut microbes) daily [34]. This is larger than the amount of fat and protein that reach the colon, which are both readily digested in the upper GI tract [10], 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 [35]. In contrast, high fibre diets (>25g per day[36]) 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[37].

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[11]. 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[38; 39]. Jarde et al. conducted a systematic review with 19 studies which found no definitive link between probiotic supplementation and improved clinical sequela. Likewise, Lindsay et al. examined the effect of probiotic supplementation on several important clinical outcomes including birthweight 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

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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[6; 40]. 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. It has been shown that self-reported BMI underestimates actual BMI in pregnancy[41].

In addition, the method of dietary assessment varied considerably across the studies. Five studies assess diet by FFQ, one by three-day food diaries, and one by IDQ. Roytio *et al.* used three-day 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.

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Of the five studies that employed FFQs, there were differences in the period of time assessed (from four to 16 weeks), and the time-point in pregnancy it was administered (two in first trimester, two in second trimester, 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 FFQs. In the Willets FFQ used in Lundgren et al, 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[42]. 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 [23].

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[1].

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

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obstetric population. Without this, findings from subgroups are difficult to interpret. Dietary analysis should be conducted in a systematic manor. Food diaries most accurately capture intake within the last week and therefore may be most appropriate compared with food-frequency questionnaires 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[16]. 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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Conflicts of Interest

Contents are the authors' own view. EFM is Technical Director at Alimentary Health Group. The authors have no other disclosures to declare.

Authors' Contributions

RS, EFM, DVS, PDC, and FMM designed research; SM, AG, RM, EOB, and DB conducted research; SM, EOB and DB analysed data; SM, EOB and DB wrote the paper; FMM had primary responsibility for final content. All authors read and approved the final manuscript.

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Table 1: ROBINS-I risk of bias results

Domain	**Chu et al., [9]**	**Mandal et al., [26]**	**Röytiö et al., [27]**	**Lundgren et al., [28]**	**Barrett et al., [29]**	**Gomez-Arango et al., [30]**	**Laitinen et al., [31]**
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**

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Table 2: Summary of results

Author	Year of publication	Title	n=	Study cohort	Country
Chu et al[25]	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 et al[26]	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 et al[27]	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 et al[28]	2018	Maternal diet during pregnancy is related with the infant stool microbiome in a delivery-mode dependent manner	145	Participants gathered from New Hampshire Birth Cohort Study	USA
Barrett et al[29]	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

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Gomez-Arango et al[30]	2018	Low dietary fiber intake increases Collinsella 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 et al[31]	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	**Mean pre-pregnancy BMI**	**Pre-term birth rate**	**Smoking status**	**Gestational Age at time-point**	**Third level education (%)**	**GDM rate**
Chu et al	30.0 ± 5.9	27.8 ± 5.9	11.5%	Not reported	Third trimester	Not reported	30%
Mandal et al	Not reported	22.9 ± 3.5	35%	15%	Second trimester 22 weeks Stool collected day 4 post-partum	46%	N/A
Röytiö et al	30.1 ± 4.7	30.2 ± 4.6 overweight / obesity	Not reported	Not reported	First trimester 13.3 weeks	50%	N/A
Lundgren et al	31.9	25.6	Not reported	4.8%	24-28 weeks	70%	11%
Barrett et al	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	Ow: 32 (29-34)	Ow: 27.9 (27-29.1)	Not reported	Not reported	First trimester	Not reported	0

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et al	Ob: 30.5 (28-34)	Ob: 34.3 (31.8-41.3) overweight / obesity			16 weeks		
Laitinen et al	30.1 ± 4.7	30.3 ± 4.6 overweight / obesity	Not reported	Not reported	First trimester 13.3 weeks	50%	N/A
Data Collection							
	Dietary Data			**Microbiome Data**			
Chu et al	Dietary Screener Questionnaire (DSQ): Captured dietary habits over past month			Infant Stool 16S rRNA sequencing on samples collected at delivery and 6 weeks post-partum			
Mandal et al	Food Frequency Questionnaire			Maternal Stool 16S rRNA sequencing on samples collected at day 4 post-partum			
Röytiö et al	3-Day Food Diary: Recorded the week before study visit			Maternal Stool 16S rRNA sequencing on samples collected at < 18 weeks gestation			
Lundgren et al	Food Frequency Questionnaire: Alternative Mediterranean Score calculated			Infant Stool 16S rRNA sequencing on samples collect at 6 weeks post-partum			
Barrett et al	Food Frequency Questionnaire: Captured dietary information from start of pregnancy			Maternal Stool 16S rRNA sequencing on samples collected at < 16 weeks gestation			
Gomez-Arango et al	Food Frequency Questionnaire: Captured dietary information from start of pregnancy			Maternal Stool 16S rRNA sequencing on samples collected at < 16 weeks gestation			
Laitinen et al	Index of Dietary Quality			Maternal Stool 16S rRNA sequencing on samples collected at < 18 weeks gestation			
Analysis Performed							

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	Measures used	Correction for multiple testing	Effect of correction factor
Chu et al	PcoA unweighted UniFrac distances, LefSe	None used	n/a
Mandal et al	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 et al	Shannon, observed OTUs, 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 et al	PERMANOVA, PcoA generalized UniFrac distances	Benjamini-Hochberg correction	Associations remained significant
Barrett et al	Chao 1, Shannon, ACE, Simpson Bray-Curtis dissimilarity, Canonical correspondence, PERMANOVA, LefSe	None used	n/a
Gomez-Arango et al	Chao 1, Shannon PcoA, LefSe, Bray-Curtis dissimilarity	None used	n/a
Laitinen et al	Chao 1, observed OTUs, 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 et al	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 Bacteroides

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Mandal et al	Vitamin D, retinol and cholesterol negatively associated with maternal gut diversity	Vitamin D, retinol and cholesterol associated with relative increased abundance of Proteobacteria. Inverse relationship was observed with Vitamin E, and Protein intake
Röytiö et al	Adherence to recommended reference intakes of dietary fibre and fat associated with increased maternal gut diversity	High-Fibre/Low-Fat intake associated with lower relative abundance of Bacteroidaceae.
Lundgren et al	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) Bifidobacterium 2) Streptococcus and Clostridium 3) Bacteroides C-section born microbiome clusters: A) Bifidobacterium B) High Clostridium, Low Streptococcus, Low Ruminococcus C) Enterobacteriaceae family
Barrett et al	Vegetarian diet did not influence alpha diversity compared with omnivorous diet	Vegetarian diet associated with increased relative abundance of Roseburia and Lachnospiraceae and decreased relative abundance of Collinsella.
Gomez-Arango et al	When corrected for Total Energy Intake, beta diversity differed by dietary fibre intake	After adjustment for TEI, high dietary fibre was associated with increase relative abundance of Holdemania, Coproccocus, Roseburia and others of similar phyla. Low dietary fibre was associated with Collinsella, Suterella, Bilophila and others.
Laitinen et al	Highest IDQ quartile was associated with greater gut microbiome diversity compared to lower IDQ quartile	Higher IDQ score associated with increased relative abundance of Coproccocus and F. prausnitzii and lower abundance of Sutterella
RCT – randomised controlled trial; V – vegetarian; C – control; Ow – overweight; Ob – obese; PcoA – principal component analysis; LefSe – linear discriminant analysis effect size; PD – phylogenetic diversity; PERMANOVA - Permutational multivariate analysis of variance; FDR – false discovery rate		

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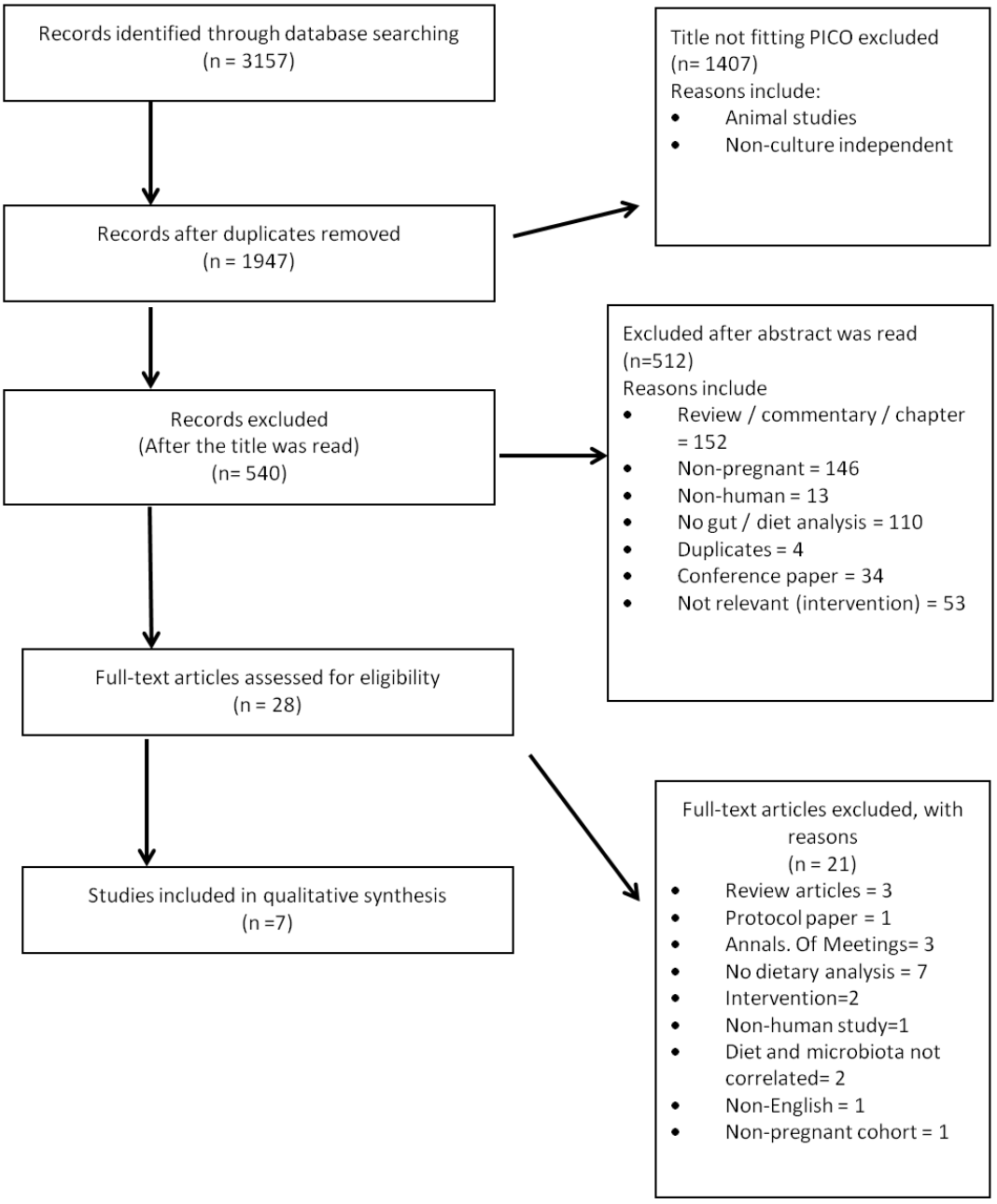
Figure Legend Figure 1: Flow diagram of study selection



Flow diagram depicting each stage of the study identification process

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