



## Improving nutrition for the prevention of gestational diabetes: Current status and perspectives

Polina V Popova, Evgenii A Pustozarov, Aleksandra S Tkachuk, Elena N Grineva

**ORCID number:** Polina V Popova 0000-0002-3697-7791; Evgenii A Pustozarov 0000-0001-8109-1319; Aleksandra S Tkachuk 0000-0002-1384-8743; Elena N Grineva 0000-0003-0042-7680.

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**Polina V Popova, Evgenii A Pustozarov, Aleksandra S Tkachuk, Elena N Grineva**, Institute of Endocrinology, Almazov National Medical Research Centre, Saint Petersburg 194156, Russia

**Polina V Popova**, Department of Faculty Therapy, Saint Petersburg Pavlov State Medical University, Saint Petersburg 197022, Russia

**Evgenii A Pustozarov**, Department of Biomedical Engineering, Saint Petersburg State Electrotechnical University, Saint Petersburg 197341, Russia

**Corresponding author:** Polina V Popova, MD, PhD, Associate Professor, Institute of Endocrinology, Almazov National Medical Research Centre, 2, Akkuratova street, Saint Petersburg 194156, Russia. [pvpopova@yandex.ru](mailto:pvpopova@yandex.ru)

### Abstract

Gestational diabetes mellitus (GDM) is a common complication of pregnancy and a serious public health problem. It carries significant risks of short-term and long-term adverse health effects for both mothers and their children. Risk factors, especially modifiable risk factors, must be considered to prevent GDM and its consequences. Observational studies have identified several nutritional and lifestyle factors associated with the risk of GDM. The results of intervention studies examining the effects of diet and lifestyle on the prevention of GDM are contradictory. Differences in the study populations, types and intensity of intervention, time frame of the intervention, and diagnostic criteria for GDM may explain the heterogeneity in the results of intervention studies. This review provides an overview of new diets and other factors that may help prevent GDM. The main results of epidemiological studies assessing the risk factors for GDM, as well as the results and methodological problems of intervention studies on the prevention of GDM and their meta-analyses, are discussed. In addition, the evidence that gene and lifestyle interactions influence the development of GDM, as well as prospects for increasing the effectiveness of interventions designed to prevent GDM, including new data on the possible uses of personalized diet therapy, are highlighted.

**Key Words:** Gestational diabetes mellitus; Risk factors; Nutrition; Prevention; Personalized medicine; Postprandial glycemic response

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**Core Tip:** Gestational diabetes mellitus (GDM) is a common complication of pregnancy and a serious public health problem. This review provides an overview of new diets and other factors that may help prevent GDM. The main results of epidemiological studies assessing the risk factors for GDM, as well as the results and methodological problems of intervention studies on the prevention of GDM and their meta-analyses, are discussed. In addition, prospects for increasing the effectiveness of interventions designed to prevent GDM, including new data on the possible use of personalized diet therapy, are highlighted.

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## INTRODUCTION

Gestational diabetes mellitus (GDM) is a common complication of pregnancy affecting approximately one in five pregnant women, according to the criteria of the International Association of the Diabetes and Pregnancy Study Groups (IADPSG)[1].

The problem of GDM prevention has attracted increasing attention from researchers in recent years, given the numerous short-term and long-term adverse effects associated with GDM on both mothers and their offspring. For women, GDM is associated with an increased risk of preeclampsia during pregnancy[2] and a significantly increased risk of type 2 DM (T2D) and comorbidities such as cardiovascular disease after pregnancy[3]. Intrauterine hyperglycemia in pregnancy potentially affects many aspects of offspring health throughout their lives. For example, babies born to mothers with GDM are more likely to be large for gestational age and thus are more likely to suffer from birth trauma[2]. Intrauterine hyperglycemia in mothers with GDM is an important factor in programming the predisposition to obesity, DM and cardiovascular disease in offspring[4-6]. The maintenance of a normal glycemic level in pregnancy is necessary to prevent adverse pregnancy outcomes and to interrupt the vicious cycle of the transmission of a predisposition to metabolic diseases in subsequent generations[7].

## RISK FACTORS FOR GDM

Changes in hormones and glucose metabolism associated with the development of GDM during pregnancy must be understood to prevent adverse outcomes such as T2D [8]. GDM occurs when insulin receptors are unable to respond adequately to changes in blood glucose levels due to the influence of hormones produced by the placenta during pregnancy, such as human placental lactogen. This insufficient response, in turn, causes an increase in blood glucose levels. Because of the similarities in the underlying pathophysiological and risk factors for GDM and T2D, factors that are effective in preventing T2D may also be successful in preventing GDM.

Some risk factors for GDM, such as advanced maternal age[9], a family history of T2D[10], polycystic ovarian syndrome[11], hypothyroidism[12], previous diagnosis of GDM, history of fetal macrosomia, overweight and obesity, are well known[13].

Fasting glycemia in the first trimester of 5.1 mmol/L or higher is a diagnostic criterion for GDM, according to the IADPSG recommendations[14], which have subsequently been adopted by most international organizations, although they are not recognized by influential medical organizations in some countries[15]. In a prospective observational study of pregnant women, we found that in 33% of women presenting first trimester fasting glycemia in the range of 5.1 mmol/L to 5.6 mmol/L, the diagnosis of GDM was confirmed by a subsequent oral glucose tolerance test (OGTT) at 24-32 wk of pregnancy[16].

Genetic factors also contribute to the etiology of GDM. Several genes have been identified as associated with the development of GDM, including polymorphic

variants of the melatonin receptor 1B (*MTNR1B*) gene, glucokinase (*GCK*), transcription factor 7 (*TCF7L2*), potassium internal rectifying channel (*KCNJ11*), regulatory subunit 1 related protein (*CDKAL1*), insulin-like growth factor 2 binding protein 2 (*IGF2BP2*), fat mass and obesity-associated protein (*FTO*), and insulin receptor substrate 1 (*IRS1*)[17-21]. However, different genes may play a predominant role in the pathogenesis of GDM in different populations. Our previous study has confirmed the association of the rs10830963 variant in the *MTNR1B* gene and rs1799884 variant in the *GCK* gene with GDM in Russian women[22].

New data also suggest a possible contribution of environmental factors to the etiology of GDM. For example, exposure to perfluorooctanoic acid, an endocrine-disrupting substance often present in some carpet-cleaning fluids, microwave corn packets, and some culinary products, has been shown to be positively associated with the risk of GDM[23].

In addition to these risk factors, data from numerous epidemiological studies indicate that dietary and lifestyle factors, both before and during pregnancy, are associated with the risk of developing GDM and play a key role in the treatment of GDM. This review will discuss the results of prospective cohort studies and randomized clinical trials (RCTs) on the effectiveness of dietary modifications in preventing GDM.

## EVIDENCE FROM OBSERVATIONAL STUDIES ON THE ASSOCIATION OF PRENATAL NUTRITION WITH THE RISK OF GDM

A major contribution to the accumulation of data on the association of preconceptional nutrition with the risk of GDM was the Nurses' Health Study II, which included 14437 nurses who have been followed in the United States since 1989 and became pregnant during the follow-up period[24-32]. A number of prepregnancy nutritional parameters were significantly associated with the risk of developing GDM: Sugary drinks[24], heme iron intake[25], fried foods[26], animal fat[27], animal protein[28], a diet low in carbohydrates but high in animal fat and protein[29], and a general Western diet high in red meat and processed meat, refined grain products, sweets, fries, and pizza[30]. For example, the risk of developing GDM increased 1.6-fold [relative risk (RR) 1.61; 95% confidence interval (CI): 1.25-2.07] with the consumption of one serving of red meat per day. Potential factors for reducing the risk of GDM included a "prudent diet" characterized by a high intake of fruit, green leafy vegetables, poultry, and fish[30], a Mediterranean diet[31], nut consumption[28] and fiber intake[32].

Similar data were obtained in the Australian population, where the "meat, snacks and sweets" type of diet was associated with an increased risk of developing GDM, and the Mediterranean type of diet was associated with a decreased risk of developing GDM[33].

Our data obtained in a survey of Russian women are consistent with the results of the aforementioned studies: high consumption of processed meat in the form of sausages was associated with an increased risk of GDM, and higher consumption of legumes and fruit was associated with a decreased risk of GDM[22].

Women who develop GDM have impaired  $\beta$ -cell function and insulin resistance, which limits their ability to cope with the metabolic problems of pregnancy[34]. Additionally, iron is an active transition metal and a strong pro-oxidant that promotes the formation of hydroxyl radicals, increasing oxidative stress. Pancreatic  $\beta$ -cells are particularly sensitive to oxidative stress because of their weak antioxidant defenses [35]. Nevertheless, following a healthy diet, such as a Mediterranean diet, may reduce the risk of GDM. Common components of healthy dietary options include fruits and vegetables, relatively small amounts of red and processed meats, and high-quality, slow-absorbing carbohydrates. Fruits and vegetables, in particular, have many antioxidant properties, in addition to providing fiber and micronutrients such as magnesium and vitamin C. The combination of all these factors has been shown to protect against metabolic disorders by counteracting free radicals and reducing systemic oxidative stress[36]. The main results of the reviewed observational studies on the association between prenatal nutrition and the risk of GDM are summarized in Table 1.

**Table 1 Summary of observational studies on the association of prenatal nutrition with the risk of gestational diabetes mellitus**

Ref.	Population, sample size	Nutritional factors/diet pattern	Comparison	RR/OR of GDM (95%CI)
Zhang <i>et al</i> [32], 2006	13110 United States women	Fiber intake	Highest <i>vs</i> lowest quintile	RR 0.67 (0.51-0.90)
Zhang <i>et al</i> [30], 2006	13110 United States women	Western diet high in red meat and processed meat, refined grain products, sweets, fries, and pizza	Highest <i>vs</i> lowest quintile	RR 1.63 (1.20-2.21)
		"Prudent diet" characterized by high intake of fruit, green leafy vegetables, poultry, and fish	Lowest <i>vs</i> highest quintile	RR 1.39 (1.08-1.80)
Chen <i>et al</i> [24], 2009	13475 United States women	Sugar-sweetened cola	5 servings per week <i>vs</i> < 1 serving per month	RR 1.22 (1.01-1.47)
Bowers <i>et al</i> [25], 2011	13475 United States women	Heme iron intake	Highest <i>vs</i> lowest quintile	RR 1.58 (1.21-2.08)
Bowers <i>et al</i> [27], 2012	13475 United States women	Animal fat	Highest <i>vs</i> lowest quintile	RR 1.88 (1.36-2.60)
Tobias <i>et al</i> [31], 2012	15254 United States women	Mediterranean diet	Highest <i>vs</i> lowest quartile	RR 0.76 (0.60-0.95)
Bao <i>et al</i> [28], 2013	15294 United States women	Animal protein	Highest <i>vs</i> lowest quintile	RR 1.49 (1.03-2.17)
Bao <i>et al</i> [26], 2014	15027 United States women	Fried foods	> 7 times per week <i>vs</i> < 1 time per week	RR 1.88 (1.34-2.64)
Bao <i>et al</i> [29], 2014	15265 United States women	Diet low in carbohydrates but high in animal fat and protein	Highest <i>vs</i> lowest quartile	RR 1.36 (1.13-1.64)
Schoenaker <i>et al</i> [33], 2015	3853 Australian women	'Meats, snacks and sweets' pattern	Bottom and top tertiles of dietary pattern scores	RR 1.35 (0.98-1.81).
		'Mediterranean-style' pattern	Bottom and top tertiles of dietary pattern scores	RR 0.85 (0.76-0.98)
Popova <i>et al</i> [22], 2017	457 Russian women	Sausage	> 3 times per week <i>vs</i> less than once per week	OR 2.2 (1.2-4.1)
		Legumes	1-2 times per week <i>vs</i> less frequent consumption	OR 0.58 (0.36-0.94)

RR: Relative risk; OR: Odds ratio; CI: Confidence interval; GDM: Gestational diabetes mellitus.

## EVIDENCE FROM OBSERVATIONAL STUDIES ON THE RELATIONSHIP BETWEEN NUTRITION DURING PREGNANCY AND THE RISK OF GDM

The evidence from observational studies on the relationship between diet during pregnancy and the risk of GDM is mixed, and a wide variety of methods for assessing dietary habits have been developed (isolating certain types of diet and consumption of specific nutrients or foods). However, several studies suggest that adherence to a Mediterranean diet during pregnancy may reduce the risk of developing GDM by 15-38%. In a multicenter study of 10 Mediterranean countries, the incidence of GDM was lower in women with better adherence to the Mediterranean diet during pregnancy (with a higher Mediterranean diet index score) by approximately 35%-38%: 8.0% *vs* 12.3%, odds ratio (OR) = 0.618,  $P = 0.030$  when using the American Diabetes Association (ADA 2010) criteria and 24.3% *vs* 32.8%, OR = 0.655,  $P = 0.004$  using the IADPSG 2012 criteria[37].

The St. Carlos GDM Prevention Study[38] also showed that among 874 Spanish women, high adherence to the Mediterranean diet was associated with a reduced risk of GDM (OR 0.35; 95%CI: 0.18-0.67) compared with women with low adherence.

However, differences in the definition of what exactly constitutes a "traditional" Mediterranean diet exist because of the differences between different Mediterranean regions. Typically, a "traditional" Mediterranean diet is characterized by large amounts of fruits, vegetables, legumes, nuts, unprocessed grains and cereals, extra virgin olive oil, moderate amounts of fish and wine, and small amounts of meat with few foods containing "empty calories"[39]. Higher consumption of red or processed meat prior to pregnancy is associated with an increased risk of developing GDM. Two meta-analyses in a healthy adult population showed that the consumption of processed

meat was associated with a higher risk of coronary heart disease (42%) and T2D (19%-32%)[40,41]. The proposed mechanism of coronary heart disease and T2D includes excess sodium and oxidative stress due to high levels of iron and glycation end products[41], but it requires further study. Because the traditional Mediterranean diet is characterized by low meat intake, the diet has been shown to be beneficial for preventing GDM.

A large cohort study from China including 3,063 pregnant women analyzed the association of four diets (vegetable, protein-rich, "prudent", and "sweets and seafood") with the risk of GDM. The vegetable type of diet was associated with a decreased risk of GDM, whereas the "sweets and seafood" type of diet was associated with an increased risk of GDM[42].

Similarly, in another Chinese prospective cohort study of 1014 women [mean prepregnancy body mass index (BMI) < 23 kg/m<sup>2</sup>], a "traditional dietary pattern" (high consumption of vegetables, fruits, and rice) was associated with a lower risk of GDM [0.40 (95%CI: 0.23-0.70)][41]. Meanwhile, a diet rich in whole-grain foods and seafood was associated with an increased risk of developing GDM [OR 1.73 (95%CI: 1.10-2.74)][43]. This finding contradicts the results of previous studies[44] and may be due to the older age of the women who followed this type of diet, which is generally considered healthier.

Another study from China including 6,299 pregnant women showed that higher intake of total protein and animal protein in mid-pregnancy was associated with an increased risk of GDM (RR 1.92, 95%CI: 1.10-3.14,  $P = 0.04$ )[45].

In our study, which included 266 women with GDM and 414 pregnant women without GDM, only higher fruit consumption (more than 12 servings per week) was associated with a reduced risk of GDM among the nutritional factors analyzed during pregnancy[22]. The association between high fruit consumption and a lower risk of developing GDM may be explained by several potential mechanisms. First, fruit is rich in fiber, which may reduce obesity and improve insulin sensitivity[46]. In addition, fiber consumption may delay gastric emptying and delay digestion and assimilation, resulting in lower plasma glucose levels after a meal[46,47]. In addition, fruits are rich in polyphenols and other antioxidant components, such as vitamin C, vitamin E and carotenoids[48,49]. These compounds may reduce the risk of GDM by reducing oxidative stress, which interferes with glucose uptake by cells.

Meanwhile, a Norwegian prospective study did not observe differences in diet among 702 women (of whom 40 had GDM) who developed GDM and those who did not[50]. Similarly, Looman *et al*[51] found no consistent correlation between diet quality and glycemia (as assessed using the 2015 Dutch Healthy Diet Index). Only a weak correlation was observed between fasting glucose levels, diet quality, and total iron intake (both  $P$  values < 0.05).

The Project Viva study in the United States, which included 1733 pregnant women who were evaluated for the association of diet type and frequency of red and processed meat consumption in the first trimester with the risk of developing GDM, obtained similar results[52]. Nutritional habits and the consumption of red and processed meat during pregnancy were not predictors of GDM diagnosis. The authors concluded that prepregnancy dietary patterns, as reflected by BMI before pregnancy, were probably more important contributors to the development of GDM than the diet during pregnancy.

The summary of observational studies on the relationship between nutrition during pregnancy and the risk of GDM is depicted in Table 2.

An important limitation of all observational studies remains the use of food frequency questionnaires to assess food intake. Nevertheless, collectively, the results of most observational studies indicate the important role of lifestyle factors during pregnancy in the development of GDM.

What is the next step in this area of research? The obvious next step appears to be a shift from the results of large observational studies to effective interventions designed to prevent GDM. Interventional studies on GDM prevention have emerged in the last 10 years.

## RANDOMIZED TRIALS OF THE EFFECT OF DIET DURING PREGNANCY ON THE RISK OF GDM

A large number of RCTs have evaluated different lifestyle interventions during pregnancy to prevent GDM. Individual studies have limited power and ability to prove the effect of diet on the risk of developing GDM. Therefore, this review will



**Table 2 Summary of observational studies on the relationship between nutrition during pregnancy and the risk of gestational diabetes mellitus**

Ref.	Population, sample size	Nutritional factors/diet pattern	Comparison	RR/OR of GDM (95%CI)
Radesky <i>et al</i> [52], 2008	1733 pregnant United States women	Diet type and frequency of red and processed meat consumption	Macronutrient energy partition and nutrient density substitution models	No association
Karamanos <i>et al</i> [37], 2014	Multicenter study of 10 Mediterranean countries, 1076 pregnant women	Mediterranean diet index (MDI), reflecting the degree of adherence to the MedDiet pattern of eating	Lower tertile of MDI (poor adherence) <i>vs</i> the upper tertile (good adherence)	OR 0.655(0.495-0.867)
He <i>et al</i> [42], 2015	3063 pregnant Chinese women	Vegetable pattern	Highest tertile <i>vs</i> lowest tertile	RR 0.79 (0.64-0.97)
		Protein-rich pattern		No association
		"Prudent" pattern		No association
		Sweets and seafood pattern		RR 1.23 (1.02-1.49)
Popova <i>et al</i> [22], 2017	680 pregnant Russian women	Fruit consumption	> 12 servings per week <i>vs</i> less consumption	OR 0.5 (0.3-0.8)
Elvebakk <i>et al</i> [50], 2018	702 pregnant Norwegian women	Intake of food groups	Women who developed GDM and women who did not develop GDM	No association
Liang <i>et al</i> [45], 2018	6299 Chinese pregnant women	Total protein	Highest tertile <i>vs</i> lowest tertile	RR 1.92 (1.10-3.14)
		Animal protein		RR 1.67 (1.19-2.93)
		Vegetable protein intake		No association
Assaf-Balut <i>et al</i> [38], 2018	874 Spanish women	Degree of adherence to a MedDiet pattern based on six food targets	High adherence (complying with 5-6 targets); moderate adherence (2-4 targets); low adherence (0-1 targets)	OR 0.35 (0.18-0.67)
Hu <i>et al</i> [43], 2019	1014 pregnant Chinese women	"Traditional pattern" (high vegetable, fruit, and rice intake)	Quartile 4 versus quartile 1	OR 0.44 (0.27-0.70)
		Whole grain-seafood pattern		OR 1.73, (1.10-2.74)

RR: Relative risk; OR: Odds ratio; CI: Confidence interval; GDM: Gestational diabetes mellitus.

mainly discuss the results of meta-analyses, which combine the results of individual studies and clarify the presence of an effect with greater certainty.

A meta-analysis by Tieu *et al* [53] that included 11 RCTs (2786 women) evaluated the effectiveness of dietary recommendations for the prevention of GDM. Five of the included studies compared dietary recommendations with standard treatment, four studies compared a low-glycemic index (GI) diet with medium or high-GI dietary recommendations, and one study compared a high-fiber diet with standard dietary recommendations. A trend toward a reduced risk of GDM (RR 0.60, 95%CI: 0.35-1.04;  $P = 0.07$ ) was observed in women who received dietary recommendations compared with the standard treatment. A subgroup analysis showed a more significant effect of dietary recommendations on reducing the risk of GDM in overweight and obese women (RR 0.39, 95%CI: 0.19-0.79) [53].

Song *et al* [54] included studies of the effects of diet, physical activity (PA) or a combination of the two during pregnancy on the risk of GDM (a total of 27 RCTs and 11487 women) in a systematic review and meta-analysis. In the pooled analysis, diet or PA resulted in an 18% (95%CI: 5-30,  $P = 0.009$ ) reduction in the risk of GDM. However, in separate analyses, the effect of PA combined with diet, diet alone, or PA alone on the risk of GDM did not reach statistical significance. In subgroup analyses, the intervention was only effective if initiated before 15 wk of gestation (RR 0.8, 95%CI: 0.66-0.97) [54].

In a systematic review involving 23 RCTs and approximately 9000 women from the Cochrane Database, Shepherd *et al* [55] compared the effect of a combination of diet and exercise with no intervention (standard management) on preventing GDM in pregnant women. This analysis showed a possible reduction in the risk of GDM (RR 0.85, 95%CI: 0.71-1.01,  $P = 0.07$ ) in the intervention group with a moderate level of

evidence.

In a recently published meta-analysis, Guo *et al*[56] examined the effectiveness of lifestyle interventions, including diet, exercise, or a combination of the two, in preventing GDM and were able to include 47 RCTs (15745 participants). As a result, the authors were able to show a significant reduction in the risk of GDM in the lifestyle intervention groups (RR 0.77, 95%CI: 0.69-0.87) and separately in studies of the effect of diet alone on GDM risk ( $n = 11$ , RR 0.75, 95%CI: 0.59-0.95). In addition, the authors were able to assess the contributions of different factors to the effectiveness of preventive interventions and identified four key aspects: high-risk intervention, early intervention, appropriate intensity and frequency of exercise, and control of weight gain during pregnancy. Interestingly, in overweight or obese women, BMI was not a predictor of intervention effectiveness. However, interventions were most effective in populations with a high prevalence of GDM rather than only overweight or obese women[56].

The summary of randomized trials on the effect of diet during pregnancy on the risk of GDM is depicted in Table 3.

## RANDOMIZED TRIALS OF THE EFFECT OF DIET BEFORE PREGNANCY ON THE RISK OF GDM

Given the data from meta-analyses concerning the benefits of early intervention, a logical assumption is that the optimal approach is to start the intervention before pregnancy. To date, few studies have been published on the effectiveness of diet and/or lifestyle changes before pregnancy on the risk of GDM. To the best of our knowledge, only two such studies have been published[57,58].

In the study by Mutsaerts *et al*[57] evaluating the effect of a 6-month lifestyle change before pregnancy on the rate of live birth in obese and infertile women, greater weight loss was achieved in the intervention group. However, no difference was observed in the incidence of GDM between groups.

In a study from Finland, high-risk women ( $n = 228$ ) planning a pregnancy were randomized into 2 groups: Lifestyle intervention or standard management[58]. The prepregnancy lifestyle intervention did not reduce the incidence of GDM. However, the lifestyle intervention was very mild. It included individual lifestyle counseling only once every 3 mo and only one group session with a nutritionist. No prepregnancy weight change was indicated, and pregnancy weight gain did not differ between the intervention group and the control group[58]. The intensity of the intervention did not appear sufficient to cause prepregnancy weight loss, and a real change in lifestyle may not have occurred. Consequently, the lack of a reduction in the risk of GDM was not surprising.

Additional studies evaluating preconception lifestyle interventions are needed. Longer, more intensive, and more frequent preconception lifestyle interventions in larger study groups might affect the incidence of GDM and perinatal and neonatal outcomes.

## PROSPECTS FOR IMPROVING THE EFFECTIVENESS OF GDM PREVENTION INTERVENTIONS

Dietary interventions aimed at reducing the risk of GDM in most studies follow a "one size fits all" approach, which provides uniform dietary recommendations for all participants in the same group. However, data on the effectiveness of these interventions for GDM prevention are inconsistent, as described above.

Among factors that potentially improve the effectiveness of GDM prevention interventions, approaches that personalize dietary recommendations are promising.

A reduction in the consumption of foods with a high GI and high glycemic load (GL) has consistently been shown to increase weight loss by reducing the postprandial glycemic response (PPGR) and insulin secretion[59-62]. In addition, minimizing the PPGR attenuates the decrease in resting energy expenditure associated with weight loss[63].

Standard dietary interventions based on GI/GL may not be sufficiently effective for weight loss and GDM prevention because people vary in their glycemic response to the same food[64], and, as shown in our studies, the addition of GI and GL to models predicting PPGR in pregnant women only marginally improved the prediction

**Table 3 Summary of randomized trials on the effect of diet during pregnancy on the risk of gestational diabetes mellitus**

Ref.	Design	Comparison	No. of participants (studies)	RR of GDM (95%CI)
Song <i>et al</i> [54], 2016	Meta-analysis, 27 RCTs (11487 women)	Lifestyle intervention of diet, PA or both <i>vs</i> standard management	11487 (27)	0.82 (0.70-0.95)
		PA plus diet <i>vs</i> standard management	6047 (14)	0.85 (0.70-1.03)
		Diet only <i>vs</i> standard management	1279 (5)	0.80 (0.58-1.10)
Tieu <i>et al</i> [53], 2017	Meta-analysis, 11 RCTs (2786 women)	Dietary recommendations <i>vs</i> standard treatment	1279 (5 RCTs)	0.60 (0.35-1.04); in overweight and obese women RR 0.39 (0.19-0.79)
		Low-glycemic index (GI) diet <i>vs</i> medium- or high-GI dietary recommendations	912 (4 RCTs)	0.91 (0.63-1.31)
		High-fiber diet <i>vs</i> standard dietary recommendations	25 (1)	No association
Shepherd <i>et al</i> [55], 2017	Meta-analysis, 23 RCTs (8918 women)	Combination of diet and exercise <i>vs</i> standard management	6633 (19)	0.85 (0.71-1.01)
Guo <i>et al</i> [56], 2019	Meta-analysis, 47 RCTs (15745 women)	Lifestyle intervention (diet, exercise, and mixed interventions) <i>vs</i> standard management	15745 (47)	0.77 (0.69-0.87)
		Diet alone <i>vs</i> standard management	2838 (11)	0.75 (0.60-0.95),

RR: Relative risk; PA: Physical activity; RCTs: Randomized clinical trials; CI: Confidence interval; GDM: Gestational diabetes mellitus.

accuracy[65]. Consequently, a proportion of individuals may experience postprandial hyperglycemia despite eating low GI/GL foods. The mismatch between lifestyle change efforts (*e.g.*, low GI/GL diet) and outcome (*e.g.*, weight loss or blood glucose control) may reduce motivation and adherence to the diet.

The reasons for differences in metabolic response are complex and widely studied. Genetic parameters and the microbiome may play a role and have great potential to explain at least part of the individual metabolic differences in food intake.

T2D is known to develop through an interaction between genetic predisposition and lifestyle, as has been confirmed in several studies [66,67]. The pathogenesis of GDM and T2D shares many factors. Therefore, researchers have assumed that GDM results from a combination of genetic risk factors and an unfavorable lifestyle. A number of new studies support the hypothesis that gene and lifestyle interactions influence the development of GDM[68]. Our study found that the association of sausage consumption with the risk of developing GDM is determined by the number of risk alleles for rs10830963 in the *MTNR1B* gene and rs1799884 in the *GCK* gene. Both genes are involved in the regulation of pancreatic islet beta-cell function and glucose homeostasis. Restriction of fatty food consumption (including sausage and sausage products) is one of the components of lifestyle changes in GDM prevention programs. Our results confirm the data reported by Grotenfelt *et al*[68] on the interaction between the rs10830963 allele and lifestyle interventions in modifying the risk of GDM. According to their study, the relative risk of GDM among women homozygous for the rs10830963 C allele was significantly lower in the intervention group than in the control group (OR = 0.16, 95%CI: 0.03-0.85, *P* = 0.014). This difference was not observed in women with the G risk allele. Further studies are needed to clarify the effects of genetic factors on the effectiveness of lifestyle changes designed to prevent GDM.

Researchers are also very interested in the microbiome as a determinant of individual metabolic differences in food intake.

In 2015, Zeevi *et al*[69] described a new machine learning algorithm that predicts individual PPGR per meal in healthy volunteers based on food intake composition, history, anthropometry, and a gut microbiome analysis. The authors showed high variability in the PPGR for the same foods among participants and suggested that universal dietary recommendations have limited utility for postprandial glucose control. Zeevi *et al*[69] also reported that individually tailored dietary recommendations based on the predicted response significantly improved the PPGR. We used a similar approach to develop models for predicting PPGR in pregnant women and obtained comparable results for accuracy, although we have not yet included microbiome data as input parameters in the models[65,70].



A promising direction to improve dietary effects is the use of mobile technology, which allows remote consultation and self-monitoring in a manner that is convenient for patients and has great potential for dissemination. We have developed a system for the remote monitoring of patients with GDM, which is a combination of software that includes a mobile app for the patient and programs to perform calculations and data analysis for the physician[71]. This system can also be used for GDM prevention programs, especially in high-risk groups.

The combination of mobile technology and providing participants with specific food recommendations tailored to their unique physiological response to food intake may increase their adherence to lifestyle changes and improve the success of weight loss and GDM prevention.

## CONCLUSION

Most observational studies have shown an association between dietary patterns before and during pregnancy and the risk of developing GDM. However, the results of randomized trials of the effect of dietary and/or lifestyle interventions on pregnant women and women planning pregnancy have been inconsistent.

The lack of effect of dietary recommendations before and during pregnancy on the risk of GDM in a number of studies can be explained by reasons such as insufficient intensity of the intervention, changes during pregnancy that prevent adherence to the recommendations (nausea, change in taste, and fatigue), and a late start and short time for lifestyle changes. In addition, individual studies have insufficient sample sizes and statistical power. Perhaps the problem of small sample size also explained the lack of reliable associations in meta-analyses published before 2019. Only the recently published and largest meta-analysis by Guo *et al*[56] showed a significant reduction in the risk of GDM in the lifestyle intervention groups and separately in studies of the effect of diet alone on GDM risk.

Most RCTs that included dietary recommendations for the prevention of GDM compared the effectiveness of the studied diet with standard dietary recommendations. Therefore, data comparing the effectiveness of different dietary options for preventing GDM are currently unavailable. Based on the data from observational studies, the benefits of the Mediterranean diet have been confirmed. Further studies are needed to clarify the optimal variant of the diet or a personalized approach to the formation of dietary recommendations to prevent the development of GDM.

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