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MINI REVIEW

Modulation of gut microbiota by diet and probiotics: potential approaches to prevent gestational diabetes mellitus

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Abstract
Gestational diabetes mellitus (GDM) is a rising global health problem that affects approximately 6% of pregnant women. Lifestyle interventions, particularly diet, and exercise are the first-line treatment, followed by pharmacotherapy, but with associated side effects to both mother and offspring. Modulation of gut microbiota may help prevent or manage GDM. Some gut bacterial groups associated with GDM are also associated with inflammatory biomarkers and gut dysbiosis. Available literature reports that low-glycaemic index diet reduces maternal fasting and 2-hour postprandial glucose and maintains a beneficial gut bacterial composition. Pre- and probiotics can aid GDM therapy by modulating gut microbiota to eubiotic status and improving glucose metabolism. Probiotics as adjuvant GDM therapy should consider bacterial strains, dosage, and treatment duration. Limitations in their use require further studies to develop specific probiotic-based GDM supplement therapy that impacts glycaemic control and inflammatory status by reducing fasting plasma glucose, insulin resistance, and improving lipid profiles of pregnant women.

Keywords: gut microbiota; pregnancy; probiotics; diet; gestational diabetes mellitus

Introduction

Gestational diabetes mellitus (GDM), defined as glucose intolerance that results in hyperglycaemia with first recognition during pregnancy (Eades et al., 2017; Hasain et al., 2020), is an increasing public health concern with a rising prevalence of 5.4% in European and 7.6% in North American pregnant women (Casagrande et al., 2018). GDM impacts maternal-foetal health causing both short- and long-term adverse effects, including higher risk of preeclampsia and caesarean delivery for mothers; and macrosomia, preterm birth, respiratory distress, and shoulder dystocia for foetuses (Metzger et al., 2008; Schneider et al., 2011; Wendland et al., 2012; Kc et al., 2015; Billionnet et al., 2017). More than half of pregnant women who develop GDM have at least one risk factor: >25 years old, body mass index (BMI) > 30 kg/m^2, history of impaired glucose tolerance, previous pregnancies with GDM or macrosomia, multiple pregnancies, family history of type 2 diabetes, among others (Lefkovits et al., 2019). GDM diagnosis is made in the first trimester if a fasting glucose test returns a plasma glucose value ≥92 and <126 mg/dL or if returning a normal value, through an oral glucose tolerance test (OGTT) made at 24–28 weeks of gestation if a fasting plasma glucose value ≥92 mg/dL or ≥180 mg/dL at one hour or ≥153

mg/dL at 2 hours (Wendland et al., 2012). Appropriate management of hyperglycaemia combined with lifestyle interventions, diet, and exercise prevents maternal obesity and GDM (Koivusalo et al., 2016; Wang et al., 2017). Other approaches are also available when diet and exercise alone are insufficient to control blood glucose levels, including pharmacological (insulin and/or oral hypoglycaemic agents, such as metformin) and non-pharmacological therapies (probiotics; Simmons, 2015). Pharmacotherapy has benefits for glucose control, especially insulin since it is unable to cross the placental barrier. However, this approach may result in side effects, including hypertensive disorders, when using insulin (Brown et al., 2017) and diarrhoea, abdominal pain, and headache, when using metformin (Dodd et al., 2018). Probiotics are defined as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" (Food and Agricultural Organization [FAO] of the United Nations and World Health Organization [WHO], 2001] and thus may be part of a non-pharmacological therapy. Gut microbiota, the group of living microorganisms colonising the gastrointestinal tract, is linked to human metabolism regulation. Alterations in gut microbiota composition are associated with metabolic diseases such as obesity, type 2 diabetes, and metabolic syndrome (Pascale et al., 2018) and can play an essential role in modulating insulin resistance (IR) and inflammatory response in GDM (Kuang et al., 2017). Diet and probiotics can affect gut microbiota composition (Wen and Duffy, 2017; Ponzo et al., 2019,b) and therefore can be a potential associative therapy for GDM if applied simultaneously.

The aim of this literature review was to compare the results of studies reporting the efficacy of both approaches (probiotics and diet) to prevent and manage GDM during pregnancy and to clarify if they could be potential therapeutic adjuvants for GDM treatment.

Current status of knowledge

The role of human gut microbiota in homeostasis

The human gastrointestinal tract is colonised by a collection of approximately 100 trillion microorganisms (Lozupone et al., 2012), whose composition is determined by host genetics, diet, immune responses, and the environment (Lynch and Pedersen, 2016). The development of our gut microbiota begins immediately at birth, being initially undifferentiated and progressively shaped by three major factors – type of delivery, breastfeeding, and weaning (Nicholson et al., 2012). In adult life, the gut microbiota has similar patterns between individuals at higher phylogenetic levels, being mainly composed of five bacteria phyla – *Bacteroidetes*, *Firmicutes*, *Proteobacteria*, *Actinobacteria*, and *Verrucomicrobia* (Tremaroli and Bäckhed, 2012). *Firmicutes* and *Bacteroidetes* are the most prevalent, representing more than 90% of the overall intestinal microbiota (Shen et al., 2013). At a genus level, some of the most frequently found bacteria are *Bifidobacterium*, *Lactobacillus*, *Bacteroides*, *Clostridium*, *Escherichia*, *Streptococcus*, and *Ruminococcus* (Conlon and Bird, 2015). At a species level, the variability is much higher, with healthy individuals having highly diverse gut microbiota (Flint et al., 2015). This complex micro-ecosystem holds a synbiotic relationship between each other (the microbes) and the host, who provides them a balanced environment to live while microbes provide the host with several benefits through a variety of functions such as modulating the intestinal barrier (Natividad and Verdu, 2013), producing bioactive compounds like short-chain fatty acids (SCFA; Topping and Clifton, 2001), maintaining host immune system (Gensollen et al., 2016), and protecting the host against ingested pathogens (Bäumler and Sperandio, 2016). Alterations in the intestinal microbiota and its metabolic pathways, termed dysbiosis (major changes in the resident microbial community with impairments for the host; Clemente et al., 2012), may contribute to the development of several chronic diseases, such as inflammatory bowel disease, multiple sclerosis, arthritis, and allergic inflammation (Kamada et al., 2013). Hence, it is important to maintain the balance of our gut microbiota composition to ensure homeostasis. Gut microbial fermentation of non-digestible foods (dietary fibres and resistant starches) maintains bowel health (Canfora et al., 2015) and leads to the production of SCFA, mainly butyrate, acetate, and propionate, via diverse biochemical pathways (Topping and Clifton, 2001). These metabolites can be used as energy sources by colonic epithelial cells or absorbed into the bloodstream (den

Besten et al., 2013). In the colon lumen, acetate, and propionate, mainly produced by *Bacteroidetes* (LeBlanc et al., 2017), release peptide YY (PPY) and glucagon-like peptide (GLP-1), which influence satiety and bowel transit; whereas butyrate, mainly produced by Firmicutes (LeBlanc et al., 2017), inhibits histone deacetylases (HDACs) and a specific G protein-coupled receptor (GPR109A), conferring anti-inflammatory effects (Koh et al., 2016), apart from modulating the expression of tight junction protein and mucins (Canfora et al., 2015). Additionally, SCFA also plays an important role in blood glucose level regulation and glucose homeostasis by inhibiting glycolysis and stimulating lipogenesis or gluconeogenesis, along with managing excessive production of cholesterol and conferring anti-carcinogenic action (Pascale et al., 2018). Further studies are needed to understand the impact of the different compounds produced by gut microbiome in the metabolism of both mother and offspring, and elucidate which microorganisms are responsible for these changes.

Modification of gut microbiota during pregnancy

Pregnancy imposes a great number of physiological adaptations. Currently, there is no specific definition of healthy gut microbiota; however, it is known that its composition is highly diverse in healthy individuals (Meijnikman et al., 2018). Studies that explored the gut microbiota composition of healthy pregnant women found some important changes associated with an increase in maternal body weight by fat deposition and new dietary habits that culminate in a progressive increase in the food intake, essential for the foetus growth (di Simone et al., 2020). Physiological changes are also part of a normal pregnancy, with maternal tissues becoming increasingly resistant to insulin in approximately 50–60% of women with normal glucose tolerance or with GDM (Kampmann et al., 2019). In addition to weight gain and adiposity, pregnant women have significantly higher leptin, insulin and IR, cholesterol, and glycated haemoglobin levels as compared with nonpregnant women (Collado et al., 2008). In the pregnancy first trimester, the gut microbiota is expected to be similar to that of a healthy nonpregnant woman, classified into different enterotypes, considering three different groups of bacteria: one enterotype characterised by the presence of *Bacteroides*; another enterotype by higher proportion of *Prevotella*; and a third enterotype dominated by *Ruminococcus* (di Simone et al., 2020). Between the first and the third trimester, gut microbiota changes substantially decreasing its diversity, with increased proportions of *Proteobacteria*, commonly associated with inflammation, while the number of butyrate-producing bacteria with anti-inflammatory effects decreases (Koren et al., 2012).

Studies comparing the intestinal microbiota between healthy-weight pregnant women and overweight and/or obese pregnant women were also considered. Gomez-Arango et al. (2016) presented that the ratio between phyla *Firmicutes* and *Bacteroidetes* was approximately 3:1 when analysing stool samples of both overweight and obese pregnant women, showing a slightly higher abundance of *Firmicutes* for obese women (Gomez-Arango et al., 2016). The higher presence of this phyla was linked by other authors with higher expression of enzymes engaged in the digestion of polysaccharide where more income of energy can be obtained from the same diet (Cani, 2013). Some correlations between specific taxa and pregnancy variables were observed. *Lachnospiraceae* and *Ruminococcaceae* families (both from *Firmicutes* phyla) were strongly correlated with leptin and positively associated with BMI. *Bacteroidaceae* relates with ghrelin that, in turn, was negatively associated with BMI, and positively correlated with *Rikenellaceae* (both from *Bacteroidetes phyla*). *Collinsella* positively correlated with insulin levels and triglycerides while *Coprococcus* (butyrate producer) correlated with gastric-inhibitory polypeptide (GIP), an incretin hormone (Gomez-Arango et al., 2016). When gestational weight gain (GWG) is excessive, pregnant women have an increased risk of developing GDM, obesity, metabolic syndrome (Carreno et al., 2012; Gilmore et al., 2015) and delivering a baby larger-for-gestational age (Carreno et al., 2012; Ferraro et al., 2012; Kim et al., 2014). In this situation, gut microbiota is associated with lower α-diversity (DiGiulio et al., 2015), and the presence of *Eisenbergiella, Lactobacillus* (Crusell et al., 2018), *Blautia*, *Ruminoccocus,* and *Feacalibacterium* (Stanislawski et al., 2017) genus and *Escherichia coli* (Santacruz et al., 2010) species. On the other hand,

Bifidobacterium and *Akkermansia muciniphila* (Collado et al., 2008; Santacruz et al., 2010), along with *Christensenella* and *Alistipes* (Crusell et al., 2018), are associated with the opposite trend. Additionally, overweight and obese pregnant women were reported to have higher levels of *Bacteroides* (Collado et al., 2008), *Staphylococcus* (Collado et al., 2008; Santacruz et al., 2010) as well as Enterobacteriaceae and *E. coli* (Santacruz et al., 2010).

Gut microbiota modifications during GDM pregnancy

Gut microbiota is involved in human metabolism regulation but can also contribute to the pathogenesis of many diseases, including GDM (Chwalba and Otto-Buczkowska, 2017; Ponzo et al., 2019a,b). During gestation, adjustments in the women's glucose metabolism occur to ensure proper glucose levels to warrant foetal growth and development combined with appropriate maternal nutrition (Angueira et al., 2015). In early gestation, fasting blood glucose (FBG) levels decrease, possibly due to dilution effects (caused by an increased plasma volume), increased glucose uptake by the placenta (Lain and Catalano, 2007; Angueira et al., 2015), and inadequate hepatic glucose production (Lain and Catalano, 2007). These levels remain constant in the second trimester and increase during the last trimester (Angueira et al., 2015). In a regular pregnancy's last trimester, maternal insulin sensitivity declines, which is considered to be advantageous to support foetal development with increased energy requirements at this stage (Koren et al., 2012). In a severe GDM pregnancy, insulin decreases an additional 40% (relatively to a healthy gestation), leading to glucose intolerance (Lain and Catalano, 2007). To balance these alterations, and due to a decreased capacity of insulin to suppress lipolysis, an increase in free fatty acids, hepatic gluconeogenesis, and severe IR occurs (Taddei et al., 2018).

In recent years, more information on the correlation between GDM and gut microbiota has become available, demonstrating a distinct microbiota profile associated with this pathology (Kuang et al., 2017; Mokkala et al., 2017; Crusell et al., 2018; Ferrocino et al., 2018; Hasan et al., 2018; Cortez et al., 2019; Liu et al., 2015; Ye et al., 2019; Ma et al., 2020; Zheng et al., 2020). At a genus level, increased abundance of *Klebsiella* (Kuang et al., 2017), *Collinsella* (Collado et al., 2008; Santacruz et al., 2010; Carreno et al., 2012; Koren et al., 2012; Jost et al., 2014; Kim et al., 2014; Priyadarshini et al., 2014; DiGiulio et al., 2015; Gomez-Arango et al., 2016; Stanislawski et al., 2017; Aatsinki et al., 2018; Crusell et al., 2018; Ferrocino et al., 2018; Meijnikman et al., 2018; Smid et al., 2018; Crusell et al., 2018), *Rothia* (Angueira et al., 2015; Chwalba and Otto-Buczkowska, 2017; Mokkala et al., 2017; Crusell et al., 2018; Taddei et al., 2018; Liu et al., 2015; Ponzo et al., 2019a,b; Zheng et al., 2020), *Eubacterium* (Kuang et al., 2017), *Ruminococcus* (Cortez et al., 2019), *Blautia* (Crusell et al., 2018; Ye et al., 2019; Zheng et al., 2020), *Prevotella* (Cortez et al., 2019; Zheng et al., 2020), *Parabacteroides* (Kuang et al., 2017; Dong et al., 2020), *Eisenbergiella* and *Tyzzerella* (Ma et al., 2020), and a reduced richness in *Akkermansia* (Cortez et al., 2019), *Marvinbryantia*, *Acetivibrio*, *Anaerosporobacter* (Jost et al., 2014), and *Roseburia* (Kuang et al., 2017; Cortez et al., 2019) were described in patients with GDM compared with normoglycemic women (Figure 1). Mokkala et al. (2017) reported changes in the gut microbiota before GDM diagnosis, indicating that higher abundance of Ruminococcaceae in the intestine, a family of bacteria important for starch digestion in the large intestine and production of SCFAs (Oriá et al., 2020), may be associated with an increased probability to develop GDM (Mokkala et al., 2017).

There is evidence suggesting associations between some bacterial taxa and GDM indicators. *Desulfovibrio*, reported as a GDM biomarker (Crusell et al., 2018), is also a known lipopolysaccharide (LPS) producer, which is one of the strongest inducers of inflammation (Cani et al., 2012), associated with IR (Kim et al., 2018) and leading to intestinal barrier damage (Sanchez-Alcoholado et al., 2017; Zhang et al., 2018a). *Collinsella* has been related to higher scores in the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) scale and insulin levels (Ferrocino et al., 2018). *Blautia* was associated with glucose intolerance (Egshatyan et al., 2016) and unfavourable metabolic profile in high BMI patients (Crusell et al., 2018; Ye et al., 2019). *Prevotella* was positively associated with increased LPS and gut inflammation mediated by pro-inflammatory cytokines (Alves et al., 2019).

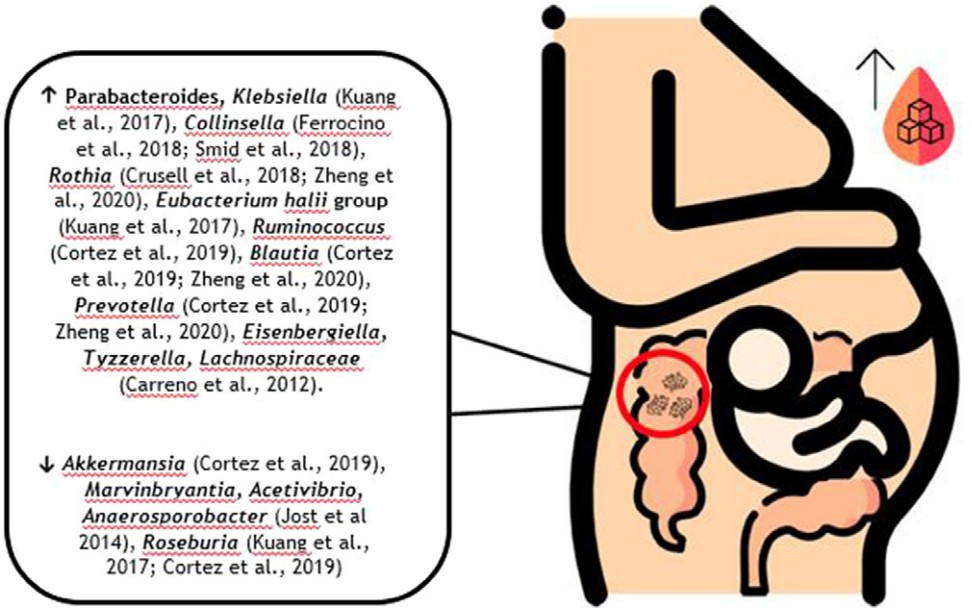

Figure 1. Possible composition of the gut microbiota in pregnant women with GDM according to the available literature.

Although such associations have been established, subjacent mechanisms concerning host and microbiota interactions remain unidentified (Angueira et al., 2015). Also, there are some controversial results since *Megasphera* and *Eggerthella* were reported to be enriched in normoglycaemic controls in some studies (Stanislawski et al., 2017; Wen and Duffy, 2017) while in others both genera were described to be enriched in the GDM group (Zheng et al., 2020). Additionally, at a phylum level, *Actinobacteria* was found simultaneously to be increased (Crusell et al., 2018) and decreased in GDM cohorts (DiGiulio et al., 2015; Cortez et al., 2019).

In an attempt to outline available information in a more visual format, Figure 1 presents the possible composition of a pregnant woman with GDM gut microbiota, mainly at the genus level, separating those currently described to be increased from those currently described as being decreased in these patients.

Finally, GDM mother's offspring gut microbiota have differences in α-richness compared with neonates of mothers without GDM, with a higher abundance of *Actinobacteria*, associated with higher levels of fasting glucose, and reduction in *Bacteroides* abundance. At a genus level, an increase of opportunistic pathogens, such as *Escherichia* and *Parabacteroides*, and a decrease in probiotic *Lactobacillus* were observed in GDM mother's offspring (Su et al., 2018; Ponzo et al., 2019b). Therefore, the influence of the mother's gut microbiota composition, blood glucose, BMI, and dietary intake on the gut microbiota of their offspring needs to be further investigated.

Interactions between diet and gut microbiota during pregnancy

The microbial community living in the gut highly depends on the host's diet, one of the most significant contributors to the modulation of intestinal microbiota and human health (Hasan and Yang, 2019). Among nutrients, the effects of complex carbohydrates (CHO) are the best studied, having an important impact on microbiota composition (Gentile and Weir, 2018). It has been reported that diets rich in CHO can modify the gut microbial composition in only a few days or weeks, because in the large intestine there is an intensive fermentative activity of resistant starch and fibres, creating a set of metabolites produced by bacteria – the human metabolome – that can be detected in the host faeces, urine, and blood that can pass the intestinal barrier (Flint et al., 2015). Dietary fibre is the energy

source for commensal SCFA-producing bacteria and its fermentation has the potential to decrease postprandial blood glucose, insulin responses and, decrease cholesterol absorption. Dietary patterns marked by low-fibre intake inhibit the growth of SCFA-producing bacteria and enable the development of other bacterial strains that use glycoproteins as energy, leading to harmful effects on the gut barrier (Gomez-Arango et al., 2017). Other studies also showed that, in early pregnancy, diets that are associated with higher ingestion of fibres, such as vegetarian diets, resulted in a diminished abundance of *Collinsella* an anaerobic bacteria that produces lactate instead of SCFA, which is associated with IR, and increased richness of *Roseburia* (butyrate-producing bacteria) when compared with omnivore diets (Barret et al., 2018). Additionally, *Prevotella* was found to be enriched in maternal microbiota related to diets with higher CHO intake, whereas *Ruminococcus* was more enriched in the cohorts ingesting vegetal protein and fat diets (García-Mantrana et al., 2020). Furthermore, in overweight and obese pregnancies higher fibre intake increased intestinal microbiota richness, while greater fat intake (saturated fatty acids, monounsaturated fatty acids, and *n*-6 polyunsaturated fatty acids) decreased its richness (Röytiö et al., 2017).

Current literature also reports the association between pro-inflammatory bacteria and dietary patterns. *Proteobacteria* were associated with a diet abundant in vitamin D, retinol, and monounsaturated fat in normal-weight pregnant women, whereas vitamin E was associated with the opposite trend (Mandal et al., 2016). One study implemented routine dietary counselling according to International Federation of Gynecology and Obstetrics (FIGO) guidelines (Hod et al., 2015) to a cohort of 41 overweight pregnant women with GDM, where participants completed a 3-day food record and it was found that only one-third accomplished the recommendations, with two-third consuming a diet rich in fat and low in fibre (Ferrocino et al., 2018). Adherent participants, whose diet was poor in saturated and total fats, showed a decreased abundance of *Bacteroides* in their gut microbiota composition, which is associated with high-fat animal-based diets (David et al., 2014). In conclusion, food and its constituents are crucial in regulating host health and disease since they can modulate the environment in which gut microbes live, as well as their diversity and metabolism.

Medical nutrition therapy in GDM

Most GDM women are diagnosed between 24 and 28 weeks of pregnancy, when there is already an increased maternal IR that tends to be higher each week (Farabi and Hernandez, 2019). Medical nutrition therapy (MNT), defined as an individualised nutritional plan developed between the woman and the dietitian (American Diabetes Association Professional Practice Committee, 2022), can be an effective first-line therapy to treat GDM. It should be a food plan that provides adequate calories for both mother and foetus, based on nutrition assessment and the control of the amount and distribution of CHO in the diet, in order to achieve adequate nourishment and normoglycaemia without ketosis and also to improve glycaemic control (Reader, 2007; Moreno-Castilla et al., 2013). For a successful treatment, individual and personalised dietary counselling and prescription should be assumed by a registered dietitian (or universal equivalent) for all pregnant women diagnosed with GDM (Duarte-Gardea et al., 2018).

The major focus of MNT is to lower postprandial plasma glucose levels, either by adjusting CHO distribution or by altering the glycaemic load (GL; Hernandez et al., 2013). The first steps of diet manipulation were taken during the 1950s and 60s, focusing on CHO restriction, with approximately 40% of total daily calories (Hernandez, 2016), considering the principle that it could help lower postprandial glucose and prevent foetal hyperinsulinemia (Mulla, 2016). Currently, it is recommended by the Institute of Medicine (United States of America – USA) a minimum of 175 g CHO/day for pregnant women, equivalent to 35% of a 2000 calories diet, with an extra 45 g compared with non-pregnant women, since an average of 33g glucose/day are required to support foetal brain development and functioning (Trumbo et al., 2002), and also 71 g of protein and 28 g of fibre. Low-CHO diets remain the conventional diet therapy for GDM in some countries. Hence, more studies are needed to

construct solid evidence about CHO restriction diets (Trumbo et al., 2002; Moreno-Castilla et al., 2016; Mulla, 2016). Moderation seems to be key, since proportions greater than 55% CHO are associated with increased postprandial plasma glucose (Filardi et al., 2019).

Considering CHO, part is categorised as complex, since their structure is resistant to digestion or even completely undigested, resulting in a slower rise in blood glucose, low-GI (Mustad et al., 2020). Worldwide, 10 clinical practice guidelines (in a total of 16 analysed) on CHO considerations for GDM recommend a low-GI diet (foods under 55 on the GI scale; Tsirou et al., 2019), as it can reduce maternal FBG and 2-hour postprandial glucose, compared with high-GI diet. Viana et al. (2014) systematically reviewed various dietary patterns and concluded that a low-GI diet was the only one confirmed as beneficial for GDM women. Moreover, this diet may also have beneficial effects on the offspring by significantly reducing FBG, postprandial glucose levels, insulin use, and risk of macrosomia (Zhang et al., 2018b; Xu and Ye, 2020). Different types of CHO have diverse impacts on gut microbiota composition. Mardinoglu et al. (2018) conducted a short-term intervention study on 10 obese individuals with non-alcoholic fat disease, in order to understand the gut microbial composition, by applying a restricted-CHO diet with increased protein for 14 days. The results show a reduction of CHO-degrading bacteria *Ruminococcus*, *Eubacterium*, *Clostridium*, and *Bifidobacterium*, and levels of SCFA, along with an increased richness in *Lactococcus*, *Eggerthella*, and *Streptococcus* (Mardinoglu et al., 2018). Another study examined the effects of a CHO-restricted diet on the gut bacteria in mice, showing a significant increase in *Clostridium* (bacteria that promote inflammation) and *Suterella* (associated with increased LPS and gut inflammation; He et al., 2020).

Regarding fibre intake, a study about the effects of high fibre with low-GI on gut microbiota in type 2 diabetes patients reported a decreased richness in *E. coli* and *Enterococcus* (opportunistic pathogens) and a significant increase in *Bifidobacterium* and *Lactobacillus* (beneficial bacteria) compared with the control group (Singh et al., 2017). *Bifidobacterium* is solidly associated with SCFA production – produced by the fermentation of microbiota-accessible carbohydrates (MACs) – decreased gut LPS levels and improved intestinal mucosal barrier. *Lactobacillus* is associated with anti-inflammatory and anti-carcinogenic effects, and also SCFA production (Singh et al., 2017). Additionally, the richness of *Lactobacillus* and *Bifidobacterium* are associated with the intake of prebiotic fibres (Moszak et al., 2020). These are indigestible fermented fibres that promote bacterial growth in the intestine with health benefits for the host, such as fructooligosaccharides (FOS), galactooligosaccharides (GOS), and inulin (Wilson and Whelan, 2017). The majority of GDM guidelines recommend an augmented quantity of fibre, with some indicating approximately 28 g/day of fibres intake (Tsirou et al., 2019).

DASH diet is another dietary pattern that has been studied for patients with GDM. Characterised by low-GI, low-energy density with high quantities of fibre and decreased levels of sodium, it was originally designed for patients with hypertension, but favourable effects were reported for metabolic syndrome and type 2 diabetes (Asemi et al., 2013a,b). The American Academy of Nutrition and Dietetics (USA) also considers this dietary pattern to be effective in improving both mother and foetal outcomes in GDM, including glucose tolerance, IR, glycosylated haemoglobin, insulin requirements, lipid profile and incidence of macrosomia (Duarte-Gardea et al., 2018), HOMA-IR results and medication needs (Yamamoto et al., 2018), systolic blood pressure and lipid profiles – these last two reported on a 4-week DASH diet in patients with GDM (Asemi et al., 2013a,b). DASH shares numerous similarities with the Mediterranean diet, except for the intake of olive oil. Fruits, vegetables, and grains are the major food sources in the DASH pattern diet, containing different fibre types (Jama et al., 2019), which may predict its positive role in GDM nutrition, as discussed above. Although there is a lack of studies directly targeting the influence of a DASH diet on GDM women's gut microbiota, it is already demonstrated that high adherence to DASH promotes the increased richness of SCFA-producing bacteria, such as *Roseburia*, whereas no adherence leads to higher urinary trimethylamine N-oxide (TMAO) levels, a microbial metabolite possibly associated with cardiovascular and neurological disorders (Filippis et al.,

2016). Further studies are required to better clarify the DASH diet role in gut microbiota modulation for GDM management.

Probiotics in GDM

Even though the adherence of the probiotics to intestinal mucosal cells is challenging, influencing its effect (O'Sullivan et al., 1992; Kullen et al., 1997), regular use of probiotics is reported to beneficially modulate intestinal microbiota composition metabolic activities in faeces (Taylor et al., 2017). Thus, maternal gut microbiota modulation with probiotic intervention is emerging as a safe approach capable of improving intestinal commensal bacteria and also providing beneficial effects for both mother and foetus health (Swartwout and Luo, 2018; Hasain et al., 2021). Currently, probiotic agents are mainly produced by gram-positive bacteria such as lactic acid bacteria, namely *Bifidobacterium* and *Lactobacillus.* Its use, particularly *L. casei*, *L. helvetica*, *L. acidophilus*, and *L. rhamnosus* are associated with an improvement of some GDM biomarkers (Pereira et al., 2018). Several other promising data suggest that probiotics may positively contribute to beneficial effects on glucose metabolism or even prevent GDM, either by probiotic-fortified foods or capsules (Dolatkhah et al., 2015; Lindsay et al., 2015; Ahmadi et al., 2016; Jafarnejad et al., 2016; Karamali et al., 2016; Wickens et al., 2017; Badehnoosh et al., 2018; Kijmanawat et al., 2019).

Seven studies assess the effect of probiotics on metabolic health in pregnant women with GDM (Table 1). Only one randomised control trial (RCT) demonstrated no impact on the metabolic health of GDM pregnant women, with the consumption of one single strain probiotic capsule, *L. salivarius*, in a dose of 1x10^9 CFU/day during 6 weeks. A double-blind, placebo-controlled study performed with 60 GDM pregnant women demonstrated that probiotic intervention with 3 strains, *L. acidophilus*, *L. casei* and *B. bifidum*, in a dose of 6x10^9 CFU/day during 6 weeks resulted in a significant decrease of FBG, insulin, HOMA-IR and HOMA for β cell function (HOMA-β) levels in the probiotic group compared with the placebo group. There were also positive results in the probiotic group concerning lipid metabolism, with considerable reductions in serum triglycerides and very low density lipoprotein (VLDL) cholesterol. Similar results were reported when administering a symbiotic supplement (probiotics plus inulin) with the same probiotic strains and doses used in Karamali et al. (2016) to GDM pregnant women, supplemented with 800 mg of inulin (a prebiotic fibre) during a 6-week-treatment, resulting in decreased insulin levels, and HOMA-IR and HOMA-β results, along with similar lipid outcomes when compared with placebo (Ahmadi et al., 2016). Another RCT involving 70 pregnant women diagnosed with GDM showed that daily consumption of a probiotic capsule containing eight different strains, *S. thermophilus*, *B. breve*, *B. longum*, *B. infantis*, *L. acidophilus*, *L. plantarum*, *L. paracasei* and *L. delbrueckii*, in a dose of 15 × 10^9 CFU during 8 weeks, had significant differences in insulin levels and HOMA-IR; however, no changes were observed in FBG and HbA1c in the probiotic group compared with the placebo group (Jafarnejad et al., 2016). Data from a double-blind, placebo-controlled, and randomised study revealed that an 8-week treatment of probiotics in a 4 × 10^9 CFU/day dose with four probiotic strains, *L. acidophilus*, *Bifidobacterium* sp., *S. thermophilus,* and *L. bulgaricus*, showed reductions in FBG, HOMA-IR and GWG (Dolatkhah et al., 2015). Moreover, a 4-week randomised double-blind and placebo-controlled study performed with a two-strain probiotic capsule containing *L. acidophilus* and *B. bifidus* in a 2 × 10^9 CFU dose in 57 GDM pregnant women, demonstrated significant improvements in glucose metabolism in the probiotic group compared with the placebo, comprising fasting plasma insulin, FBG, and HOMA-IR (Kijmanawat et al., 2019). Two other RCTs conducted with the same number of participants (n = 60, 30 in the probiotic group, 30 in placebo group) and the same three strains of probiotics, *L. acidophilus*, *L. casei* and *L. bifidum*, and doses (6 × 10^9 CFU/day) but with different treatment duration and type of participants, 6 weeks with GDM pregnant women (Badehnoosh et al., 2018) and 12 weeks with healthy pregnant women (Ahmadi et al., 2016), have both exhibited positive results in the probiotic group. In GDM pregnant women probiotic treatment significantly reduced FBG and other inflammatory biomarkers, total glutathione, high

Table 1. Studies of probiotics in GDM diagnosed women during gestation.

References	Dietary intervention/ assessment	Intervention/ control	Duration (weeks)	Probiotic strains	Dosage (CFU)	Outcomes
Lindsay et al. (2015)	Low glycaemic index (3-day food record)	Probiotic/ placebo (48/52)	6	*L. salivarius*	1×10^9	↔ Fasting plasma glucose ↔ HOMA-IR ↔ C-peptide ↓ Total cholesterol ↓ LDL cholesterol ↔ Triglycerides ↔ Gestational weight gain
Dolatkhah et al. (2015)	Usual dietary habits (24-h recall questionnaire of 3 days)	Probiotic/ placebo (29/27)	8	*L. acidophilus*, *Bifidobacterium*, *S. thermophilus*, *L. bulgaricus*	4×10^9 (1×10^9 each strain)	↓ Fasting plasma glucose ↓ HOMA-IR ↓ Gestational weight gain
Karamali et al. (2016)	Usual dietary habits (3-day food record)	Probiotic/ placebo (30/30)	6	*L. acidophilus*, *L. casei*, *B. bifidum*	6×10^9 (2×10^9 each strain)	↓ Fasting plasma glucose ↓ HOMA-IR ↓ HOMA-β ↓ Serum insulin levels ↑ QUICKI ↓ VLDL cholesterol ↓ Triglycerides
Jafarnejad et al. (2016)	Usual dietary habits (24-h recall questionnaire of 3 days)	Probiotic/ placebo (37/35)	8	*B. longum*, *B. infantis*, *L. acidophilus*, *L. plantarum*, *L. paracasei*, *L. delbrueckki* subsp. bulgaricus	15×10^9	↔ Fasting plasma glucose ↓ HOMA-IR ↓ Serum insulin levels ↓ IL-6 ↓ TNF-α ↓ hs-CRP ↔ HbA1c
Ahmadi et al. (2016)	Usual dietary habits (3-day food record)	Synbiotic/ placebo (35/35)	6	*L. acidophilus*, *L. casei*, *B. bifidum*	4×10^9 (2×10^9 each strain)	↔ Fasting plasma glucose ↓ Serum insulin levels ↓ HOMA-IR ↓ HOMA-β ↑ QUICKI ↓ Triglycerides ↓ VLDL cholesterol

Table 1. *Continued*

References	Dietary intervention/ assessment	Intervention/ control	Duration (weeks)	Probiotic strains	Dosage (CFU)	Outcomes
Badehnoosh et al. (2018)	Usual dietary habits (3-day food record)	Probiotic/ placebo (30/30)	6	*L. acidophilus, L. casei, B. bifidum*	6×10^9 (2×10^9 each strain)	↓ Fasting plasma glucose ↓ hs-CRP ↓ Plasma MDA concentrations ↑TAC levels ↔ Gestational weight gain
Kijmanawat et al. (2019)	No specific diet-controlled GDM (3-day food record)	Probiotic/ placebo (28/29)	4	*L. acidophilus, B. bifidum*	2×10^9 (1×10^9 each strain)	↓ Fasting plasma glucose ↓ Fasting plasma insulin ↓ HOMA-IR ↔ Gestational weight gain

↔ No significant differences between probiotic and control groups; ↓significantly lower in the probiotic group compared with the control; ↑significantly higher in the probiotic group compared with the control.HbA1c, glycosylated haemoglobin; HOMA-IR, homeostatic model of assessment of insulin resistance; HOMA-β, homeostatic model assessment for B-cell function; hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin 6; MDA, malondialdehyde; QUICKI, quantitative insulin sensitivity check index; TAC, total antioxidant capacity; TNF-α, tumour necrosis factor alpha; VLDL, very low density lipoprotein.

sensitivity C-reactive protein, malondialdehyde, and nitric oxide (Badehnoosh et al., 2018), whereas in healthy pregnant women substantially diminished insulin levels, HOMA-IR and HOMA-β (Ahmadi et al., 2016).

Hasain et al. (2021) conducted a meta-analysis on this subject and reported a significant reduction in different glycaemic control markers as FPG, fasting serum insulin, and HOMA-IR in women with GDM when a probiotic supplementation is performed, in a dose between 10^6 and 10^9 CFU. However, no significant impact was observed when comparing the data for total cholesterol levels, which presents a discrepancy with the previous results presented. The studies included in this analysis used multispecies probiotics, including *Lactobacillus* and *Bifidobacterium*, similar to the previous studies presented.

Current literature reveals that probiotic therapy may be an important non-pharmacological approach in terms of improving glycaemic control in pregnant women diagnosed with GDM. Probiotic mechanisms of action for treating diabetes mellitus are diverse and depend on different aspects (Khursheed et al., 2019). Anti-diabetic effects emerge when the administration of probiotics is accomplished, homeostasis is recovered, along with diminished LPS levels, supporting the synthesis of different SCFA (butyrate, acetate, and propionate) on the intestine. This leads to an increased release of incretin hormones (like GLP-1), stimulating insulin secretion and delaying gastric emptying, which affects blood glucose levels and reduces intestinal permeability, by improving tight junction proteins, thus diminishing inflammation, oxidative stress, glucose intolerance, and IR (Sanchez-Alcoholado et al., 2017; Khursheed et al., 2019).

However, additional studies are needed to clarify the underlying mechanisms of action through which probiotic therapy improve glycaemic control in GDM pregnant women and determine variables such as what strains, dosage and duration of probiotic treatment confer the highest benefits during gestation. Hsu et al. (2018) reported the influence of maternal therapy with *Lactobacillus casei* probiotic and inulin prebiotic for hypertension treatment in rat's offspring, showing a protective effect when a high fructose diet is administered during pregnancy and lactation. However, the mechanism behind the effect on the offspring is still not clear, as it may be due to a direct consequence of the probiotic passage through the milk or the placenta or the modification of the mother's metabolism. Other studies evaluated the use of probiotics to manage offspring overweight. The meta-analysis developed by Wang et al. (2020) reveals the decrease of the newborn birth weight when women with GDM are treated with probiotics. On the other hand, the intake of probiotic by obese pregnant women has the opposite effect, increasing the newborn birth weight.

Discrepancies between studies are also present. Badehnoosh et al. (2018) and Karamali et al. (2018) observed a positive effect of 6 weeks probiotic therapy with *L. acidophilus*, *L. casei*, and *B. bifidum* on offspring birth weight from women with GDM, while Kijmanawat et al. (2019) observed that supplementation with only *L. acidophilus* and *B. bifidum* during 4 weeks do not produce any effect on the infant weight. The success of the probiotic intake seems to be dependent on the type of probiotic strains used, being cocktails with higher diversity of microorganism more beneficial. The duration of treatment also appears to influence the effect of the treatment, with Wang et al. (2020) analysis indicating the need of at least 6 weeks to see effects.

Although proven safe and without adverse effects both for mother and offspring (Didari et al., 2014), additional studies need to elucidate the modification not only in the mother's metabolism and gut microbiome but also in the offspring. All of this should be taken in consideration when recommending probiotic treatment to pregnant women diagnosed with GDM.

Conclusion

Gut microbiota suffers alterations during healthy and pathological gestations like GDM. Modulating its composition through diet and probiotics can be a valid non-pharmacological preventive approach to reduce adverse GDM outcomes in both mother and offspring. Dietary management without probiotics, particularly with a low-GI approach, the currently most recommended diet for patients with GDM,

showed benefits in reducing maternal FBG and 2-hour postprandial glucose, apart from being associated with beneficial gut bacteria, such as *Bifidobacterium* and *Lactobacillus*. As reviewed, probiotic supplements may ameliorate glycaemic control and inflammatory status of GDM pregnant women, demonstrating the ability to reduce fasting plasma glucose, IR, and improved lipid profiles. However, further high-quality studies are needed to verify the effectiveness of dietary interventions with probiotics as well as the definition of the bacterial strains, doses, and duration of treatment that have the best clinical significance for GDM pregnant women. Achieving this will securely increase the use of probiotic supplementation in GDM diets to better contribute to healthier GDM pregnancies and post-partum outcomes for both mother and offspring.

Author contribution. Conceptualisation and writing – original draft: M.C.C.; Writing – review and editing: S.A. and S.G.P.; Supervision: S.G.P.

Significance statement. With the increase of gestational diabetes mellitus (GDM) and the universal difficulties in the pharmacological management of diseases during pregnancy, the role of diet interventions with probiotics supplementation is incrementally becoming more important. Current literature contributes relevant information on the best approach to manage GDM through medical nutrition therapy, particularly regarding carbohydrates, lipids, and fibre intake, combined with probiotics supplementation. That is the theme that this manuscript reviews highlights, including future approaches to propel this field of work.

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References

Aatsinki A-K, **Uusitupa H-M**, **Munukka E**, **Pesonen H**, **Rintala A**, **Pietilä S**, **Lahti L**, **Eerola E**, **Karlsson L** and **Karlsson H** (2018) Gut microbiota composition in mid-pregnancy is associated with gestational weight gain but not prepregnancy body mass index. *Journal of Women's Health (2002)* **27**(10), 1293–1301. https://doi.org/10.1089/jwh.2017.6488

Ahmadi S, **Jamilian M**, **Tajabadi-Ebrahimi M**, **Jafari P** and **Asemi Z** (2016) The effects of synbiotic supplementation on markers of insulin metabolism and lipid profiles in gestational diabetes: A randomised, double-blind, placebo-controlled trial. *The British Journal of Nutrition* **116**(8), 1394–1401. https://doi.org/10.1017/S0007114516003457

American Diabetes Association Professional Practice Committee (2022) Management of diabetes in pregnancy: Standards of medical care in diabetes. *Diabetes Care* **45**, S232–S243. https://doi.org/10.2337/dc22-S015

Angueira AR, **Ludvik AE**, **Reddy TE**, **Wicksteed B**, **Lowe Jr WL** and **Layden BT** (2015) New insights into gestational glucose metabolism: Lessons learned from 21st century approaches. *Diabetes* **64**(2), 327–334. https://doi.org/10.2337/db14-0877

Asemi Z, **Samimi M**, **Tabassi Z**, **Sabihi SS** and **Esmaillzadeh A** (2013a) A randomized controlled clinical trial investigating the effect of DASH diet on insulin resistance, inflammation, and oxidative stress in gestational diabetes. *Nutrition* **29**(4), 619–624. https://doi.org/10.1016/j.nut.2012.11.020

Asemi Z, **Tabassi Z**, **Samimi M**, **Fahiminejad T** and **Esmaillzadeh A** (2013b) Favourable effects of the dietary approaches to stop hypertension diet on glucose tolerance and lipid profiles in gestational diabetes: A randomised clinical trial. *The British Journal of Nutrition* **109**(11), 2024–2030. https://doi.org/10.1017/S0007114512004242

Badehnoosh B, **Karamali M**, **Zarrati M**, **Jamilian M**, **Bahmani F**, **Tajabadi-Ebrahimi M**, **Jafari P**, **Rahmani E** and **Asemi Z** (2018) The effects of probiotic supplementation on biomarkers of inflammation, oxidative stress and pregnancy outcomes in gestational diabetes. *The Journal of Maternal-Fetal & Neonatal Medicine* **31**(9), 1128–1136. https://doi.org/10.1080/14767058.2017.1310193

Barrett HL, **Gomez-Arango LF**, **Wilkinson SA**, **McIntyre H**, **Callaway L**, **Morrison M** and **Dekker Nitert M** (2018) A vegetarian diet is a major determinant of gut microbiota composition in early pregnancy. *Nutrients* **10**(7). https://doi.org/10.3390/nu10070890

Bäumler AJ and **Sperandio V** (2016) Interactions between the microbiota and pathogenic bacteria in the gut. *Nature* **535**(7610), 85–93. https://doi.org/10.1038/nature18849

Billionnet C, **Mitanchez D**, **Weill A**, **Nizard J**, **Alla F**, **Hartemann A** and **Jacqueminet S** (2017) Gestational diabetes and adverse perinatal outcomes from 716,152 births in France in 2012. *Diabetologia* **60**(4), 636–644. https://doi.org/10.1007/s00125-017-4206-6

Brown J, **Grzeskowiak L**, **Williamson K** *et al.* (2017) Insulin for the treatment of women with gestational diabetes. *Cochrane Database of Systematic Reviews*. Nov 5;**11**(11):CD012037. https://doi.org/10.1002/14651858.cd012037.pub2 PMID: 29103210; PMCID: PMC6486160.

Canfora EE, **Jocken JW** and **Blaak EE** (2015) Short-chain fatty acids in control of body weight and insulin sensitivity. *Nature Reviews. Endocrinology* **11**(10), 577–591. https://doi.org/10.1038/nrendo.2015.128

Cani PD (2013) Gut microbiota and obesity: Lessons from the microbiome. *Briefings in Functional Genomics.* **12**(4), 381–387. https://doi.org/10.1093/bfgp/elt014

Cani PD, **Osto M**, **Geurts L** and **Everard A** (2012) Involvement of gut microbiota in the development of low-grade inflammation and type 2 diabetes associated with obesity. *Gut Microbes* **3**(4), 279–288. https://doi.org/10.4161/gmic.19625

Carreno CA, **Clifton RG**, **Hauth JC**, **Myatt L**, **Roberts JM**, **Spong CY**, **Varner MW**, **Thorp JM Jr**, **Mercer BM**, **Peaceman AM**, **Ramin SM**, **Carpenter MW**, **Sciscione A**, **Tolosa JE**, **Saade GR**, **Sorokin Y** and **Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network** (2012) Excessive early gestational weight gain and risk of gestational diabetes mellitus in nulliparous women. *Obstetrics and Gynecology* **119** (6), 1227–1233. https://doi.org/10.1097/AOG.0b013e318256cf1a

Casagrande SS, **Linder B** and **Cowie CC** (2018) Prevalence of gestational diabetes and subsequent type 2 diabetes among U.S. women. *Diabetes Research and Clinical Practice* **141**, 200–208. https://doi.org/10.1016/j.diabres.2018.05.010

Chwalba A and **Otto-Buczkowska E** (2017) Participation of the microbiome in the pathogenesis of diabetes mellitus. *Clinical Diabetology* **6**(5), 178–181. https://doi.org/10.5603/DK.2017.0029

Clemente JC, **Ursell LK**, **Parfrey LW** and **Knight R** (2012) The impact of the gut microbiota on human health: An integrative view. *Cell* **148**(6), 1258–1270. https://doi.org/10.1016/j.cell.2012.01.035

Collado MC, **Isolauri E**, **Laitinen K** and **Salminen S** (2008) Distinct composition of gut microbiota during pregnancy in overweight and normal-weight women. *The American Journal of Clinical Nutrition* **88**(4), 894–899. https://doi.org/10.1093/ajcn/88.4.894

Conlon MA and **Bird AR** (2015) The impact of diet and lifestyle on gut microbiota and human health. *Nutrients* **7**(1), 17–44. https://doi.org/10.3390/nu7010017

Cortez RV, **Taddei CR**, **Sparvoli LG**, **Ângelo AGS**, **Padilha M**, **Mattar R** and **Daher S** (2019) Microbiome and its relation to gestational diabetes. *Endocrine* **64**(2), 254–264. https://doi.org/10.1007/s12020-018-1813-z

Crusell MKW, **Hansen TH**, **Nielsen T**, **Allin KH**, **Rühlemann MC**, **Damm P**, **Vestergaard H**, **Rørbye C**, **Jørgensen NR**, **Christiansen OB**, **Heinsen FA**, **Franke A**, **Hansen T**, **Lauenborg J** and **Pedersen O** (2018) Gestational diabetes is associated with change in the gut microbiota composition in third trimester of pregnancy and postpartum. *Microbiome* **6**(1), 89. https://doi.org/10.1186/s40168-018-0472-x

David LA, **Maurice CF**, **Carmody RN**, **Gootenberg DB**, **Button JE**, **Wolfe BE**, **Ling AV**, **Devlin AS**, **Varma Y**, **Fischbach MA**, **Biddinger SB**, **Dutton RJ** and **Turnbaugh PJ** (2014) Diet rapidly and reproducibly alters the human gut microbiome. *Nature* **505**(7484), 559–563. https://doi.org/10.1038/nature12820

de Brito Alves JL, **de Oliveira Y**, **Carvalho NNC**, **Cavalcante RGS**, **Pereira Lira MM**, **Nascimento LCP**, **Magnani M**, **Vidal H**, **Braga VA** and **de Souza EL** (2019) Gut microbiota and probiotic intervention as a promising therapeutic for pregnant women with cardiometabolic disorders: Present and future directions. *Pharmacological Research* **145**(104252), 104252. https://doi.org/10.1016/j.phrs.2019.104252

de Filippis F, **Pellegrini N**, **Vannini L**, **Jeffery IB**, **la Storia A**, **Laghi L**, **Serrazanetti DI**, **di Cagno R**, **Ferrocino I**, **Lazzi C**, **Turroni S**, **Cocolin L**, **Brigidi P**, **Neviani E**, **Gobbetti M**, **O'Toole PW** and **Ercolini D** (2016) High-level adherence to a mediterranean diet beneficially impacts the gut microbiota and associated metabolome. *Gut* **65**(11), 1812–1821. https://doi.org/10.1136/gutjnl-2015-309957

de Melo Pereira GV, **de Oliveira Coelho B**, **Magalhães Júnior AI**, **Thomaz-Soccol V** and **Soccol CR** (2018) How to select a probiotic? A review and update of methods and criteria. *Biotechnology Advances* **36**(8), 2060–2076. https://doi.org/10.1016/j.biotechadv.2018.09.003

den Besten G, **van Eunen K**, **Groen AK**, **Venema K**, **Reijngoud DJ** and **Bakker BM** (2013) The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. *Journal of Lipid Research* **54**(9), 2325–2340. https://doi.org/10.1194/jlr.R036012

di Simone N, **Santamaria Ortiz A**, **Specchia M**, **Tersigni C**, **Villa P**, **Gasbarrini A**, **Scambia G** and **D'Ippolito S** Recent Insights on the maternal microbiota: Impact on pregnancy outcomes. *Frontiers in Immunology* **11**, 528202. https://doi.org/10.3389/fimmu.2020.528202

Didari T, **Solki S**, **Mozaffari S**, **Nikfar S** and **Abdollahi M** (2014) A systematic review of the safety of probiotics. *Expert Opinion on Drug Safety* **13**(2), 227–239. https://doi.org/10.1517/14740338.2014.872627

DiGiulio DB, **Callahan BJ**, **McMurdie PJ**, **Costello EK**, **Lyell DJ**, **Robaczewska A**, **Sun CL**, **Goltsman DSA**, **Wong RJ**, **Shaw G**, **Stevenson DK**, **Holmes SP** and **Relman DA** (2015) Temporal and spatial variation of the human microbiota during pregnancy. *Proceedings of the National Academy of Sciences of the United States of America* **112**(35), 11060–11065. https://doi.org/10.1073/pnas.1502875112

Dodd JM, **Grivell RM**, **Deussen AR**, **Hague WM** and **Cochrane Pregnancy and Childbirth Group** (2018) Metformin for women who are overweight or obese during pregnancy for improving maternal and infant outcomes. *Cochrane Database of Systematic Reviews* **7**, CD010564. https://doi.org/10.1002/14651858.CD010564.pub2

Dolatkhah N, **Hajifaraji M**, **Abbasalizadeh F**, **Aghamohammadzadeh N**, **Mehrabi Y** and **Mesgari Abbasi M** (2015) Is there a value for probiotic supplements in gestational diabetes mellitus? A randomized clinical trial. *Journal of Health, Population, and Nutrition* **33**(1), 25. https://doi.org/10.1186/s41043-015-0034-9

Dong L, **Han L**, **Duan T**, **Lin S**, **Li J** and **Liu X** (2020) Integrated microbiome–metabolome analysis reveals novel associations between fecal microbiota and hyperglycemia-related changes of plasma metabolome in gestational diabetes mellitus. *RSC Advances* **10**(4), 2027–2036. https://doi.org/10.1039/C9RA07799E

Duarte-Gardea MO, **Gonzales-Pacheco DM**, **Reader DM**, **Thomas AM**, **Wang SR**, **Gregory RP**, **Piemonte TA**, **Thompson KL** and **Moloney L** (2018) Academy of nutrition and dietetics gestational diabetes evidence-based nutrition practice guideline. *Journal of the Academy of Nutrition and Dietetics* **118**, 1719–1742. https://doi.org/10.1016/j.jand.2018.03.014

Eades CE, **Cameron DM** and **Evans JMM** (2017) Prevalence of gestational diabetes mellitus in Europe: A meta-analysis. *Diabetes Research and Clinical Practice* **129**, 173–181. https://doi.org/10.1016/j.diabres.2017.03.030

Egshatyan L, **Kashtanova D**, **Popenko A**, **Tkacheva O**, **Tyakht A**, **Alexeev D**, **Karamnova N**, **Kostryukova E**, **Babenko V**, **Vakhitova M** and **Boytsov S** (2016) Gut microbiota and diet in patients with different glucose tolerance. *Endocrine Connections* **5**(1), 1–9. https://doi.org/10.1530/EC-15-0094

Farabi SS and **Hernandez TL** (2019) Low-carbohydrate diets for gestational diabetes. *Nutrients* **11**(8), 1737. 1https://doi.org/0.3390/nu11081737

Ferraro ZM, **Barrowman N**, **Prud'homme D**, **Walker M**, **Wen SW**, **Rodger M** and **Adamo KB** (2012) Excessive gestational weight gain predicts large for gestational age neonates independent of maternal body mass index. *The Journal of Maternal-Fetal & Neonatal Medicine* **25**(5), 538–542. https://doi.org/10.3109/14767058.2011.638953

Ferrocino I, **Ponzo V**, **Gambino R**, **Zarovska A**, **Leone F**, **Monzeglio C**, **Goitre I**, **Rosato R**, **Romano A**, **Grassi G**, **Broglio F**, **Cassader M**, **Cocolin L** and **Bo S** (2018) Changes in the gut microbiota composition during pregnancy in patients with gestational diabetes mellitus (GDM). *Scientific Reports* **8**(1), 12216. 1https://doi.org/0.1038/s41598-018-30735-9

Filardi T, **Panimolle F**, **Crescioli C**, **Lenzi A** and **Morano S** (2019) Gestational diabetes mellitus: The impact of carbohydrate quality in diet. *Nutrients* **11**(7), 1549. https://doi.org/10.3390/nu11071549

Flint HJ, **Duncan SH**, **Scott KP** and **Louis P** (2015) Links between diet, gut microbiota composition and gut metabolism. *The Proceedings of the Nutrition Society* **74**(1), 13–22. https://doi.org/10.1017/S0029665114001463

Food and Agricultural Organization (FAO) of the United Nations, World Health Organization (WHO) (2001) A joint FAO/WHO expert consultation on the health and nutritional properties of powder milk with live lactic acid bacteria. Available at http://www.fao.org/3/a-a0512e.pdf (accessed 1 June 2023).

García-Mantrana I, **Selma-Royo M**, **González S**, **Parra-Llorca A**, **Martínez-Costa C** and **Collado MC** (2020) Distinct maternal microbiota clusters are associated with diet during pregnancy: Impact on neonatal microbiota and infant growth during the first 18 months of life. *Gut Microbes* **11**(4), 962–978. https://doi.org/10.1080/19490976.2020.1730294

Gensollen T, **Iyer SS**, **Kasper DL** and **Blumberg RS** (2016) How colonization by microbiota in early life shapes the immune system. *Science* **352**(6285), 539–544. https://doi.org/10.1126/science.aad9378

Gentile CL and **Weir TL** (2018) The gut microbiota at the intersection of diet and human health. *Science* **362**(6416), 776–780. https://doi.org/10.1126/science.aau5812

Gilmore LA, **Klempel-Donchenko M** and **Redman LM** (2015) Pregnancy as a window to future health: Excessive gestational weight gain and obesity. *Seminars in Perinatology* **39**(4), 296–303. https://doi.org/10.1053/j.semperi.2015.05.009

Gomez-Arango LF, **Barrett HL**, **McIntyre HD**, **Callaway LK**, **Morrison M**, **Dekker Nitert M** and **SPRING Trial Group** (2016) Connections between the gut microbiome and metabolic hormones in early pregnancy in overweight and obese women. *Diabetes* **65**(8), 2214–2223. https://doi.org/10.2337/db16-0278

Gomez-Arango LF, **Barrett HL**, **Wilkinson SA**, **Callaway LK**, **McIntyre HD**, **Morrison M** and **Dekker Nitert M** (2018) Low dietary fiber intake increases Collinsella abundance in the gut microbiota of overweight and obese pregnant women. *Gut Microbes* **9**, 189–201. https://doi.org/10.1080/19490976.2017.1406584

Hasain Z, **Che Roos N**, **Rahmat F**, **Mustapa M**, **Raja Ali R** and **Mokhtar N** (2021) Diet and pre-intervention washout modifies the effects of probiotics on gestational diabetes mellitus: A comprehensive systematic review and meta-analysis of randomized controlled trials. *Nutrients* **13**(9), 3045. https://doi.org/10.3390/nu13093045

Hasain Z, **Mokhtar NM**, **Kamaruddin NA**, **Mohamed Ismail NA**, **Razalli NH**, **Gnanou JV** and **Raja Ali RA** (2020) Gut microbiota and gestational diabetes mellitus: A review of host-gut microbiota interactions and their therapeutic potential. *Frontiers in Cellular and Infection Microbiology* **10**, 188. https://doi.org/10.3389/fcimb.2020.00188

Hasan S, **Aho V**, **Pereira P**, **Paulin L**, **Koivusalo SB**, **Auvinen P** and **Eriksson JG** (2018) Gut microbiome in gestational diabetes: A cross-sectional study of mothers and offspring 5 years postpartum. *Acta Obstetricia et Gynecologica Scandinavica* **97**(1), 38–46. https://doi.org/10.1111/aogs.13252

Hasan N and **Yang H** (2019) Factors affecting the composition of the gut microbiota, and its modulation. *PeerJ* **7**, e7502. https://doi.org/10.7717/peerj.7502

He C, **Wu Q**, **Hayashi N**, **Nakano F**, **Nakatsukasa E** and **Tsuduki T** (2020) Carbohydrate-restricted diet alters the gut microbiota, promotes senescence and shortens the life span in senescence-accelerated prone mice. *The Journal of Nutritional Biochemistry* **78**(108326), 108326. https://doi.org/10.1016/j.jnutbio.2019.108326

Hernandez TL (2016) Carbohydrate content in the GDM diet: Two views: View 1: Nutrition therapy in gestational diabetes: The case for complex carbohydrates. *Diabetes Spectrum: A Publication of the American Diabetes Association* **29**(2), 82–88. https://doi.org/10.2337/diaspect.29.2.82

Hernandez Tl, **Anderson Ma**, **Chartier-Logan C**, **Friedman JE** and **Barbour LA** (2013) Strategies in the nutritional management of gestational diabetes. *Clinical Obstetrics and Gynecology* **56**(4), 803–815. https://doi.org/10.1097/GRF.0b013e3182a8e0e5

Hod M, **Kapur A**, **Sacks DA**, **Hadar E**, **Agarwal M**, **di Renzo GC**, **Roura LC**, **McIntyre HD**, **Morris JL** and **Divakar H** (2015) The International Federation of Gynecology and Obstetrics (FIGO) initiative on gestational diabetes mellitus: A pragmatic guide for diagnosis, management, and care. *International Journal of Gynaecology and Obstetrics* **131**(Suppl 3), S173–S211. https://doi.org/10.1016/S0020-7292(15)30033-3

Hsu CN, **Lin YJ**, **Hou CY** and **Tain YL** (2018) Maternal administration of probiotic or prebiotic prevents male adult rat offspring against developmental programming of hypertension induced by high fructose consumption in pregnancy and lactation. *Nutrients* **10**(9), 1229. https://doi.org/10.3390/nu10091229

Jafarnejad S, **Saremi S**, **Jafarnejad F** and **Arab A** (2016) Effects of a multispecies probiotic mixture on glycemic control and inflammatory status in women with gestational diabetes: A randomized controlled clinical trial. *Journal of Nutrition and Metabolism* **2016**, 5190846. https://doi.org/10.1155/2016/5190846

Jama HA, **Beale A**, **Shihata WA** and **Marques FZ** (2019) The effect of diet on hypertensive pathology: Is there a link via gut microbiota-driven immunometabolism? *Cardiovascular Research* **115**(9), 1435–1447. https://doi.org/10.1093/cvr/cvz091

Jost T, **Lacroix C**, **Braegger C** and **Chassard C** (2014) Stability of the maternal gut microbiota during late pregnancy and early lactation. *Current Microbiology* **68**(4), 419–427. https://doi.org/10.1007/s00284-013-0491-6

Kamada N, **Seo S-U**, **Chen GY** and **Núñez G** (2013) Role of the gut microbiota in immunity and inflammatory disease. *Nature Reviews. Immunology* **13**(5), 321–335. https://doi.org/10.1038/nri3430

Kampmann U, **Knorr S**, **Fuglsang J** and **Ovesen P** (2019) Determinants of maternal insulin resistance during pregnancy: An updated overview. *Journal of Diabetes Research* **2019**, 5320156. https://doi.org/10.1155/2019/5320156

Karamali M, **Dadkhah F**, **Sadrkhanlou M**, **Jamilian M**, **Ahmadi S**, **Tajabadi-Ebrahimi M**, **Jafari P** and **Asemi Z** (2016) Effects of probiotic supplementation on glycaemic control and lipid profiles in gestational diabetes: A randomized, double-blind, placebo-controlled trial. *Diabetes & Metabolism* **42**(4), 234–241. https://doi.org/10.1016/j.diabet.2016.04.009

Karamali M, **Nasiri N**, **Taghavi Shavazi N**, **Jamilian M**, **Bahmani F**, **Tajabadi-Ebrahimi M** and **Asemi Z** (2018) The effects of synbiotic supplementation on pregnancy outcomes in gestational diabetes. *Probiotics and Antimicrobial Proteins* **10**(3), 496–503. https://doi.org/10.1007/s12602-017-9313-7/tables/4

Kc K, **Shakya S** and **Zhang H** (2015) Gestational diabetes mellitus and macrosomia: A literature review. *Annals of Nutrition & Metabolism* **66**(Suppl 2), 14–20. https://doi.org/10.1159/000371628

Khursheed R, **Singh SK**, **Wadhwa S**, **Kapoor B**, **Gulati M**, **Kumar R**, **Ramanunny AK**, **Awasthi A** and **Dua K** (2019) Treatment strategies against diabetes: Success so far and challenges ahead. *European Journal of Pharmacology* **862**(172625), 172625. https://doi.org/10.1016/j.ejphar.2019.172625

Kijmanawat A, **Panburana P**, **Reutrakul S** and **Tangshewinsirikul C** (2019) Effects of probiotic supplements on insulin resistance in gestational diabetes mellitus: A double-blind randomized controlled trial. *Journal of Diabetes Investigation* **10**(1), 163–170. https://doi.org/10.1111/jdi.12863

Kim YA, **Keogh JB** and **Clifton PM** (2018) Probiotics, prebiotics, synbiotics and insulin sensitivity. *Nutrition Research Reviews* **31**(1), 35–51. https://doi.org/10.1017/S095442241700018X

Kim SY, **Sharma AJ**, **Sappenfield W**, **Wilson HG** and **Salihu HM** (2014) Association of maternal body mass index, excessive weight gain, and gestational diabetes mellitus with large-for-gestational-age births. *Obstetrics and Gynecology* **123**(4), 737–744. https://doi.org/10.1097/AOG.0000000000000177

Koh A, **de Vadder F**, **Kovatcheva-Datchary P** and **Bäckhed F** (2016) From dietary fiber to host physiology: Short-chain fatty acids as key bacterial metabolites. *Cell* **165**(6), 1332–1345. https://doi.org/10.1016/j.cell.2016.05.041

Koivusalo SB, **Rönö K**, **Klemetti MM**, **Roine RP**, **Lindström J**, **Erkkola M**, **Kaaja RJ**, **Pöyhönen-Alho M**, **Tiitinen A**, **Huvinen E**, **Andersson S**, **Laivuori H**, **Valkama A**, **Meinilä J**, **Kautiainen H**, **Eriksson JG** and **Stach-Lempinen B** (2016) Gestational diabetes mellitus can be prevented by lifestyle intervention: The Finnish gestational diabetes prevention study (RADIEL): A randomized controlled trial. *Diabetes Care* **39**(1), 24–30. https://doi.org/10.2337/dc15-0511

Koren O, **Goodrich JK**, **Cullender TC**, **Spor A**, **Laitinen K**, **Kling Bäckhed H**, **Gonzalez A**, **Werner JJ**, **Angenent LT**, **Knight R**, **Bäckhed F**, **Isolauri E**, **Salminen S** and **Ley RE** (2012) Host remodeling of the gut microbiome and metabolic changes during pregnancy. *Cell* **150**(3), 470–480. https://doi.org/10.1016/j.cell.2012.07.008

Kuang Y-S, **Lu J-H**, **Li S-H**, **Li JH**, **Yuan MY**, **He JR**, **Chen NN**, **Xiao WQ**, **Shen SY**, **Qiu L**, **Wu YF**, **Hu CY**, **Wu YY**, **Li WD**, **Chen QZ**, **Deng HW**, **Papasian CJ**, **Xia HM** and **Qiu X** (2017) Connections between the human gut microbiome and gestational diabetes mellitus. *Gigascience* **6**(8), 1–12. https://doi.org/10.1093/gigascience/gix058

Kullen MJ, **Amann MM**, **O'Shaughnessy MJ**, **O'Sullivan DJ**, **Busta FF** and **Brady LJ** (1997) Differentiation of ingested and endogenous Bifidobacteria by DNA fingerprinting demonstrates the survival of an unmodified strain in the gastrointestinal tract of humans. *The Journal of Nutrition* **127**(1), 89–94. https://doi.org/10.1093/jn/127.1.89

Lain KY and **Catalano PM** (2007) Metabolic changes in pregnancy. *Clinical Obstetrics and Gynecology* **50**(4), 938–948. https://doi.org/10.1097/GRF.0b013e31815a5494

LeBlanc JG, **Chain F**, **Martín R**, **Bermúdez-Humarán LG**, **Courau S** and **Langella P** (2017) Beneficial effects on host energy metabolism of short-chain fatty acids and vitamins produced by commensal and probiotic bacteria. *Microbial Cell Factories* **16**(1), 79. https://doi.org/10.1186/s12934-017-0691-z

Lefkovits YR, **Stewart ZA** and **Murphy HR** (2019) Gestational diabetes. *Medicine (Abingdon)*. **47**(2), 114–118. https://doi.org/10.1016/j.mpmed.2018.11.006

Lindsay KL, **Brennan L**, **Kennelly MA**, **Maguire OC**, **Smith T**, **Curran S**, **Coffey M**, **Foley ME**, **Hatunic M**, **Shanahan F** and **McAuliffe FM** (2015) Impact of probiotics in women with gestational diabetes mellitus on metabolic health: A randomized controlled trial. *American Journal of Obstetrics and Gynecology***212**, 496.e1–e11. https://doi.org/10.1016/j.ajog.2015.02.008

Liu H, **Pan L-L**, **Lv S**, **Yang Q**, **Zhang H**, **Chen W**, **Lv Z** and **Sun J** (2015) Alterations of gut microbiota and blood lipidome in gestational diabetes mellitus with hyperlipidemia. *Frontiers in Physiology* **10**, 1015. https://doi.org/10.3389/fphys.2019.01015

Lozupone CA, **Stombaugh JI**, **Gordon JI**, **Jansson JK** and **Knight R** (2012) Diversity, stability and resilience of the human gut microbiota. *Nature* **489**(7415), 220–230. https://doi.org/10.1038/nature11550

Lynch SV and **Pedersen O** (2016) The human intestinal microbiome in health and disease. *The New England Journal of Medicine* **375**(24), 2369–2379. https://doi.org/10.1056/NEJMra1600266

Ma S, **You Y**, **Huang L**, **Long S**, **Zhang J**, **Guo C**, **Zhang N**, **Wu X**, **Xiao Y** and **Tan H** (2020) Alterations in gut microbiota of gestational diabetes patients during the first trimester of pregnancy. *Frontiers in Cellular and Infection Microbiology* **10**, 58. https://doi.org/10.3389/fcimb.2020.00058

Mandal S, **Godfrey KM**, **McDonald D**, **Treuren WV**, **Bjørnholt JV**, **Midtvedt T**, **Moen B**, **Rudi K**, **Knight R**, **Brantsæter AL**, **Peddada SD** and **Eggesbø M** (2016) Fat and vitamin intakes during pregnancy have stronger relations with a pro-inflammatory maternal microbiota than does carbohydrate intake. *Microbiome* **4**(1), 55. https://doi.org/10.1186/s40168-016-0200-3

Mardinoglu A, **Wu H**, **Bjornson E**, **Zhang C**, **Hakkarainen A**, **Räsänen SM**, **Lee S**, **Mancina RM**, **Bergentall M**, **Pietiläinen KH**, **Söderlund S**, **Matikainen N**, **Ståhlman M**, **Bergh PO**, **Adiels M**, **Piening BD**, **Granér M**, **Lundbom N**, **Williams KJ**, **Romeo S**, **Nielsen J**, **Snyder M**, **Uhlén M**, **Bergström G**, **Perkins R**, **Marschall HU**, **Bäckhed F**, **Taskinen MR** and **Borén J** (2018) An integrated understanding of the rapid metabolic benefits of a carbohydrate-restricted diet on hepatic steatosis in humans. *Cell Metabolism* **27**(3), 559–571.e5. https://doi.org/10.1016/j.cmet.2018.01.005

Meijnikman AS, **Gerdes VE**, **Nieuwdorp M** and **Herrema H** (2018) Evaluating causality of gut microbiota in obesity and diabetes in humans. *Endocrine Reviews* **39**(2), 133–153. https://doi.org/10.1210/er.2017-00192

Metzger BE, **Lowe LP**, **Dyer AR**, *et al.* (2008) Hyperglycemia and adverse pregnancy outcomes. *The New England Journal of Medicine* **358**(19), 1991–2002. https://doi.org/10.1056/NEJMoa0707943

Mokkala K, **Houttu N**, **Vahlberg T**, **Munukka E**, **Rönnemaa T** and **Laitinen K** (2017) Gut microbiota aberrations precede diagnosis of gestational diabetes mellitus. *Acta Diabetologica* **54**(12), 1147–1149. https://doi.org/10.1007/s00592-017-1056-0

Moreno-Castilla C, **Hernandez M**, **Bergua M**, **Alvarez MC**, **Arce MA**, **Rodriguez K**, **Martinez-Alonso M**, **Iglesias M**, **Mateu M**, **Santos MD**, **Pacheco LR**, **Blasco Y**, **Martin E**, **Balsells N**, **Aranda N** and **Mauricio D** (2013) Low-carbohydrate diet for the treatment of gestational diabetes mellitus: A randomized controlled trial. *Diabetes Care* **36**(8), 2233–2238. https://doi.org/10.2337/dc12-2714

Moreno-Castilla C, **Mauricio D** and **Hernandez M** (2016) Role of medical nutrition therapy in the management of gestational diabetes mellitus. *Current Diabetes Reports* **16**(4), 22. https://doi.org/10.1007/s11892-016-0717-7

Moszak M, **Szulińska M** and **Bogdański P** (2020) You are what you eat-the relationship between diet, microbiota, and metabolic disorders - a review. *Nutrients* **12**(4), 1096. https://doi.org/10.3390/nu12041096

Mulla WR (2016) Carbohydrate content in the GDM diet: Two views: View 2: Low-carbohydrate diets should remain the initial therapy for gestational diabetes. *Diabetes Spectrum: A Publication of the American Diabetes Association* **29**(2), 89–91. https://doi.org/10.2337/diaspect.29.2.89

Mustad VA, **Huynh DTT**, **López-Pedrosa JM**, **Campoy C** and **Rueda R** (2020) The role of dietary carbohydrates in gestational diabetes. *Nutrients* **12**(2), 385. https://doi.org/10.3390/nu12020385

Natividad JMM and **Verdu EF** (2013) Modulation of intestinal barrier by intestinal microbiota: Pathological and therapeutic implications. *Pharmacological Research* **69**(1), 42–51. https://doi.org/10.1016/j.phrs.2012.10.007

Nicholson JK, **Holmes E**, **Kinross J**, **Burcelin R**, **Gibson G**, **Jia W** and **Pettersson S** (2012) Host-gut microbiota metabolic interactions. *Science* **336**(6086), 1262–1267. https://doi.org/10.1126/science.1223813

Oriá RB, **Empadinhas N** and **Malva JO** (2020) Editorial: Interplay between nutrition, the intestinal microbiota and the immune system. *Frontiers in Immunology* **11**, 1758. https://doi.org/0.3389/fimmu.2020.01758

O'Sullivan MG, **Thornton G**, **O'Sullivan GC** and **Collins JK** (1992) Probiotic bacteria: Myth or reality? *Trends in Food Science & Technology* **3**, 309–314. https://doi.org/10.1016/s0924-2244(10)80018-4

Pascale A, **Marchesi N**, **Marelli C**, **Coppola A**, **Luzi L**, **Govoni S**, **Giustina A** and **Gazzaruso C** (2018) Microbiota and metabolic diseases. *Endocrine* **61**(3), 357–371. https://doi.org/10.1007/s12020-018-1605-5

Ponzo V, **Fedele D**, **Goitre I**, **Leone F**, **Lezo A**, **Monzeglio C**, **Finocchiaro C**, **Ghigo E** and **Bo S** (2019a) Diet-gut microbiota interactions and gestational diabetes mellitus (GDM). *Nutrients* **11**(2), 330. https://doi.org/10.3390/nu11020330

Ponzo V, **Ferrocino I**, **Zarovska A**, **Amenta MB**, **Leone F**, **Monzeglio C**, **Rosato R**, **Pellegrini M**, **Gambino R**, **Cassader M**, **Ghigo E**, **Cocolin L** and **Bo S** (2019b) The microbiota composition of the offspring of patients with gestational diabetes mellitus (GDM). *PLoS One* **14**(12), e0226545. https://doi.org/10.1371/journal.pone.0226545

Priyadarshini M, **Thomas A**, **Reisetter AC**, **Scholtens DM**, **Wolever TMS**, **Josefson JL** and **Layden BT** (2014) Maternal short-chain fatty acids are associated with metabolic parameters in mothers and newborns. *Translational Research* **164**(2), 153–157. https://doi.org/10.1016/j.trsl.2014.01.012

Reader DM (2007) Medical nutrition therapy and lifestyle interventions. *Diabetes Care* **30**, S188–S193. https://doi.org/10.2337/dc07-s214

Röytiö H, **Mokkala K**, **Vahlberg T** and **Laitinen K** (2017) Dietary intake of fat and fibre according to reference values relates to higher gut microbiota richness in overweight pregnant women. *The British Journal of Nutrition* **118**(5), 343–352. https://doi.org/10.1017/S0007114517002100

Sanchez-Alcoholado L, **Castellano-Castillo D**, **Jordán-Martínez L**, **Moreno-Indias I**, **Cardila-Cruz P**, **Elena D**, **Muñoz-Garcia AJ**, **Queipo-Ortuño MI** and **Jimenez-Navarro M** (2017) Role of gut microbiota on cardio-metabolic parameters and immunity in coronary artery disease patients with and without type-2 diabetes mellitus. *Frontiers in Microbiology* **8**, 1936. https://doi.org/10.3389/fmicb.2017.01936

Santacruz A, **Collado MC**, **García-Valdés L**, **Segura MT**, **Martín-Lagos JA**, **Anjos T**, **Martí-Romero M**, **Lopez RM**, **Florido J**, **Campoy C** and **Sanz Y** (2010) Gut microbiota composition is associated with body weight, weight gain and biochemical parameters in pregnant women. *The British Journal of Nutrition* **104**(1), 83–92. https://doi.org/10.1017/S0007114510000176

Schneider S, **Hoeft B**, **Freerksen N**, **fischer B**, **Roehrig S**, **Yamamoto S** and **Maul H** (2011) Neonatal complications and risk factors among women with gestational diabetes mellitus: Gestational diabetes mellitus. *Acta Obstetricia et Gynecologica Scandinavica* **90**(3), 231–237. https://doi.org/10.1111/j.1600-0412.2010.01040.x

Shen J, **Obin MS** and **Zhao L** (2013) The gut microbiota, obesity and insulin resistance. *Molecular Aspects of Medicine* **34**(1), 39–58. https://doi.org/10.1016/j.mam.2012.11.001

Simmons D (2015) Prevention of gestational diabetes mellitus: Where are we now? *Diabetes, Obesity & Metabolism* **17**(9), 824–834. https://doi.org/10.1111/dom.12495

Singh RK, **Chang H-W**, **Yan D**, **Lee KM**, **Ucmak D**, **Wong K**, **Abrouk M**, **Farahnik B**, **Nakamura M**, **Zhu TH**, **Bhutani T** and **Liao W** (2017) Influence of diet on the gut microbiome and implications for human health. *Journal of Translational Medicine* **15**(1), 73. https://doi.org/10.1186/s12967-017-1175-y

Smid MC, **Ricks NM**, **Panzer A**, **Mccoy AN**, **Azcarate-Peril MA**, **Keku TO** and **Boggess KA** (2018) Maternal gut microbiome biodiversity in pregnancy. *American Journal of Perinatology* **35**(1), 24–30. https://doi.org/10.1055/s-0037-1604412

Stanislawski MA, **Dabelea D**, **Wagner BD**, **Sontag MK**, **Lozupone CA** and **Eggesbø M** (2017) Pre-pregnancy weight, gestational weight gain, and the gut microbiota of mothers and their infants. *Microbiome* **5**(1), 113. https://doi.org/10.1186/s40168-017-0332-0

Su M, **Nie Y**, **Shao R**, **Duan S**, **Jiang Y**, **Wang M**, **Xing Z**, **Sun Q**, **Liu X** and **Xu W** (2018) Diversified gut microbiota in newborns of mothers with gestational diabetes mellitus. *PLoS One* **13**(10), e0205695. https://doi.org/10.1371/journal.pone.0205695

Swartwout B and **Luo XM** (2018) Implications of probiotics on the maternal-neonatal interface: Gut microbiota, immunomodulation, and autoimmunity. *Frontiers in Immunology* **9**, 2840. https://doi.org/10.3389/fimmu.2018.02840

Taddei CR, **Cortez RV**, **Mattar R**, **Torloni MR** and **Daher S** (2018) Microbiome in normal and pathological pregnancies: A literature overview. *American Journal of Reproductive Immunology* **80**, e12993. https://doi.org/10.1111/aji.12830

Taylor B, **Woodfall G**, **Sheedy K**, **O'Riley M**, **Rainbow K**, **Bramwell E** and **Kellow N** (2017) Effect of probiotics on metabolic outcomes in pregnant women with gestational diabetes: A systematic review and meta-analysis of randomized controlled trials. *Nutrients* **9**(5), 461. https://doi.org/10.3390/nu9050461

Topping DL and **Clifton PM** (2001) Short-chain fatty acids and human colonic function: Roles of resistant starch and nonstarch polysaccharides. *Physiological Reviews* **81**(3), 1031–1064. 1https://doi.org/0.1152/physrev.2001.81.3.1031

Tremaroli V and **Bäckhed F** (2012) Functional interactions between the gut microbiota and host metabolism. *Nature* **489**(7415), 242–249. https://doi.org/10.1038/nature11552

Trumbo P, **Schlicker S**, **Yates AA**, **Poos M** and **Food and Nutrition Board of the Institute of Medicine, The National Academies** (2002) Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. *Journal of the American Dietetic Association* **102**(11), 1621–1630. https://doi.org/10.1016/s0002-8223(02)90346-9

Tsirou E, **Grammatikopoulou MG**, **Theodoridis X**, **Gkiouras K**, **Petalidou A**, **Taousani E**, **Savvaki D**, **Tsapas A** and **Goulis DG** (2019) Guidelines for medical nutrition therapy in gestational diabetes mellitus: Systematic review and critical appraisal. *Journal of the Academy of Nutrition and Dietetics* **119**(8), 1320–1339. https://doi.org/10.1016/j.jand.2019.04.002

Viana LV, **Gross JL** and **Azevedo MJ** (2014) Dietary intervention in patients with gestational diabetes mellitus: A systematic review and meta-analysis of randomized clinical trials on maternal and newborn outcomes. *Diabetes Care* **37**(12), 3345–3355. https://doi.org/10.2337/dc14-1530

Wang C, **Tung YT**, **Chang HC** *et al.* (2020) Effect of probiotic supplementation on newborn birth weight for mother with gestational diabetes mellitus or overweight/obesity: A systematic review and meta-analysis. *Nutrients*, **12**(11), 3477. https://doi.org/10.3390/nu12113477

Wang C, **Wei Y**, **Zhang X**, **Zhang Y**, **Xu Q**, **Sun Y**, **Su S**, **Zhang L**, **Liu C**, **Feng Y**, **Shou C**, **Guelfi KJ**, **Newnham JP** and **Yang H** (2017) A randomized clinical trial of exercise during pregnancy to prevent gestational diabetes mellitus and improve pregnancy outcome in overweight and obese pregnant women. *American Journal of Obstetrics and Gynecology* **216**(4), 340–351. https://doi.org/10.1016/j.ajog.2017.01.037

Wen L and **Duffy A** (2017) Factors influencing the gut microbiota, inflammation, and type 2 diabetes. *The Journal of Nutrition* **147**(7), 1468S–1475S. https://doi.org/10.3945/jn.116.240754

Wendland EM, **Torloni MR**, **Falavigna M**, **Trujillo J**, **Dode MA**, **Campos MA**, **Duncan BB** and **Schmidt MI** (2012) Gestational diabetes and pregnancy outcomes-a systematic review of the World Health Organization (WHO) and the International Association of Diabetes in pregnancy study groups (IADPSG) diagnostic criteria. *BMC Pregnancy and Childbirth* **12**(1), 23. https://doi.org/10.1186/1471-2393-12-23

Wickens KL, **Barthow CA**, **Murphy R**, **Abels PR**, **Maude RM**, **Stone PR**, **Mitchell EA**, **Stanley TV**, **Purdie GL**, **Kang JM**, **Hood FE**, **Rowden JL**, **Barnes PK**, **Fitzharris PF** and **Crane J** (2017) Early pregnancy probiotic supplementation with *lactobacillus rhamnosus* HN001 may reduce the prevalence of gestational diabetes mellitus: A randomised controlled trial. *The British Journal of Nutrition* **117**(6), 804–813. https://doi.org/10.1017/S0007114517000289

Wilson B and **Whelan K** (2017) Prebiotic inulin-type fructans and galacto-oligosaccharides: Definition, specificity, function, and application in gastrointestinal disorders: Prebiotic fructans and GOS. *Journal of Gastroenterology and Hepatology* **32** (Suppl 1), 64–68. https://doi.org/10.1111/jgh.13700

Xu J and **Ye S** (2020) Influence of low-glycemic index diet for gestational diabetes: A meta-analysis of randomized controlled trials. *The Journal of Maternal-Fetal & Neonatal Medicine* **33**(4), 687–692. https://doi.org/10.1080/14767058.2018.1497595

Yamamoto JM, **Kellett JE**, **Balsells M**, **García-Patterson A**, **Hadar E**, **Solà I**, **Gich I**, **van der Beek EM**, **Castañeda-Gutiérrez E**, **Heinonen S**, **Hod M**, **Laitinen K**, **Olsen SF**, **Poston L**, **Rueda R**, **Rust P**, **van Lieshout L**, **Schelkle B**, **Murphy HR** and **Corcoy R** (2018) Gestational diabetes mellitus and diet: A systematic review and meta-analysis of randomized controlled trials examining the impact of modified dietary interventions on maternal glucose control and neonatal birth weight. *Diabetes Care* **41**(7), 1346–1361. https://doi.org/10.2337/dc18-0102

Ye G, **Zhang L**, **Wang M**, **Chen Y**, **Gu S**, **Wang K**, **Leng J**, **Gu Y** and **Xie X** (2019) The gut microbiota in women suffering from gestational diabetes mellitus with the failure of glycemic control by lifestyle modification. *Journal Diabetes Research* **2019**, 6081248. https://doi.org/10.1155/2019/6081248

Zhang R, **Han S**, **Chen G-C**, **Li ZN**, **Silva-Zolezzi I**, **Parés GV**, **Wang Y** and **Qin LQ** (2018a) Effects of low-glycemic-index diets in pregnancy on maternal and newborn outcomes in pregnant women: A meta-analysis of randomized controlled trials. *European Journal of Nutrition* **57**(1), 167–177. https://doi.org/10.1007/s00394-016-1306-x

Zhang Q, **Yu H**, **Xiao X**, **Hu L**, **Xin F** and **Yu X** (2018b) Inulin-type fructan improves diabetic phenotype and gut microbiota profiles in rats. *PeerJ* **6**, e4446. https://doi.org/10.7717/peerj.4446

Zheng W, **Xu Q**, **Huang W**, **Yan Q**, **Chen Y**, **Zhang L**, **Tian Z**, **Liu T**, **Yuan X**, **Liu C**, **Luo J**, **Guo C**, **Song W**, **Zhang L**, **Liang X**, **Qin H** and **Li G** (2020) Gestational diabetes mellitus is associated with reduced dynamics of gut microbiota during the first half of pregnancy. *mSystems* **5**(2). https://journals.asm.org/doi/epub/10.1128/msystems.00109-20

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