THE ASSOCIATION OF GENETIC AND DIETARY EXPOSURES WITH GESTATIONAL DIABETES MELLITUS RISK

THE ASSOCIATION OF GENETIC AND DIETARY EXPOSURES WITH GESTATIONAL DIBETES MELLITUS RISK

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TITLE: The association of genetic and dietary exposures with gestational diabetes mellitus risk

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LAY ABSTRACT

Gestational diabetes mellitus (GDM) is glucose intolerance that first appears during pregnancy. Although lifestyle modification is the cornerstone of GDM management, dietary recommendations for GDM prevention are sparse. The overarching objective of this thesis is to describe the relationships between diets, foods, and nutrients and GDM and metabolic disorders of pregnancy and to understand whether carbohydrate quality can modify a genetic predisposition to diabetes.

In the systematic literature reviews, high-quality evidence showed that red meat increases GDM risk. Moderate-quality evidence showed that several dietary factors also influence the risk of GDM and metabolic disorders of pregnancy, but most of the existing evidence is of low-quality. More high-quality studies are needed before dietary interventions can be implemented.

In our genetic study, we observed that carbohydrate quality may modify the genetic risk of diabetes in South Asians but not in White-Caucasians and conclude that carbohydrate quality may provide only a limited assessment of overall diet quality.

ABSTRACT

Background: Although lifestyle modification is the cornerstone of GDM management, the evidence base on which dietary recommendations to prevent GDM is diverse and has not been synthesized in a consistent fashion.

Objectives: The overall objective of this thesis is to assess the relationship of diet patterns, foods, and nutrients with GDM risk. Specifically, we seek to:

1) Quantify the relationship between dietary factors and GDM and metabolic disorders of pregnancy;
2) Compare the effects of dietary factors on markers of glycemic control, such as fasting glucose, fasting insulin, Hb_{A1c}, and the homeostatic model assessment for insulin resistance (HOMA-IR);
3) Assess the association and interaction between carbohydrate quality, and genetic load on the risk of developing GDM using data from 2 prospective birth cohort studies.

Methods: We follow the approach set by the Cochrane Group's Handbook for Systematic Review of Interventions to conduct meta-analyses and assess the quality of the evidence using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach. We analyze prospective cohort data of 2,504 women from the CHILD and START studies, which enrolled women of White-Caucasian and South Asian ethnicity. We quantify carbohydrate quality by deriving the glycemic index and load (GL), and total and added sugar intake. We construct a gene score using 102 loci that were

previously associated with type 2 diabetes in genome-wide association studies.

Results: 1) The meta-analysis identified high-quality evidence that red meat increases GDM risk; however, most associations of foods and nutrients with GDM and other metabolic disorders of pregnancy are of low-quality; 2) The network meta-analysis identified that most dietary interventions given with gestational weight gain advice will lower fasting glucose; 3) In South Asians, a high GL coupled with a high genetic load increased GDM risk six fold, but a high total sugar intake in the presence of a high genetic load reduced GDM risk. This paradoxical finding may be explained by a high correlation between total sugars and other healthy foods.

Conclusions: Few valid associations between dietary factors and GDM risk exist. GL and total sugars may modify the genetic risk of GDM in South Asians but not in White-Caucasians. Further research is needed to determine effective interventions that can assist women in adopting healthier eating habits during pregnancy.

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ABBREVIATIONS

ADA	American Diabetes Association
AHA	American Heart Association
Apo-B	Apolipoprotein-B
$AUC_{glucose}$	Area-under-the-cure glucose
BiB	Born in Bradford
BG	Blood glucose
BMI	Body mass index
BP	Blood pressure
CIs	Confidence intervals
CrIs	Credible intervals
CCS	Canadian Cardiovascular Society
CHILD	Canadian Healthy Infant Longitudinal Development
CHO	Carbohydrate
CNF	Canadian Nutrient Files
CVD	Cardiovascular disease
DASH	Dietary Approach to Stop Hypertension
DBP	Diastolic blood pressure
DC	Diabetes Canada
DIAGRAM	DIAbetes Genetics Replication And Meta-analysis

DIC	Deviance information criterion
DOHaD	Developmental Origins of Health and Disease
EPIC	European Prospective Investigation into Cancer and Nutrition
EVOO	Extra-virgin olive oil
FAMILY	Family Atherosclerosis Monitoring In early life
FFQ	Food frequency questionnaire
FG	Fasting glucose
FI	Fasting insulin
GDM	Gestational diabetes mellitus
GH	Gestational hypertension
GI	Glycemic index
GL	Glycemic load
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
GRS	Genetic risk score
GWAS	Genome-wide association study
GWG	Gestational weight gain
HAPO	Hyperglycemia and Adverse Pregnancy Outcomes
HbA1c	Hemoglobin-A1c
HDP	Hypertensive disorders of pregnancy
HOMA-IR	Homeostatic model assessment for insulin resistance
HPFS	Health Professional Follow-up Study

HR	Hazard ratio
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IOM	Institute of Medicine
IQR	Interquartile range
IRR	Incidence rate ratios
JAGS	Just Another Gibbs Sampler
LDL-C	Low density lipoprotein cholesterol
LGA	Large for gestational age
MAGIC	Meta-Analyses of Glucose and Insulin-related traits Consortium
MD	Mean differences
MeD	Median differences
MUFA	Monounsaturated fatty acid
NDDG	National Diabetes Data Group
NHS	Nurses' Health Study
NICE	National Institute for Health and Care Excellence
NMA	Network meta-analysis
non-HDL-C	non-high-density lipoprotein cholesterol
NOS	Newcastle-Ottawa scale
NDSR	Nutrition Data Systems for Research
OGTT	Oral glucose tolerance test
OR	Odds ratio

PAR	Population attributable risk
PCOS	Polycystic ovarian syndrome
PREDIMED	Prevención con Dieta Mediterránea
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PUFA	Polyunsaturated fatty acid
RCT	Randomized controlled trials
RR	Risk ratio
SBP	Systolic blood pressure
SDI	Social disadvantage index
SMBG	Self-monitoring of blood glucose
SNP	Single nucleotide polymorphism
SOGC	Society of Obstetrics and Gynecology of Canada
SSB	Sugar-sweetened beverages
START	SouTh Asian biRth cohorT
SUCRA	Surface Under the Cumulative Ranking
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TG	Triglycerides
UK	United Kingdom
US	United States
USDA	United States Department of Agriculture

WHO World Health Organization

DECLARATION OF ACADEMIC ACHIEVEMENT

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CHAPTER 1. INTRODUCTION

1.1. Overview of glucose metabolism in pregnancy

Progressive insulin resistance occurs during pregnancy, even in women who do not have diabetes mellitus (**Figure 1.1.**).[1] During early pregnancy, insulin sensitivity is largely similar to pre-pregnancy levels. Blood insulin increases with a corresponding drop in fasting glucose, and adipose tissues converts the glucose into fat so that there is an energy reserve to meet the metabolic demands of the growing fetus later in pregnancy.[2,3,4] By late pregnancy, hepatic glucose production increases by 16-30% and insulin sensitivity decreases by 30-50%.[3-5] This increasing insulin insensitivity shunts glucose to the feto-placental unit, facilitating fetal growth.[1]

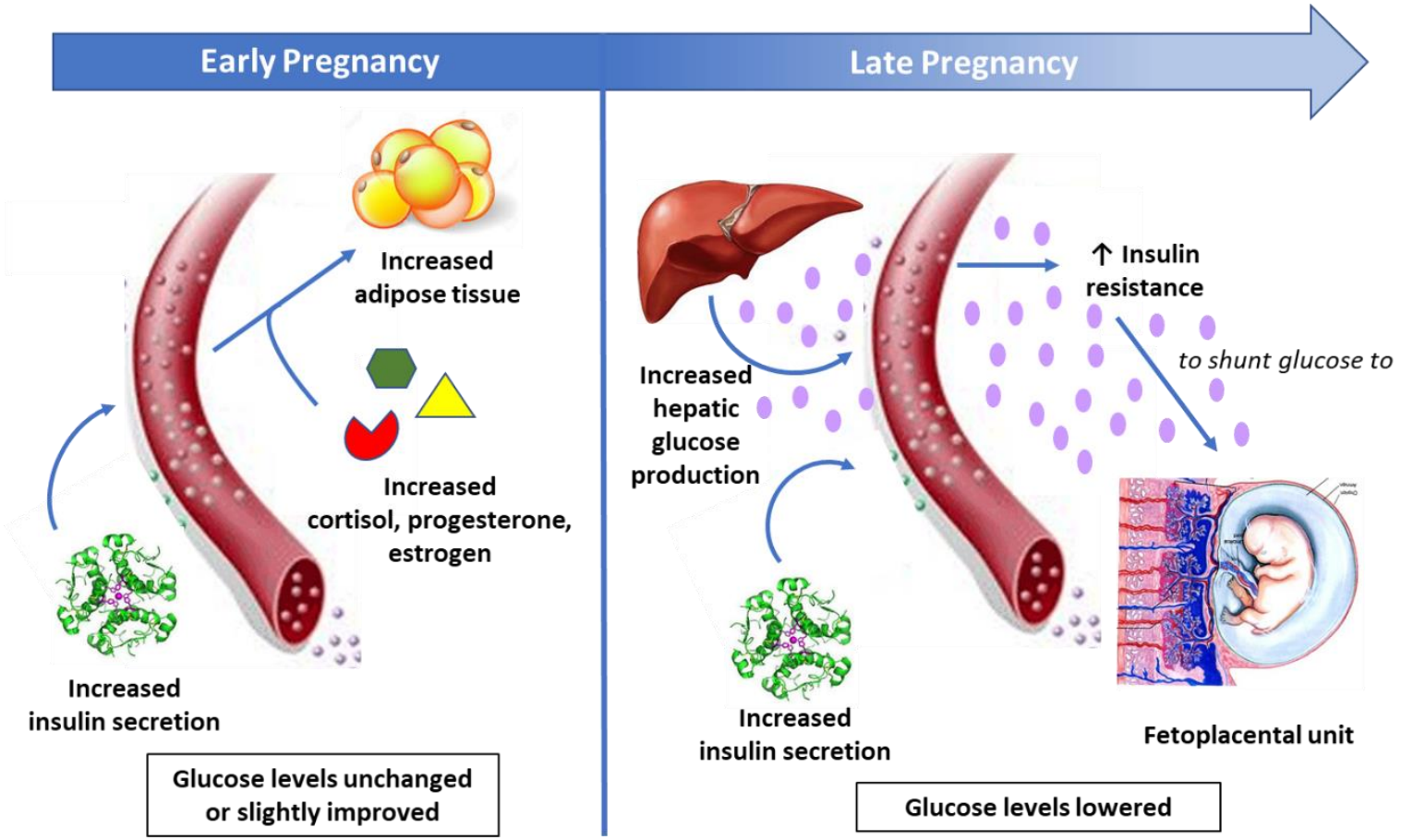
1.2. Gestational diabetes mellitus

For many years, health organizations defined GDM as any degree of glucose intolerance first recognized during pregnancy, regardless of whether the condition may have predated or persisted after pregnancy.[6] Many investigators and clinicians regarded this definition to be imprecise and lacked association with clinically important outcomes such as Caesarean delivery and shoulder dystocia.[7-9] Today, most health organizations define GDM as diabetes that occurs during pregnancy and resolves during post-partum, usually within six weeks.[10,11] The precise mechanism underlying GDM is unknown but most women with GDM have insulin resistance and pancreatic β-cell insufficiency.

1.3. Diagnosis of gestational diabetes mellitus

Diabetes organizations have not reached a consensus on the method and criteria on

Figure 1.1. Glucose metabolism in early vs late pregnancy.



Purple circles represent glucose molecule

which to diagnose GDM (**Table 1.1.**). The National Diabetes Data Group (NDDG) and Carpenter and Coustan criteria were once the accepted methods of screening and diagnosing GDM. The intent behind these criteria was to identify women at high risk of developing diabetes after pregnancy, but they did not reliably identify those who were at increased risk of adverse pregnancy outcomes.[12,13] To address this important gap, investigators at Northwestern University (Illinois, USA) designed the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) Study, which included ~25,000 women from nine countries. The HAPO study established a relationship between maternal hyperglycemia and adverse outcomes (e.g. birth weight >90th percentile, primary caesarean section, neonatal hypoglycaemia, and cord C-peptide >90th percentile) and a one-step approach to establishing the diagnosis of GDM using a 75-g oral glucose tolerance test (OGTT).[14,15] Based on the findings from the HAPO Study, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) defined GDM using the following criteria, fasting glucose [FG] ≥ 5.1 mmol/L, 1-hour blood glucose [BG]≥ 10.0 mmol/L, or 2-hours BG≥ 8.5 mmol/L. The IADPSG recommends the adoption of this criteria by all health organizations to establish an universal GDM screening process.

The World Health Organization (WHO)[15] and the American Diabetes Association (ADA)[6] adopted these criteria as their own in 2015 but many other health organizations including Diabetes Canada (DC) and the National Institute for Health and Care Excellence (NICE) have not, citing concerns over clinical implications.[11,16,17] There is still yet to be a universal standard recommendation for the diagnosis of GDM.

Table 1.1. Diagnostic criteria of GDM used by various health organizations

Organization	Gestational week at which screening should be conducted	Diagnostic test	Diagnostic criteria
NDDG, 1979[12]	-	100g OGTT	FG ≥ 5.8 mmol/L 1-hour BG ≥ 10.6 mmol/L 2-hour BG ≥ 9.2 mmol/L 3-hour BG ≥ 8.0 mmol/L
Carpenter and Coustan, 1982[13]	-	100g OGTT	FG≥ 5.3 mmol/L 1-hour BG≥ 10.0 mmol/L 2-hour BG ≥ 8.6 mmol/L 3-hour BG7.8 mmol/L
WHO, 2013[16]	Anytime during pregnancy	75g OGTT	FG: 5.1-6.9 mmol/L 1-hour BG≥ 10.0 mmol/L 2-hour BG 8.5-11.0 mmol/L
IADPSG, 2015[15]	24-28 or; anytime during pregnancy if at high risk of GDM	75g OGTT	FG≥ 5.1 mmol/L 1-hour BG≥ 10.0 mmol/L 2-hours BG≥ 8.5 mmol/L
NICE, 2015[17]	Anytime during pregnancy and only to those at high risk for GDM	75g OGTT	FG≥ 5.6 mmol/L 2-hour BG≥ 7.8 mmol/L
ADA, 2016[6]	24-28 (only in women with no overt diabetes pre-	75g OGTT or 50g OGTT	75g OGTT FG≥ 5.1 mmol/L 1-hour BG≥ 10.0 mmol/L

	pregnancy and first trimester)		2-hour BG≥ 8.5 mmol/L <u>50g OGTT</u> If 1-hour BG≥ 7.8 mmol/L proceed to perform 100g OGTT and use either Carpenter & Coustan or NDDG diagnostic criteria
DC, 2018[18]	24-28; if at high-risk for T2DM, use Hb_{A1c} test at first antenatal visit	50g OGTT (preferred) 75g OGTT (alternate)	<u>50g OGTT</u> 1-hour BG≥ 11.1 mmol/L or; 1-hour BG: 7.8-11.0 mmol/L + 75g OGTT results where FG≥ 5.3 mmol/L, 1-hour BG≥ 10.6 mmol/L, or 2-hour≥ 9.0 mmol/L <u>75g OGTT</u> FG≥ 5.1 mmol/L 1-hour BG≥ 10.0 mmol/L 2-hour BG≥ 8.5 mmol/L

Abbreviations: ADA, American Diabetes Association; BG, blood glucose; CHO, carbohydrate; DC, Diabetes Canada; FG, fasting glucose; GDM, gestational diabetes mellitus; Hb_{A1c}, hemoglobin A1C; IADPSG, International Association for the Diabetes and Pregnancy Study Group; NDDG, National Diabetes Data Group; NICE, National Institute for Health and Care Excellence; OGTT, oral glucose tolerance test; T2DM, type 2 diabetes mellitus; WHO, world health organization.

1.3.1. Criticisms of the IADPSG diagnostic criteria

The IADPSG based its diagnostic criteria for GDM using the findings from the HAPO Study, owing to the study's extensive efforts to standardize procedures for participant enrollment, laboratory analyses, data collection, and data analysis.[15] The HAPO Study found that FG, 1-hr BG, and 2-hr BG values were all positively and linearly associated with the frequency of adverse outcomes.[19,20] The IADPSG Panel could not locate any demarcation point along these associations where the frequency of adverse outcome became extremely high.[14] As such, the IADPSG chose their threshold for GDM diagnosis based on the average concentration of BG at which the odds ratio (OR) for the adverse outcomes was 1.75, a decision which has been criticized on several grounds.[15,20]

First, the diagnostic criteria are arbitrary. Although the investigators defined these thresholds *a priori*, the justification was not based on biology.[15] Second, the diagnostic criteria for GDM are thought to overmedicalize women with modest outcome benefits. Using these cut-offs, some experts in the field have criticized that this threshold would overmedicalized women with modest outcome benefits. Using these cut-offs, the diagnosis of GDM would apply to ~17-25% of women compared to the 7-10% using current diagnostic criteria such as the ones adopted by DC.[15] Treating a larger number of "less hyperglycaemic" women may reach a point where therapy may turn out to be useless, or worse, harmful. Furthermore, increasing the diagnosis of GDM have cost and workload implications.[11,21] It is unclear if increasing the number of GDM diagnoses will bring important benefits to women and their infants as well as it being cost-effective

Finally, a universal GDM diagnostic criteria does not capture important population differences. Even within the HAPO study, the prevalence of GDM varied across the 15 study sites.[22] These variations may reflect important underlying differences in the studied population, including ethnicity, obesity, socioeconomic status, and age, amongst others. These are all putative risk factors for GDM. GDM risk is higher in certain ethnic groups (e.g. South Asians, Indigenous people) and in those with higher body mass index (BMI).[23,24] Applying different diagnostic criteria would impact the choice of strategies to detect and diagnose GDM.

1.4. The burden of gestational diabetes mellitus

In 2010, GDM complicated 54.5 out of 1000 deliveries in Canada (excluding Quebec).[25] This prevalence increased by 34% since 2004/2005 (40.8 per 1000 deliveries).[25] Although a more recent review of the frequency of GDM in Canada is unavailable, its occurrence is likely to have increased given the positive trend in the past.

The prevalence of GDM also differs by ethnicity. Women of Asian and Indigenous have the highest rates of GDM, the former of which is the fastest-growing ethnic minority group in Canada.[26,27] As such, ethnic-specific GDM diagnostic criteria may be useful to prevent GDM and its complications in higher-risk populations.[28]

There is also a considerable economic cost associated with GDM. There is also a considerable economic cost associated with GDM. Though Canadian data are lacking, we can draw similar observations from other countries. A 2009 Finnish study reported the total cost of treating women with GDM (i.e. during pregnancy and post-partum) to be

€6,432 compared to €5,143 in women without GDM, which largely arises from more healthcare provider visits and hospitalizations.[29] These estimates of economic burden are likely conservative as they do not consider distal costs, including the increased development and treatment of long-term sequelae.

1.5. Complications of gestational diabetes mellitus

1.5.1. Pregnant women complications

GDM increases maternal risk of type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD). In a meta-analysis of 20 cohort studies with a mean follow-up duration of 8.60 years, a history of GDM increased the risk of T2DM by 7.43 (95% CIs [confidence intervals]: 4.79, 11.51) compared to those who were normoglycemic during pregnancy.[30] A later cohort analysis conducted in the United Kingdom (UK) of >40,000 women that followed participants for a median of 2.9 years confirmed these findings. The lifetime relative risk of T2DM, comparing women with a history of GDM to those without, was 21.96 (95% CI: 18.31, 26.34) after adjustment for age, social disadvantage, BMI, and smoking.[31]

Although cohort studies have associated GDM with CVD risk,[31-33] not every guideline has reflected this relationship. Only the 2011 American Heart Association (AHA) recognizes GDM as a major risk factor of CVD.[34] The 2001 Canadian Cardiovascular Society (CCS) did not acknowledge GDM as a CVD risk factor, citing a lack of evidence to support that women with a history of GDM are at increased CVD risk even if they do not develop T2DM.[35] NICE in the UK makes no mention of GDM in their guidelines on CVD risk

assessment.[36]

Since the publications of these guidelines, three large cohort studies have investigated the association between GDM and CVD.[31-33] The relationship between GDM, T2DM, and CVD risk, however, still remains unclear. A Canadian cohort study of over 1 million pregnancies showed that women with GDM and did not develop T2DM had an increased risk of CVD (hazard ratio [HR]= 1.30 [95% CIs: 1.07, 1.59]) over a median follow-up of 10.0 years.[32] A similar finding was seen in the Nurses' Health Study (NHS) II of 89,479 women and a follow-up duration of 26 years (adjusted-HR= 1.30 [95% CIs: 0.99, 1.71]).[33] Finally, a large cohort study of >40,000 women living in the UK found inconclusive results due to low statistical power.[31] Of the 14 women with GDM who developed ischemic heart disease, only 5 also developed T2DM in the postpartum period. The difference in findings between the Canadian cohort and NHS may relate to the different co-variates that were adjusted in the models including BMI and ethnicity. Taken together, women with a history of GDM are at increased risk of CVD later in life but it is unclear if this relationship is independent of T2DM. Larger cohort studies, where the analyses adjust for important confounding factors, are needed.

1.5.2. Infant complications

GDM can affect fetal growth and development. Hyperglycemia at conception and during the first trimester increases the risk of fetal malformation and spontaneous abortion.[20] During the second and third trimesters, excessive fetal growth, neonatal hypoglycaemia, jaundice, polycythaemia, and stillbirth may occur.[15]

Offspring of women who had diabetes during pregnancy are at increased risk of obesity, insulin resistance, and T2DM during childhood and adolescence.[37,38] This may reflect heredity, shared environment between the women and her children, or perhaps be an independent effect of exposure to diabetes *in utero.*[20] Several studies have reported findings that support the latter. First, offspring of women with GDM have a higher risk of developing obesity or T2DM than the offspring of fathers with diabetes.[39] Second, offspring of mothers with type 1 diabetes mellitus (T1DM), who are generally not obese, have higher BMI by adolescence and more impaired glucose tolerance than offspring of mothers without diabetes.[40] Third, in sibling pairs discordant for exposure to maternal diabetes, offspring born after the women developed diabetes had a higher BMI and a higher risk of developing T2DM than offspring born before their mother developed diabetes.[39] These findings suggest that diabetes during pregnancy could be an important contributor to the risk of developing obesity and T2DM later in life.

1.6. Gestational diabetes mellitus risk factors

GDM risk factors can be broadly classified as non-modifiable or modifiable risk factors. About 50% of women who develop GDM display one or more of the following risk factors.[19] Non-modifiable risk factors include increased age, increased BMI, and South or East Asian ethnicity, whereas modifiable risk factors include low vegetable or fruit intake, and physical inactivity.[10,17,18,41] Other recognized risk factors include history of delivering a macrosomic infant, a previous history of GDM, diagnosis of polycystic ovarian syndrome (PCOS), and corticosteroid use.[11] In the NHS II, 28.0% to 46.2% of GDM cases were

attributable to overweight and obesity,[42,43] 10% attributable to physical inactivity, 12% attributable to unhealthy diet, and 3% attributable to smoking.[43] These four modifiable risk factors accounted for 49.2% of all cases of GDM in this population.[43] The SouTh Asian biRth cohorT (START) reported similar findings among South Asians in Canada (population attributable risk [PAR] of overweight/obesity and low quality diet= 37.3%).[44]

1.7. Genetic determinants of gestational diabetes mellitus

Although there is a general recognition that GDM has a genetic basis, few studies have directly examined the genetic determinants of GDM.[45] This gap in the literature reflects the unique challenges in studying GDM. A study of the genetic basis for any given phenotype requires twin concordance rates, familial risk estimates, or heritability studies. For GDM, the conduct of genetic studies is complicated by the need to identify and enrol related individuals with GDM, the lack of a routine and universally-standardized GDM screening process and the low prevalence of GDM in some populations.[46] These difficulties can lead to ascertainment bias, poor estimates of heritability, and inability to assemble a sufficiently large sample for genetic studies of GDM.

Most genetic studies on GDM used a candidate gene approach. The candidate gene approach targets associations of mutations within pre-specified genes of interests, which are often ones that previous studies have shown a significant association with T2DM. Using this approach, studies have identified the following genes to increased GDM risk: TCF7L2, GCK, KCNJ11, KCNQ1, CDKAL1, IGF2BP2, MTNR1B, and IRS1 (**Table 1.2.**).[47] Most of these genes are linked to impaired β-cell function or its development.[48]

Only one genome-wide association study (GWAS) on GDM is available to date.[49] GWAS is a hypothesis-free driven observational study performed to identify single nucleotide polymorphisms (SNPs) associated with GDM risk; they do not pre-specify which genes to examine. The study identified two SNPS, one located in an intron of CDKAL1 (rs7754840) and one near MTNR1B (rs10830962), associated with GDM risk in women of Korean descent at genome-wide significance level ($p = 6.65 \times 10^{-16}$ and $p = 2.49 \times 10^{-13}$, respectively). The gene function of CDKAL1 is unknown, but previous studies linked MTNR1B to increased FG.[45] Taken together, the current state of the literature suggests a similar genetic architecture between GDM and T2DM. However, because most of the studies that support this conclusion uses the candidate gene approach, this conclusion may be biased as this approach relies on previous studies of T2DM and may preclude discoveries of genetic variants unique to GDM. To confirm the genetic basis of GDM, future studies should focus on using an unbiased approach such as GWAS.

1.8. Dietary determinants of gestational diabetes mellitus

The evidence to support the role of diet in the development of GDM is sparse. When GDM first received recognition as a distinctive form of diabetes in the 1950's, many had hypothesized that GDM would share many of the same risk factors as T2DM, including diet. Although health organizations currently emphasize diet and lifestyle modifications as cornerstone in GDM management, few have actually made any dietary recommendations for GDM prevention (**Table 1.3.**).[10,17,18,50] This may due the lack of data supporting the role of diet in the prevention of GDM from randomized controlled trials

Table 1.2. Candidate genes associated with GDM in meta-analyses

Gene	Chromosome	Encoded Protein	Protein Function
IRS1	2	Insulin Receptor Substrate 1	Insulin signaling pathway
IGF2BP2	3	Insulin-like Growth Factor 2 mRNA binding Protein 2	Regulate protein translation
CDKAL1	6	CDK5 Regulatory subunit associated protein 1 like-1	Glucose-stimulated insulin secretion
GCK	7	Glucokinase	Regulation of insulin secretion
TCF7L2	10	Transcription factor 7-like 2	Regulation of insulin secretion
MTNR1B	11	Melatonin Receptor 1B	Antagonize insulin release
CKNJ11	11	Potassium inwardly rectifying channel subfamily J, member 11	Regulation of insulin secretion
KCNQ1	11	Protein voltage-gated channel KQT-like subfamily, member 1	Regulation of insulin secretion

(RCTs).

Most dietary interventions (low glycemic index [GI], high-unsaturated-to-saturated-fat ratio, high protein diet, healthy diet) have failed to show an effect on incidence of GDM.[51-55] The lack of effect may not necessarily mean that diets cannot reduce GDM risk. Most of the RCTs that reported a null finding achieved a smaller than planned dietary contrast between the dietary intervention and its comparator, enrolled a small number of participants, and introduced the dietary intervention during second trimester (mean= 15.6 weeks) which may be too late for an intervention to have an effect.

Table 1.3. Dietary recommendations to prevent and manage gestational diabetes mellitus risk in selected guidelines

Guideline	Recommendation for prevention	Recommendation for management
ADA, 2015[10]	-	• Manage first with diet and exercise; medications should be added if needed
NICE, 2015[17]	-	• Provide nutrition counselling • If glycemic targets are not met within 2 weeks from nutritional therapy alone, insulin therapy should be initiated
WHO, 2015[50]	-	• Manage first with diet and exercise; medications should be added if needed
DC, 2018[18]	• counsel on healthy eating and prevention of excessive GWG in early pregnancy, ideally before 15 weeks of gestation	• Provide nutrition counselling • Emphasise healthy eating and foods with a low GI should replace those with a high GI • Start medication if diet and physical activity if blood glucose targets are not met within 1-2 weeks

Abbreviations: ADA, American Diabetes Association; CHO, carbohydrate; DC, Diabetes Canada; GI, glycemic index; GWG, gestational weight gain; IADPSG, International Association for the Diabetes and Pregnancy Study Group; NICE, National Institute for Health and Care Excellence.

As such, larger and higher quality RCTs that start interventions earlier than second trimester (e.g. pre-pregnancy) are needed to clarify the effects of diet on GDM risk.

1.8.1. Carbohydrate quantity vs carbohydrate quality

The conventional approach to the prevention and treatment of GDM is restriction of carbohydrate (CHO) intake.[56] This approach is motivated by the observation that individuals who suffered from GDM have high BG levels and limiting CHO intake lowers postprandial hyperglycemia.[57] However, current evidence does not support CHO restriction in the prevention of GDM. In the NHS II, average total daily CHO intake does not significantly associate with GDM risk.[58] Furthermore, adherence to a low-CHO diet is difficult because many women report an increased desire for desserts and sweets during pregnancy. Replacing carbohydrate with fat is one option, but previous studies have found that higher total fat intake may exacerbate insulin resistance.[56,59] The lack of success to prevent GDM using a CHO restriction approach has led to a paradigm shift to focus on CHO quality.

The evidence to support CHO quality and GDM prevention is mixed. In the NHS II, low GI and glycemic load (GL), and high intakes of whole grains and dietary fibre were protective against GDM.[58] Dietary patterns such as the Dietary Approach to Stop Hypertension (DASH)-style and Mediterranean-style eating patterns which emphasize whole grains and restrict refined CHO and sugar-sweetened beverages (SSBs), reduced GDM risk,[33] whereas higher adherence to a Western dietary pattern, higher in refined CHO and SSBs, increased GDM risk.[60] In RCTs of low GI diets, investigators reported no difference in GDM incidence between diets. However, these trials typically do not achieve the planned contrast in the GI between diets (i.e. <7-units), leaving them underpowered

to show a clinical effect. [53,55,61] Thus, it remains uncertain whether CHO quality may modify GDM risk.

1.9. Gene-diet interaction on gestational diabetes mellitus

Few studies have examined whether gene-diet interactions may modify GDM risk. Such studies can advance our understanding of the biology and pathophysiology of GDM and potentially improve GDM risk stratification and reduce clinical events.[62,63] Gene–diet interaction studies could also contribute to explaining some of the phenotypic variance that is not accounted for by common variants.[64]

Only one RCT and one prospective cohort study have examined gene-diet interactions and their influence on GDM risk. The RCT showed that individuals homozygous for the C-allele of rs10830963 (MTNR1B) responded better to a lifestyle intervention (diet, physical activity, and weight gain advice) than those with alternative genotypes (e.g. CG or GG).[65] The prospective cohort study showed no significant interaction between a variant of the HLA-DRB1 gene and diet on GDM risk.[66] These studies, although novel to the field, are limited by their small sample size and therefore statistical power (n_{RCT}= 226 and n_{cohort}= 712), examination of a single genetic loci (MTNR1B in RCT and HLA-DRB1 in cohort study), and to a single homogenous population of either European (in the RCT) or Asian (in the cohort study) ancestry. Future research should build on these existing finding by increasing the sample size, enhancing the biological relevance by combining several SNPs to build a single gene score, and examining a multi-ethnic sample population.

1.10. Other cardiometabolic considerations associated with pregnancy

1.10.1. Overweight, obesity, and gestational weight gain

Gestational weight gain (GWG) is one of the most important therapeutic targets for cardiometabolic risk management. Nearly 50% of women exceed the recommended GWG particularly those who are overweight or obese entering pregnancy.[67] Excessive GWG increases risk of caesarean delivery and postpartum weight retention for the mother and LGA infants, macrosomia, and childhood overweight or obesity for the offspring.[68,69] Diet or exercise interventions during pregnancy can help reduce excessive weight gain and therefore modify the risk for adverse perinatal outcomes.[70,71]

1.10.2. Hypertensive disorders of pregnancy and blood pressure

Hypertensive disorders of pregnancy (HDP) remain the leading cause of complications in women and perinatal morbidity and mortality.[72] Women with HDP have high blood pressure (BP), which most health organizations defined as ≥140mmHg systolic (SBP) and/or ≥90 mmHg diastolic (DBP) blood pressure. Four types of HDP exist: 1) chronic hypertension, which is hypertension developed before pregnancy or before 20 weeks of gestation; 2) gestational hypertension (GH), which is hypertension developed after 20 weeks of gestation; 3) pre-eclampsia, which is hypertension that occurs during pregnancy coupled with other adverse effects such as proteinuria and; 4) other hypertensive effects such as white-coat effect.[73] Studies have reported that women with HDP have increased post-partum CVD risk;[30,74,75] however, the exact physiological mechanism to explain this relationship is contentious with some studies suggesting an overlap of pre-pregnancy risk

factors rather than a direct influence of HDP.[76]

The first-line of therapy for the prevention and treatment of HDP is medications. Guidelines also recommend calcium supplementation in women whose calcium intakes from food are low. Diet and lifestyle interventions are generally not recommended apart from calcium supplementation because these is insufficient primary data on which to base recommendations for prevention and treatment.[77]

1.10.3. Blood lipids

Blood lipids are not routinely assessed during pregnancy; however emerging evidence suggest that women's lipid profile during pregnancy may affect women's risk for adverse pregnancy complications and postpartum CVD risk.[78] Several studies have identified proatherogenic patterns in lipid concentrations (e.g. increased Lp(a), triglycerides [TG], and small dense atherogenic LDL particles, and lower HDL-C levels) that precede clinical manifestations of preeclampsia.[78] Furthermore, women who have higher concentrations of small dense LDL fractions during pregnancy tend to have increased risk of CVD later in life.[78] More studies are neded to elucidate the relationship between lipid profiles during pregnancy and pregnancy complications.

CHAPTER 2. THE CONSISTENCY OF THE EVIDENCE BETWEEN DIETARY FACTORS AND GESTATIONAL DIABETES MELLITUS AND METABOLIC DISORDERS OF PREGNANCY

2.1. Introduction

Metabolic disorders of pregnancy include GDM, GWG, and HDP (pre-eclampsia and GH). These disorders affect women's health not only during their pregnancy but may have lasting influence on their cardiometabolic risk later in life.[79] Physiologic and metabolic changes during pregnancy may unmask pre-existing pancreatic β-cell insufficiency and insulin insensitivity, endothelial dysfunction, and vascular or metabolic disease.[80] Women with GDM are more likely to develop future T2DM, chronic hypertension, and ischemic heart disease than women who had a normoglycemic pregnancy,[31,33] and those who had excessive GWG are more likely to retain their pregnancy weight gain than those who gained weight in the ranges consistent with the Institute of Medicine (IOM) guidelines.[81,82] Similarly, women with a history of HDP are at similar risk for post-partum T2DM and CVD as women with a history of GDM.[83] Studies have documented these relationships predominantly in White-Caucasians, but other studies have found that other ethnic groups share these relationships as well.[84,85]

Furthermore, infants born to women with GDM, HDP, and/or excessive GWG are more likely to experience complications during birth and later in life. The Developmental Origins of Health and Disease (DOHaD) hypothesis posits that an infant's metabolism adapts to meet the demands of the *in utero* environment (e.g. overnutrition, insulin resistance, restricted placental blood flow) and this programming influences the growing

infant's risk for metabolic syndrome later in life.[86] For example, infants born to women with GDM have increased risk of fetal overgrowth (e.g. large-for-gestational age [LGA] or macrosomia), adiposity, and insulin resistance;[87,88] infants born to women who experienced excessive GWG have increased risk of high birthweight and increased BMI and adiposity in childhood;[89-91] and infants born to women with HDP have increased risk of stillbirth, preterm delivery, and/or small for gestational age, likely because of restricted blood flow across the feto-placental unit.[92-94] Thus, prevention of these metabolic disorders of pregnancy has great potential to improve infant health outcomes.

Dietary modification either through reducing energy intake and/or by changing dietary components during pregnancy may lower the risk of metabolic disorders of pregnancy. In observational studies, adherence to a "healthy" diet that emphasizes fruits, vegetables, whole grain foods, has a high white-to-red meat ratio, and minimizes added sugars and *trans* fats, increased the likelihood of adequate GWG and reduces the risk of developing pre-eclampsia.[95,96] In cohort studies, high pre-pregnancy body weight and low diet quality is responsible for 35-40% of GDM cases.[43,44] Despite these findings, most current major health organizations stop short of making dietary recommendations for the prevention of metabolic disorders of pregnancy because of the lack of intervention studies evaluating the effectiveness of diet. Only DC, WHO, and the Society of Obstetrics and Gynecology of Canada (SOGC) have made dietary recommendations for GDM management; however, even these recommendations are vague (e.g. "nutrition counselling on healthy eating should be provided") and/or based on low-quality evidence

such as expert consensus.[18,50,97]

Although many studies have evaluated the association of dietary factors with GWG, GDM, and fewer for HDP, it has been difficult for experts and guidelines committees to reach consensus on the quality and consistency of the evidence, which has resulted in weak or no recommendations. This is partly due to the diversity and variety of diets, foods, and nutrients that have been studied as well as the often-contradictory findings from cohort studies and RCTs. Ideally, unbiased, systematic reviews of relevant evidence should inform the development of dietary recommendations. Thus, the purpose is to: 1) systematically review the evidence for the relationship of various dietary factors with GWG, GDM, HDP, and blood lipids; 2) assess the quality of evidence and; 3) compare the findings between cohort studies and RCTs.

2.2. Methods

2.2.1. Protocol and registration

We followed the Cochrane Handbook for Systematic Review of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement for the conduct and reporting of the meta-analysis.[98,99] The *a priori* protocol is available at PROSPERO (CRD42016042534).

2.2.2. Data source

We searched electronic databases (MEDLINE, EMBASE, and Cochrane Central) from inception through December 7, 2017**,** supplemented by a search of registered protocols in clinicaltrials.gov and a manual search of the references of included reports. **Appendix**

Table 2.1 details an example of the search strategy used. BJK and VH independently reviewed the titles and abstracts of each report. We reviewed full-text reports that passed title and abstract screening in duplicate and any disagreement was resolved by consensus with RJdS.

2.2.3. Study selection and eligibility criteria

We included prospective cohort studies, nested case-control studies, and RCTs that assessed the relation of dietary pattern or food with outcomes of interest. Except for GDM (usually tested at 24-28 weeks gestation) and HDP (usually diagnosed after 20 weeks of gestation), outcomes of interest were measured ≥36 weeks. Studies must have followed women for ≥2-weeks, a minimum duration that the DC recommend achieving glycemic targets using diet therapy alone.[18] We excluded studies of diets, foods, or supplements designed to correct undernutrition. We imposed no language restrictions.

2.2.4. Data extraction

Pairs of reviewers (VH with BJK, RA, PT, or AN) independently extracted relevant data from eligible reports onto a spreadsheet using previously tested template.[100] We extracted study author, title, study design, sample size, health status of participants, age, ethnicity, pre-pregnancy BMI or weight, gestational age at enrollment, smoking status, country of conduct, and the diagnostic criteria used by studies to define outcomes. In addition to the above, we extracted data relating to the following from cohort studies: method of dietary assessment, the gestational period at which studies evaluated dietary intake, the exposure, the statistical models and the covariates included in the models; and for RCTs,

gestational week at which the investigators initiated the intervention, and follow-up duration.

2.2.5. Quality assessment

We assessed the risk of bias of each report with a modified Newcastle-Ottawa Scale (NOS) for cohort studies and the Cochrane Risk of Bias Tool for RCTs.[98,101] We modified the NOS so that each awarded star was equivalent to receiving a point, for a maximum of 9 points. A score of 0-3 was high risk of bias, 4-6 was unclear, and 7-9 was low risk of bias. Two independent reviewers completed the assessments (VH with BJK, RA, PT, or AN) and any disagreement was resolved with a third party (RJdS).

We used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to assess the confidence in the effect estimates derived from the body of evidence (quality of evidence) by outcome.[102] Four outcomes were possible from this assessment, ranging from very low (⊕◯◯◯) to high (⊕⊕⊕⊕).

2.2.6. Exposure definitions

We harmonized the definition of various dietary patterns to maintain consistency amongst dietary factors. **Appendix Table 2.2.** details the harmonized definitions for each dietary pattern in our analysis.

2.2.7. Outcome definitions

The primary outcome was appropriate GWG. Secondary outcomes related to GWG (inadequate GWG, excessive GWG, GWG), glycemia (GDM, FG, 1- hour and 2-hour OGTT results, and hypoglycemic events), HDP (pre-eclampsia, GH, SBP, DBP), and blood lipids

(LDL-C, non-HDL-C, TG, and Apo-B).

2.2.8. Population attributable risk (PAR)

We calculated the PAR for dietary associations that were of high quality according to the GRADE approach. We estimated the prevalence of exposure using data from three Canadian birth cohorts that enrolled mostly women in their second trimester: Canadian Healthy Infant Longitudinal Development (CHILD),[103] Family Atherosclerosis Monitoring In early life (FAMILY),[104] and START.[105] Recruitment occurred in the provinces of British Columbia (CHILD), Manitoba (CHILD), and Ontario (CHILD, FAMILY, and START).

2.2.9. Statistical analysis

The relative risk (RR) comparing extreme levels of exposure or intake (highest vs. lowest quantile) was the principal effect measure for dichotomous outcomes. We calculated the RR with the corresponding 95% CIs for the most-adjusted (i.e. the multivariable association measure with the highest number of covariates) and least-adjusted estimates reported in each cohort study. Models were "most-adjusted" if they included at least age, pre-pregnancy BMI, and total energy intake as co-variates and "least-adjusted" if they were crude models or models that that did not adjust for all three above co-variates. The mean difference was the principal effect measure for continuous outcomes. Where there were ≥10 reports, we performed a DerSimonian and Laird random effects meta-analysis, which yields conservative CIs around RR in the presence of heterogeneity, and when fewer than 10 studies were available, we performed a fixed effect estimates meta-analysis. We used Review Manager 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration,

Copenhagen, Denmark) to conduct the meta-analysis.

2.2.10. Heterogeneity

We assessed heterogeneity with Cochran's Q-statistic and quantified it with the I^2 statistic and supplemented this with a visual inspection of forest plots because statistical techniques can overestimate heterogeneity. When >10 reports were available, we planned *a priori* to conduct subgroup analyses to explain heterogeneity. We also planned to assess publication bias by visual inspection of funnel plots and statistically using Duval and Tweedie's trim-and-fill, where at least 10 studies were available.

2.2.11. Subgroup analysis

The total energy content of the diet potentially confounds the effect of foods on outcomes because energy intake determines GWG independent of dietary composition.[106] To assess the potential for confounding of dietary effects by total energy, we stratified RCTs according to whether the design of the intervention and comparator arms were matched for total energy intake. A dietary comparison is "energy-neutral" when the intended energy intake for both the intervention and comparator arms were similar, and "energy-conscious" when the energy intake was lower in the intervention than the comparator arm.

2.3. Results

2.3.1. Literature search

We identified 11,667 reports from the electronic databases and manual search. We included 68 cohort studies (n= 584,276 participants)[43,44,58,60,95,107-169] and 54 RCTs (n=

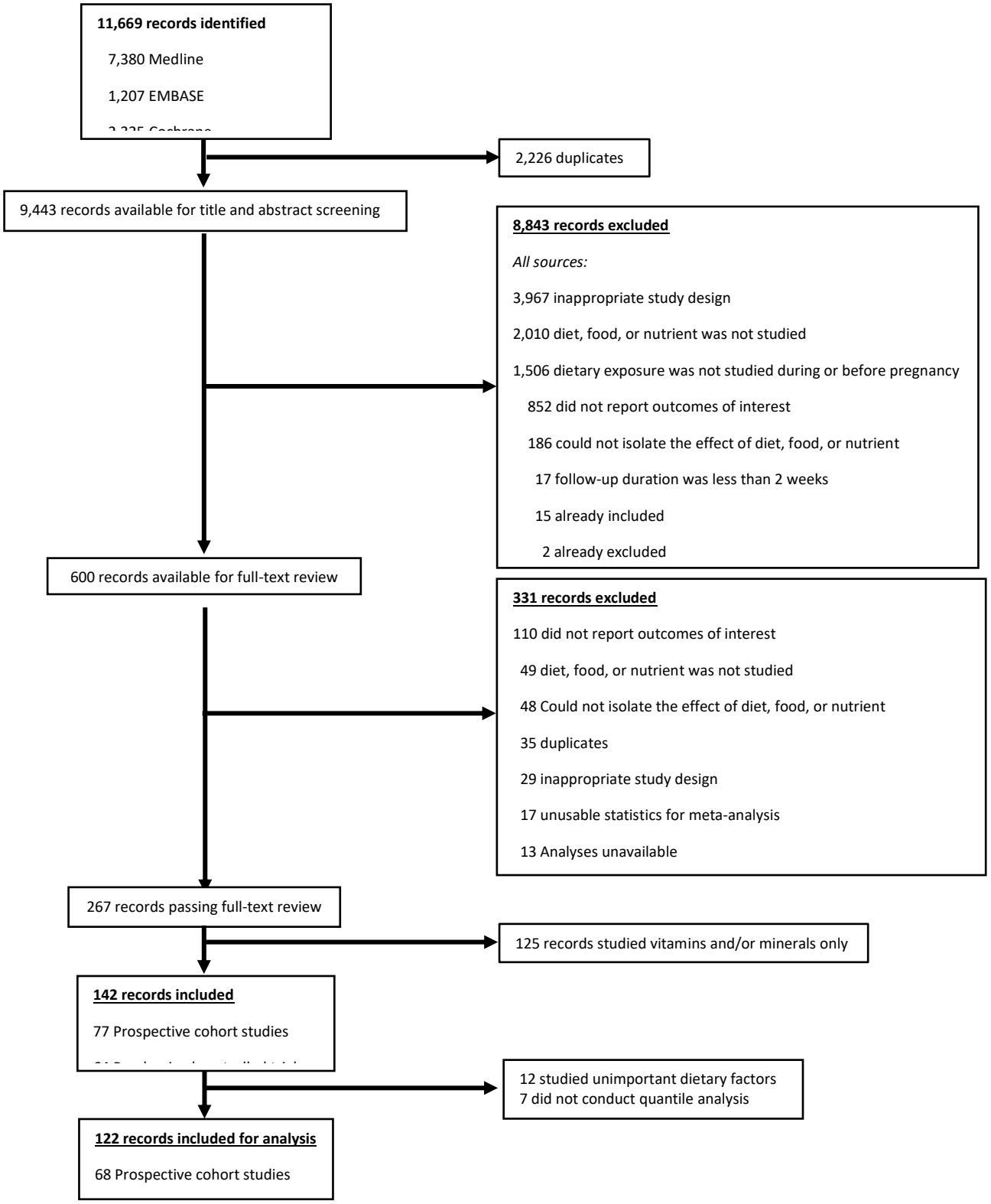
10,158 participants), of which 41 RCTs were energy-neutral (n=8,198)[51-55,61,170-204] and 10 RCTs were energy-conscious (n= 1,960)[96,205-213] (**Figure 2.1**).

2.3.2. Study characteristics

The cohort studies recruited women between 1959 and 2016 and involved women who were apparently healthy. Women were, on average, in their late-twenties at enrolment (median= 29.80 years) with a median pre-pregnancy BMI of 23.75 kg/m^2. Most studies used food frequency questionnaires (FFQs) (45 studies; 66.18%) and assessed dietary intakes during pregnancy (35 studies; 62.50%). Most studies originated in North America (31 studies; 49.21%) and Europe (22 studies; 34.92%). Sixty-three of the dietary association received a low risk of bias assessment (70.00%) (**Appendix Table 2.3.**). **Appendix Tables 2.4.** to **2.6**. details the study characteristics grouped by reported outcomes.

The RCTs recruited women between 1987 and 2016, and most women experienced gestational dysglycemia (22 trials; 47.83%) or were relatively healthy (18 trials; 39.13%). The dietary intervention began at a median of 19.80 weeks of pregnancy. The median age was 30.00 years and pre-pregnancy BMI was 25.48 kg/m^2. Most trials originated in Europe (21 trials; 44.68%), North America (15 trials; 31.91%), and some in Asia (11 trials; 23.40%). The median follow-up duration was 16 weeks (range: 3 to 31). Most RCTs were at low risk of bias due to random sequence generation, incomplete outcome data, and selective reporting; and at unclear risk of bias due to allocation concealment and blinding of reporting; and at unclear risk of bias due to allocation

Figure 2.1. Flow of the Literature Search



concealment and blinding of participants and personnel (**Appendix Figure 2.1.**). **Appendix Tables 2.7.** to **2.10**. details the study characteristics grouped by reported outcomes.

2.3.3. Glycemia and gestational diabetes mellitus

Thirty-one cohort studies (n= 207,326) reported outcomes relating to glycemia (**Appendix Figure 2.2.** compares the least-adjusted and most adjusted models). GDM risk (RR [95% CIs]; GRADE quality) increased with higher red meat (2.13 [1.68, 2.70]; high), total meat (1.68 [1.07, 2.64]; low), processed meat (1.51 [1.19, 1.91]; low), unprocessed meat (1.60 [1.22, 2.11]; low), and animal protein (1.49 [1.03, 2.16]; low) intakes; fried food (1.78 [1.27, 2.49]; moderate), adherence to Western diet (1.50 [1.15, 1.95]; low), processed food (1.88 [1.29, 2.74]; very low), GL (1.61 [1.03, 2.56]; low), and total monounsaturated fatty (MUFA) (1.55 [1.03, 2.34]; low) (**Table 2.1.;** GRADE tables in **Appendix Table 2.11.**). GDM risk decreased with higher adherence to a low-fat diet (0.71 [0.53, 0.95]; low), DASH-style diet (0.66 [0.53, 0.82]; low), healthy diet (0.63 [0.54, 0.75]; moderate), Mediterranean-style diet (0.68 [0.56, 0.82]; low), Prudent diet (0.70 [0.56, 0.87]; low), nuts and peanuts (0.73 [0.57, 0.95]; low), energy-restriction (0.36 [0.21, 0.62]; very low), whole grains (0.61 [0.39, 0.96]; low), total fibre (0.72 [0.56, 0.93]; very low), cereal fibre (0.76 [0.59, 0.98]; very low), fruit fibre (0.67 [0.51, 0.88]; very low), lower dietary cholesterol (0.63 [0.49, 0.80]; low), and vegetable protein (0.69 [0.50, 0.96]; low). We estimate that the PAR for red meat intake and GDM to be 7.26% for red meat intake and GDM.

Seventeen energy-balanced (n= 3,528) and six energy-conscious (n= 1,409) RCTs

reported on glycemic outcomes (**Table 2.1.;** GRADE table in **Appendix Tables 2.12.** and **2.13.**). GDM risk (RR [95% CIs]; GRADE quality) increased on a low-fat diet (1.37 [1.05, 1.79]; moderate). GDM risk decreased with higher energy (0.61; [0.39, 0.97]; moderate) and unsaturated fat intake (0.73 [0.56, 0.95]; moderate).

FG increased on a low-CHO and high-fat diet (**Table 2.1.;** GRADE tables in **Appendix Tables 2.12.** to **2.13.**). However, change in FG decreased on a low-fat diet, GL, complex CHO, GI, unsaturated fat, and higher energy intakes.

2.3.4. Gestational weight gain

Twenty-three cohort studies (n= 103,555) reported on outcomes relating to GWG. All but one reported least-adjusted associations between the dietary factor and GWG outcomes (**Appendix Figures 2.3.** to **2.6;** GRADE tables in **Appendix Table 2.14.**).

Twenty-nine energy-balanced (n=5,879) and nine energy-conscious (n=1,704) RCTs reported on outcomes related to GWG. The likelihood of achieving adequate GWG (RR [95% CIs]; GRADE quality) increased with adherence to a Mediterranean-style diet (2.40 [1.77, 3.25]; moderate) and with a healthy diet prescribed along with GWG advice (1.60 [1.28, 2.00]; moderate). The likelihood of excessive GWG decreased with lower GI (0.74 [0.61, 0.90]; very low) (**Table 2.2**.; GRADE tables in **Appendix Tables 2.15. and 2.16**.).

GWG decreased with greater adherence to any of four diets: a low-fat diet, a diabetes management diet, a low-CHO and high-fat diet, and a low-CHO diet with GWG advice. GWG increased with adherence to a low-CHO diet and to higher intakes of fish oil (**Table 2.2.; Appendix Figure 2.5.;** GRADE tables in **Appendix Tables 2.15.** and **2.16.**). No

Table 2.1. Summary MDs and 95% CIs for the association between each dietary factor and diabetes outcomes.*

	Cohort Studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational diabetes mellitus									
Higher red meat	2 (18,592)	2.13 (1.68, 2.70)	⊕⊕⊕⊕ HIGH	-	-	-	-	-	-
Higher fried foods	1 (15,027)	1.78 (1.27, 2.49)	⊕⊕⊕◯ MODERATE	-	-	-	-	-	-
Higher PUFA-to-SFA ratio	1 (13,475)	0.98 (0.77, 1.24)	⊕⊕⊕◯ MODERATE	-	-	-	-	-	-
Higher adherence to low-fat diet	2 (13,800)	0.71 (0.53, 0.95)	⊕⊕◯◯ LOW	1 (874)	1.37 (1.05, 1.79)	⊕⊕⊕◯ MODERATE	-	-	-
Higher adherence to DASH-style diet	1 (15,245)	0.66 (0.53, 0.82)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher adherence to healthy eating	1 (14,437)	0.75 (0.59, 0.95)	⊕⊕◯◯ LOW	1 (631)	0.92 (0.55, 1.52)	⊕◯◯◯ VERY LOW	1 (272)	1.20 (0.33, 4.28)	⊕⊕◯◯ LOW
Higher adherence to Mediterranean-style diet	2 (19,107)	0.68 (0.56, 0.82)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher adherence to Prudent diet	2 (13,278)	0.70 (0.56, 0.87)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher adherence to Western diet	2 (16,963)	1.50 (1.15, 1.95)	⊕⊕◯◯ LOW	-	-	-	-	-	-

Table 2.1. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and diabetes outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational diabetes mellitus									
Higher total dairy foods	1 (15,294)	0.95 (0.90, 1.01)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher total meats	1 (3,298)	1.68 (1.07, 2.64)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher processed meat	2 (18,592)	1.51 (1.19, 1.91)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher unprocessed meat	1 (15,294)	1.60 (1.22, 2.11)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher fish	2 (18,705)	0.96 (0.79, 1.15)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher nuts and peanuts	1 (15,294)	0.73 (0.57, 0.95)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Lower glycemic load	1 (13,110)	0.62 (0.39, 0.97)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher whole grains	1 (3,414)	0.61 (0.39, 0.96)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher cereal fibre	1 (13,110)	0.76 (0.59, 0.98)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher fruit fibre	1 (13,110)	0.67 (0.51, 0.88)	⊕⊕◯◯ LOW	-	-	-	-	-	-

Table 2.1. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and diabetes outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational diabetes mellitus									
Higher MUFA	1 (13,475)	1.55 (1.03, 2.34)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Lower trans fat	1 (13,475)	0.99 (0.90, 1.09)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Lower dietary cholesterol	2 (16,633)	0.63 (0.49, 0.80)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher animal protein	1 (15,294)	1.49 (1.03, 2.16)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher vegetable protein	1 (15,294)	0.69 (0.50, 0.96)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher adherence to low-CHO diet	2 (13,435)	1.29 (0.86, 1.93)	⊕◯◯◯ VERY LOW	-	-	-	1 (232)	0.58 (0.29, 1.16)	⊕⊕⊕◯ MODERATE
Higher adherence to high-protein diet	2 (15,619)	0.92 (0.80, 1.05)	⊕◯◯◯ VERY LOW	1 (185)	1.34 (0.74, 2.41)	⊕⊕◯◯ LOW	-	-	-
Higher processed foods	2 (4,074)	1.88 (1.29, 2.74)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher vegetables	2 (4,021)	1.00 (0.99, 1.01)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-

Table 2.1. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and diabetes outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational diabetes mellitus									
Higher low-fat dairy foods	1 (3,414)	0.57 (0.32, 1.03)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher seafoods	2 (3,447)	0.83 (0.69, 1.00)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher poultry	2 (18,592)	1.01 (0.81, 1.26)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher eggs	3 (18,620)	0.98 (0.91, 1.06)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher legumes	1 (15,294)	1.06 (0.84, 1.34)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher nuts and seeds	1 (168)	0.94 (0.76, 1.17)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher total SSBs	1 (168)	0.99 (0.97, 1.01)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher vegetable oil	1 (168)	0.80 (0.59, 1.10)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Lower energy	1 (1,135)	0.36 (0.21, 0.62)	⊕◯◯◯ VERY LOW	-	-	-	2 (309)	0.61 (0.39, 0.97)	⊕⊕⊕◯ MODERATE
Lower glycemic index	1 (13,110)	0.77 (0.59, 1.00)	⊕◯◯◯ VERY LOW	3 (1491)	0.87 (0.60, 1.26)	⊕◯◯◯ VERY LOW	-	-	-

Table 2.1. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and diabetes outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational diabetes mellitus									
Higher total fibre	2 (13,435)	0.72 (0.56, 0.93)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher vegetable fibre	1 (13,110)	0.87 (0.67, 1.13)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Lower saturated fat	1 (13,475)	1.13 (0.79, 1.60)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher PUFA	1 (13,475)	1.01 (0.77, 1.33)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher n-3	1 (13,475)	1.03 (0.78, 1.36)	⊕◯◯◯ VERY LOW	1 (140)	1.13 (0.39, 3.25)	⊕⊕◯◯ LOW	-	-	-
Higher fish oil/DHA and EPA	1 (3,279)	1.16 (0.74, 1.82)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Lower n-6	1 (13,475)	1.22 (0.89, 1.67)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher unsaturated fat	-	-	-	1 (874)	0.73 (0.56, 0.95)	⊕⊕⊕◯ MODERATE	-	-	-
Higher unsaturated-to-saturated fat ratio	-	-	-	1 (117)	1.44 (0.83, 2.49)	⊕◯◯◯ VERY LOW	-	-	-

Table 2.1. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and diabetes outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Impaired glucose tolerance									
Higher unsaturated-to-saturated fat ratio	-	-	-	1 (130)	1.03 (0.41, 2.59)	⊕◯◯◯ VERY LOW	-	-	-
Fasting glucose (mmol/L)									
Higher adherence to low-CHO and high-fat diet	-	-	-	1 (12)	0.46 (0.05, 0.87)	⊕⊕◯◯ LOW	-	-	-
Higher adherence to low-fat diet	-	-	-	1 (874)	-0.20 (-0.32, -0.08)	⊕⊕◯◯ LOW	-	-	-
Lower glycemic load	-	-	-	1 (83)	-0.31 (-0.55, -0.07)	⊕⊕◯◯ LOW	-	-	-
Higher complex CHO	-	-	-	1 (12)	-0.46 (-0.87, -0.05)	⊕⊕◯◯ LOW	-	-	-
Higher MUFA	-	-	-	1 (25)	0.50 (-0.17, 1.17)	⊕⊕◯◯ LOW	-	-	-
Lower glycemic index	-	-	-	4 (241)	-0.40 (-0.50, -0.31)	⊕◯◯◯ VERY LOW	-	-	-

Table 2.1. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and diabetes outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Fasting glucose (mmol/L)									
Higher unsaturated-to-saturated fat ratio	-	-	-	1 (130)	0.04 (-0.10, 0.18)	⊕◯◯◯ VERY LOW	-	-	-
Higher unsaturated fat	-	-	-	2 (958)	-0.17 (-0.28, -0.05)	⊕◯◯◯ VERY LOW	-	-	-
Lower energy	-	-	-	-	-	-	3 (649)	-0.50 (-0.58, -0.42)	⊕◯◯◯ VERY LOW
1-hour OGTT (mmol/L)									
Higher adherence to high-protein diet	-	-	-	1 (185)	0.10 (-0.33, 0.53)	⊕⊕◯◯ LOW	-	-	-
2-hour OGTT (mmol/L)									
Higher adherence to high-protein diet	-	-	-	1 (185)	0.21 (-0.14, 0.56)	⊕⊕◯◯ LOW	-	-	-
Lower energy	-	-	-	-	-	-	1 (50)	0.30 (-0.41, 1.01)	⊕⊕◯◯ LOW

Table 2.1. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and diabetes outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Number of hypoglycaemic events									
Higher adherence to diabetes management diet	-	-	-	1 (50)	5.00 (-3.19, 13.19)	⊕⊕⊕◯ MODERATE	-	-	-
Higher total fibre	-	-	-	1 (50)	-5.00 (-13.19, 3.19)	⊕⊕⊕◯ MODERATE	-	-	-

Abbreviations: CHO, carbohydrate; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MD, mean difference; MUFA, monounsaturated fatty acids; n-3, omega-3; n-6, omega-6; OGTT, oral glucose tolerance test; PUFA, polyunsaturated fatty acids; RD, risk difference; RR, relative risk; SFA, saturated fatty acids.

* RCTs were divided into energy-neutral and energy-conscious. Energy-neutral RCTs include RCTs, where the intended energy intake for both the intervention and comparator arms were similar, and energy-conscious refers to RCTS, where the energy intake was lower in the intervention than the comparator arm.

† Effect estimates are RR or MD or RD (95% CIs). Relative risk (RR) was reported in gestational diabetes mellitus and impaired glucose tolerance. Mean difference (MD) was reported in fasting glucose, and 1-hour and 2-hour OGTT. Risk difference (RD) was reported in number of hypoglycemic events.

‡ Quality of evidence as assessed by GRADE.

other dietary exposures reported significant association with GWG measures.

2.3.5. Hypertensive disorders of pregnancy

Twenty-four cohort studies (n= 343,068) reported outcomes relating to HDP (**Appendix Figures 2.7.** and **2.8.;** GRADE tables in **Appendix Table 2.17.**). Pre-eclampsia risk (RR [95% CIs]; GRADE quality) increased PUFA (2.61 [1.29, 5.29]; moderate), processed foods (1.21 [1.03, 1.42]; low), and sugar-sweetened beverages (SSBs) (1.27 [1.05, 1.54]; very low) (**Table 2.3.**). Conversely, pre-eclampsia risk decreased with lower energy (0.27 [0.11, 0.65]; moderate), higher adherence to Nordic diet (0.86 [0.79, 0.94]; moderate), DASH-style diet (0.74 [0.65, 0.84]; low), healthy diet (0.72 [0.62, 0.84]; low), vegetables (0.79 [0.62, 0.99]; low), total fibre (0.28 [0.11, 0.73]; very low), insoluble (0.35 [0.14, 0.88]; very low), and soluble fibre (0.30 [0.11, 0.83]; very low). No other dietary component reported significant association with pre-eclampsia or GH.

Twenty-three energy-balanced (n= 4,444) and six energy-conscious (n= 1,034) RCTs reported on outcomes relating to HDP (**Table 2.3.**; GRADE tables in **Appendix Tables 2.18.** and **2.19.**). Pre-eclampsia risk (RR [95% CIs]; GRADE quality) decreased on a diabetes management diet (0.46 [0.24, 0.89]; moderate) and GH risk decreased on a low-CHO diet with GWG advice provided (0.21 [0.06, 0.75]; moderate).

SBP decreased with higher dark chocolate intakes (**Table 2.3.;** GRADE tables in **Appendix Tables 2.18.** and **2.19.**). Both SBP and DBP decreased with higher fish oil intake. No other dietary components reported significant effects on HDP measures.

Table 2.2. Summary MDs and 95% CIs for the association between each dietary factor and body weight outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Inadequate weight gain									
Lower glycemic index	-	-	-	3 (736)	1.27 (1.00, 1.62)	⊕◯◯◯ VERY LOW	-	-	-
Higher adherence to healthy eating	-	-	-	-	-	-	1 (307)	0.53 (0.27, 1.07)	⊕⊕⊕◯ MODERATE
Adequate weight gain									
Higher adherence to Mediterranean-style diet	-	-	-	1 (120)	2.40 (1.77, 3.25)	⊕⊕⊕◯ MODERATE	-	-	-
Higher n-3	-	-	-	1 (150)	1.58 (0.80, 3.15)	⊕⊕⊕◯ MODERATE	-	-	-
Higher adherence to high protein diet	-	-	-	1 (185)	1.11 (0.52, 2.33)	⊕⊕◯◯ LOW	-	-	-
Lower glycemic index	-	-	-	3 (736)	1.12 (0.93, 1.35)	⊕◯◯◯ VERY LOW	-	-	-
Higher unsaturated-to-saturated fat ratio	-	-	-	1 (156)	1.23 (0.81, 1.89)	⊕◯◯◯ VERY LOW	-	-	-
Higher adherence to healthy eating	-	-	-	-	-	-	2 (579)	1.60 (1.28, 2.00)	⊕⊕⊕◯ MODERATE

Table 2.2. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and body weight outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Excessive weight gain									
Lower glycemic index	-	-	-	4 (833)	0.74 (0.61, 0.90)	⊕◯◯◯ VERY LOW	-	-	-
Higher unsaturated-to-saturated fat ratio	-	-	-	1 (156)	0.87 (0.60, 1.26)	⊕◯◯◯ VERY LOW	-	-	-
Higher adherence to healthy eating	-	-	-	-	-	-	1 (307)	0.95 (0.75, 1.21)	⊕⊕⊕◯ MODERATE
Gestational weight gain (kg)									
Higher adherence to low-CHO diet	-	-	-	1 (68)	0.71 (0.06, 1.36)	⊕⊕◯◯ LOW	1 (232)	-13.59 (-19.29, -7.89)	⊕◯◯◯ VERY LOW
Adherence to low-fat diet	-	-	-	1 (874)	-0.20 (-0.32, -0.08)	⊕⊕◯◯ LOW	-	-	-
Adherence to high-protein diet	-	-	-	1 (185)	-0.28 (-1.67, 1.11)	⊕⊕◯◯ LOW	-	-	-
Higher adherence to DASH-style diet	-	-	-	2 (85)	-1.63 (-4.31, 1.05)	⊕⊕◯◯ LOW	-	-	-
Higher adherence to diabetes management diet	-	-	-	2 (981)	-2.57 (-4.99, -0.15)	⊕⊕◯◯ LOW	-	-	-
Low glycemic load	1 (1,186)	-0.82 (-1.92, 0.28)	⊕◯◯◯ VERY LOW	2 (121)	-0.48 (-1.95, 1.00)	⊕⊕◯◯ LOW	-	-	-

Table 2.2. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and body weight outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational weight gain (kg)									
Higher complex CHO	-	-	-	1 (12)	0.60 (-3.32, 4.52)	⊕⊕◯◯ LOW	-	-	-
Higher n-3	-	-	-	1 (150)	0.25 (-0.97, 1.47)	⊕⊕◯◯ LOW	-	-	-
Higher fish oil/DHA and EPA	-	-	-	3 (200)	0.70 (0.16, 1.23)	⊕⊕◯◯ LOW	-	-	-
Low-CHO and high-fat diet	-	-	-	3 (182)	-0.87 (-1.46, -0.27)	⊕◯◯◯ VERY LOW	-	-	-
Higher adherence to healthy eating	-	-	-	1 (576)	0.30 (-0.50, 1.10)	⊕◯◯◯ VERY LOW	2 (292)	-2.54 (-5.31, 0.24)	⊕⊕◯◯ LOW
Higher adherence to Mediterranean-style diet	-	-	-	2 (397)	0.34 (-0.20, 0.88)	⊕◯◯◯ VERY LOW	-	-	-
Higher total dairy foods	-	-	-	1 (49)	0.20 (-5.90, 6.30)	⊕◯◯◯ VERY LOW	-	-	-
Higher chocolate	-	-	-	1 (90)	-1.40 (-7.50, 4.70)	⊕◯◯◯ VERY LOW	-	-	-
Lower glycemic index	-	-	-	5 (1571)	0.00 (-0.49, 0.49)	⊕◯◯◯ VERY LOW	-	-	-

Table 2.2. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and body weight outcomes.*

	Cohort studies			Energy-neutral RCTs			Energy-conscious RCTs		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational weight gain (kg)									
Higher total fibre	-	-	-	2 (70)	-0.32 (-7.46, 6.82)	⊕◯◯◯ VERY LOW	-	-	-
Higher unsaturated-to-saturated fat ratio	-	-	-	1 (156)	-0.10 (-1.70, 1.50)	⊕◯◯◯ VERY LOW	-	-	-
Higher unsaturated fat	-	-	-	2 (958)	0.33 (-0.27, 0.94)	⊕◯◯◯ VERY LOW	-	-	-
Lower energy	-	-	-	-	-	-	5 (1323)	-1.93 (-4.86, 1.00)	⊕◯◯◯ VERY LOW

Abbreviations: CHO, carbohydrate; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MD, mean difference; n-3, omega-3; RR, relative risk

* RCTs were divided into energy-neutral and energy-conscious. Energy-neutral RCTs include RCTs, where the intended energy intake for both the intervention and comparator arms were similar, and energy-conscious refers to RCTS, where the energy intake was lower in the intervention than the comparator arm.

† Relative risk (RR) was reported in inadequate gestational weight gain, adequate weight gain, and excessive weight gain. Mean difference (MD) was reported in gestational weight gain.

‡Quality of evidence as assessed by GRADE.

2.3.6. Blood lipids

Eight energy-balanced RCTs (n= 824) reported blood lipid outcomes (**Appendix Table 2.20.**; GRADE tables in **Appendix Table 2.21.**). LDL-C decreased with higher adherence to a Mediterranean-style diet. Non-HDL-C decreased with higher unsaturated fat, MUFA, and fish oil and increased with higher GI. TG decreased with low GL and unsaturated fat intakes. No other dietary interventions reported significant effects on blood lipid measures.

2.3.7. Consistency of findings between cohort studies and RCTs

Six dietary comparisons had data available from both cohort studies and RCTs for the GDM analysis, 5 for pre-eclampsia, 1 for GH, and 1 for GWG as continuous measure. The directions of these relationships were similar for most of these dietary associations: cohort studies and RCTs agreed for energy restriction and GDM (n_{cohort}= 1 and n_{RCT}= 2; protective), high protein diet and GDM (n_{cohort}= 2 and n_{RCT}= 1; null), low GI and GDM (n_{cohort}= 1 and n_{RCT}= 3; null), high omega-3 (n-3) and GDM (n_{cohort}= 1 and n_{RCT}= 1; null), low-fat intake and pre-eclampsia (n_{cohort}=1 and n_{RCT}= 1; null), high n-3 and pre-eclampsia (n_{cohort}= 1 and n_{RCT}= 1; null), high fish oil and pre-eclampsia (n_{cohort}= 1 and n_{RCT}= 4; null), and high n-3 and GH (n_{cohort}= 1 and n_{RCT}= 5; null). Cohort studies and RCTs did not agree in the other 4 dietary comparisons. Only energy restriction significantly reduced GDM risk in both cohorts and RCTs (**Figure 2.2.**).

2.4. Discussion

We have synthesized the literature examining the association of 60 dietary factors with

Table 2.3. Summary MDs and 95% CIs for the association between each dietary factor and hypertensive disorders of pregnancy outcomes.*

	Cohort studies			Energy-neutral trials			Energy-conscious trials		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Pre-eclampsia									
Low energy	1 (3,133)	0.27 (0.11, 0.65)	⊕⊕⊕◯ MODERATE	-	-	-	3 (274)	1.03 (0.55, 1.92)	⊕◯◯◯ VERY LOW
Higher PUFA	1 (3,133)	2.61 (1.29, 5.29)	⊕⊕⊕◯ MODERATE	-	-	-	-	-	-
Higher adherence to Nordic diet	1 (72,072)	0.86 (0.79, 0.94)	⊕⊕⊕◯ MODERATE	-	-	-	-	-	-
Higher adherence to DASH-style diet	1 (28,192)	0.74 (0.65, 0.84)	⊕⊕◯◯ LOW	4 (163)	0.99 (0.34, 2.92)	⊕⊕◯◯ LOW	-	-	-
Higher adherence to healthy diet	1 (23,423)	0.72 (0.62, 0.84)	⊕⊕◯◯ LOW	-	-	-	2 (528)	0.52 (0.22, 1.23)	⊕⊕◯◯ LOW
Higher processed foods	1 (23,423)	1.21 (1.03, 1.42)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher fruits	1 (32,933)	0.79 (0.67, 0.93)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher vegetables	1 (28,192)	0.79 (0.62, 0.99)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher desserts and sweets	1 (23,423)	0.90 (0.77, 1.05)	⊕⊕◯◯ LOW	-	-	-	-	-	-
Higher adherence to low-fat diet	1 (3,133)	1.99 (0.75, 5.31)	⊕◯◯◯ VERY LOW	1 (874)	1.54 (0.59, 4.02)	⊕⊕◯◯ LOW	-	-	-

Table 2.3. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and hypertensive disorders of pregnancy outcomes.*

	Cohort studies			Energy-neutral trials			Energy-conscious trials		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Pre-eclampsia									
Higher adherence to high-protein diet	1 (3,133)	0.60 (0.27, 1.34)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher seafoods	1 (3,279)	1.25 (0.55, 2.84)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher total SSBs	1 (32,933)	1.27 (1.05, 1.54)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher honey	1 (33,549)	0.90 (0.78, 1.03)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher total fibre	1 (1,538)	0.28 (0.11, 0.73)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher insoluble fibre	1 (1,538)	0.35 (0.14, 0.88)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher soluble fibre	1 (1,538)	0.30 (0.11, 0.83)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher added sugar	2 (36,126)	1.08 (0.91, 1.28)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher saturated fat	1 (3,133)	0.40 (0.12, 1.32)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher MUFA	1 (3,133)	1.11 (0.50, 2.43)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-

Table 2.3. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and hypertensive disorders of pregnancy outcomes.*

	Cohort studies			Energy-neutral trials			Energy-conscious trials		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Pre-eclampsia									
Higher fish oil/DHA and EPA	1 (3,279)	0.63 (0.33, 1.21)	⊕◯◯◯ VERY LOW	4 (1,536)	0.56 (0.16, 1.92)	⊕⊕◯◯ LOW	-	-	-
Higher n-3	1 (3,133)	1.80 (0.89, 3.65)	⊕◯◯◯ VERY LOW	1 (54)	0.33 (0.01, 7.84)	⊕⊕◯◯ LOW	-	-	-
Lower n-6	1 (3,133)	1.90 (0.98, 3.70)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Lower trans fat	1 (63,226)	1.02 (0.87, 1.20)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher adherence to diabetes management diet	-	-	-	1 (931)	0.46 (0.24, 0.89)	⊕⊕⊕◯ MODERATE	-	-	-
Higher adherence to Mediterranean-style diet	-	-	-	1 (290)	0.92 (0.34, 2.48)	⊕◯◯◯ VERY LOW	-	-	-
Higher chocolate	-	-	-	1 (90)	0.00* (-0.04, 0.04)	⊕⊕◯◯ LOW	-	-	-
Lower glycemic load	-	-	-	1 (84)	1.00 (0.06, 15.47)	⊕⊕◯◯ LOW	-	-	-
Higher unsaturated fat	-	-	-	1 (874)	0.65 (0.25, 1.70)	⊕⊕◯◯ LOW	-	-	-
Higher adherence to low-CHO diet	-	-	-	-	-	-	1 (232)	0.64 (0.26, 1.58)	⊕⊕◯◯ LOW

Table 2.3. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and hypertensive disorders of pregnancy outcomes.*

	Cohort studies			Energy-neutral trials			Energy-conscious trials		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational hypertension									
Higher seafoods	1 (3,279)	1.13 (0.79, 1.60)	⊕◯◯◯ VERY LOW	-	-	-	-	-	-
Higher fish oil/DHA and EPA	1 (3,279)	1.14 (0.85, 1.53)	⊕◯◯◯ VERY LOW	5 (1,731)	1.02 (0.86, 1.21)	⊕⊕⊕◯ MODERATE	-	-	-
Higher adherence to diabetes management diet	-	-	-	1 (931)	0.75 (0.47, 1.20)	⊕⊕⊕◯ MODERATE	-	-	-
Higher adherence to low-fat diet	-	-	-	1 (874)	1.42 (0.69, 2.93)	⊕⊕◯◯ LOW	-	-	-
Higher chocolate	-	-	-	1 (90)	0.00* (-0.04, 0.04)	⊕⊕◯◯ LOW	-	-	-
Lower glycemic index	-	-	-	1 (20)	0.33 (0.02, 7.32)	⊕⊕◯◯ LOW	-	-	-
lower glycemic load	-	-	-	1 (84)	0.35 (0.01, 8.34)	⊕⊕◯◯ LOW	-	-	-
Higher unsaturated fat	-	-	-	1 (874)	0.70 (0.34, 1.46)	⊕⊕◯◯ LOW	-	-	-
Higher adherence to low-CHO and high-fat diet	-	-	-	1 (150)	3.08 (0.64, 14.78)	⊕◯◯◯ VERY LOW	-	-	-
Higher adherence to Mediterranean-style diet	-	-	-	1 (259)	0.98 (0.48, 2.01)	⊕◯◯◯ VERY LOW	-	-	-

Table 2.3. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and hypertensive disorders of pregnancy outcomes.*

	Cohort studies			Energy-neutral trials			Energy-conscious trials		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Gestational hypertension									
Lower energy	-	-	-	-	-	-	1 (50)	0.29 (0.04, 2.44)	⊕⊕◯◯ LOW
Higher adherence to low-CHO diet	-	-	-	-	-	-	1 (232)	0.21 (0.06, 0.75)	⊕⊕⊕◯ MODERATE
Higher adherence to healthy diet	-	-	-	-	-	-	1 (272)	0.80 (0.12, 5.48)	⊕⊕◯◯ LOW
Systolic blood pressure (mmHg)									
Higher adherence to low-fat diet	-	-	-	1 (874)	0.00 (-0.00, 0.00)	⊕⊕◯◯ LOW	-	-	-
Higher total dairy foods	-	-	-	1 (49)	-1.00 (-5.53, 3.53)	⊕⊕◯◯ LOW	-	-	-
Higher dark chocolate	-	-	-	1 (90)	-6.70 (-11.23, -2.17)	⊕⊕◯◯ LOW	-	-	-
Lower glycemic load	-	-	-	1 (38)	-2.00 (-7.37, 3.37)	⊕⊕◯◯ LOW	-	-	-
Higher unsaturated fat	-	-	-	1 (874)	0.00 (-0.00, 0.00)	⊕⊕◯◯ LOW	-	-	-
Higher MUFA	-	-	-	1 (27)	1.00 (-14.31, 16.31)	⊕◯◯◯ VERY LOW	-	-	-
Higher fish oil/DHA & EPA	-	-	-	5 (1,498)	-2.57 (-2.68, -2.46)	⊕◯◯◯ VERY LOW	-	-	-

Table 2.3. CONTINUED. Summary MDs and 95% CIs for the association between each dietary factor and hypertensive disorders of pregnancy outcomes.*

	Cohort studies			Energy-neutral trials			Energy-conscious trials		
Dietary factors	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**	***n* studies (*n* women)**	**Effect estimate†**	**Quality of evidence‡**
Diastolic blood pressure (mmHg)									
Higher adherence to low-fat diet	-	-	-	1 (874)	1.00 (-0.96, 2.96)	⊕⊕◯◯ LOW	-	-	-
Higher total dairy foods	-	-	-	1 (49)	1.00 (-2.19, 4.19)	⊕⊕◯◯ LOW	-	-	-
Higher chocolate	-	-	-	1 (90)	-2.90 (-6.09, 0.29)	⊕⊕◯◯ LOW	-	-	-
Lower glycemic load	-	-	-	1 (38)	-2.00 (-5.80, 1.80)	⊕⊕◯◯ LOW	-	-	-
Higher unsaturated fat	-	-	-	1 (874)	1.00 (-0.96, 2.96)	⊕⊕◯◯ LOW	-	-	-
Higher fish oil/DHA & EPA	-	-	-	5 (1,498)	-4.08 (-4.65, -3.51)	⊕⊕◯◯ LOW	-	-	-
High MUFA	-	-	-	1 (27)	1.00 (-8.80, 10.80)	⊕◯◯◯ VERY LOW	-	-	-

Abbreviations: CHO, carbohydrate; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MD, mean difference; MUFA, monounsaturated fatty acids; n-3, omega-3; n-6, omega-6; PUFA, polyunsaturated fatty acids; RR, relative risk; SSBs, sugar-sweetened beverages.

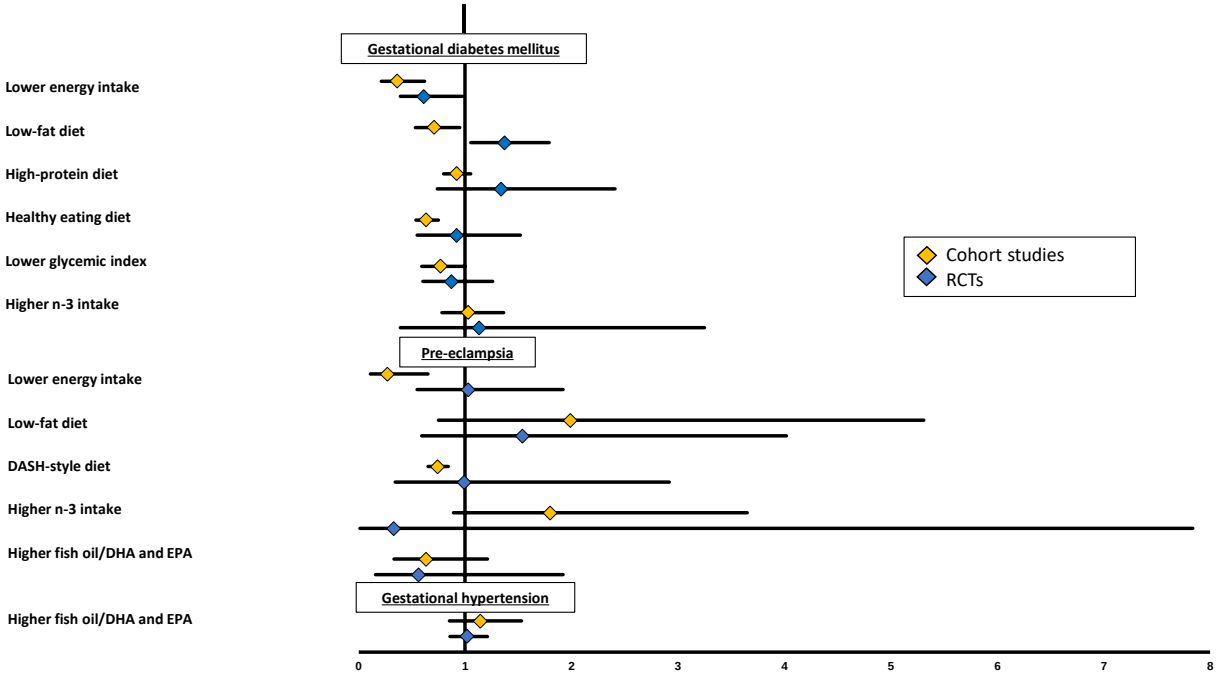
* RCTs were divided into energy-neutral and energy-conscious. Energy-neutral RCTs include RCTs, where the intended energy intake for both the intervention and comparator arms were similar, and energy-conscious refers to RCTS, where the energy

intake was lower in the intervention than the comparator arm.

† Relative risk (RR) was reported in pre-eclampsia and gestational hypertension. Mean difference (MD) was reported in systolic and diastolic blood pressure.

‡ Quality of evidence as assessed by GRADE.

Figure 2.2. Consistency of the evidence from cohort studies and randomized control trials.



18 pregnancy outcomes. Of the 214 associations, the strongest evidence was for a 113% increased risk of GDM with higher intakes of red meat. We also found that a healthy diet and the Mediterranean diet may protect against several common metabolic disorders of pregnancy. Where data was available in both cohort studies and RCTs, only energy restriction showed a consistent protection against GDM risk in both study designs. However, much of the body of evidence of our systematic review and meta-analysis was of poor quality (81.12%).

2.4.1. Association of red meat intake and GDM risk

We have the highest confidence in the finding that higher red meat intake increases GDM risk. The two cohort studies on which this is based were of high methodological quality (i.e. NOS= 9), found a strong association dose-response (i.e. RR >2.0 comparing the highest to lowest exposure), and provided a highly precise measure of association in a large sample (i.e. >15,000). Our findings are congruent with the findings of a harmful association between red meat and T2DM.[214-216] In our study, every serving of red meat (e.g. 3-oz) increases the risk of GDM by 74% (95% CIs: 46, 108%). Two components of red meat that are likely involved in affecting diabetes risk are cholesterol and heme-iron. Dietary cholesterol impairs insulin sensitivity via increased hepatic cholesterol esters[217,218] and high intakes of heme-iron can cause β-cell dysfunction and insulin resistance, via increased oxidative stress.[219] Furthermore, methods of processing and preparing red meat can create by-products such as nitrosamines or advanced glycation end products, which other studies have shown to impair β-cell function.[220]

2.4.2. Association of dietary patterns and risk of metabolic disorders of pregnancy

Most major health organizations including DC, NICE, SOGC, and WHO recommend women to follow a healthy diet during pregnancy.[18,50,97,221] The precise definition of a healthy diet varies, but foods generally common to healthful dietary patterns include fruits and vegetables, whole grains, legumes, nuts, and lean meat. Overall, we have moderate confidence in the finding that a healthy dietary pattern supports a healthy pregnancy. This means that we believe the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Across the metabolic disorder spectrum, we found evidence that following a healthy diet may reduce GDM risk by 37% (95% CIs: 25, 46%), pre-eclampsia by 28% (95% CIs: 16, 38%), and when combined with GWG advice, increases the likelihood of adequate GWG by 160% (95% CIs: 128, 200%). Although these findings are congruent with current dietary guidelines for the management of GDM,[18,50,97,221] the evidence on which these findings are based on is of low quality and lacks consistency. For example, though cohort studies show that a healthy diet is protective against GDM, this was not the case in RCTs. Further, while a healthy diet with GWG advice increases the likelihood of adequate GWG, it did not appear to modify the risk of inadequate or excessive GWG.

Healthy eating may still be beneficial for women during pregnancy despite these incongruency. Drawing from findings in studies in the non-pregnant population (men and women), healthy eating patterns improved body weight, T2DM, and CVD risk.[222-225] These findings have resulted in several major health organization recommending healthy eating

patterns to manage metabolic risk in non-pregnant populations.[226-229] Furthermore, following a healthy diet may displace unhealthy foods from the diet such as SSBs, refined CHO, and fried foods, which are features of a "Western" diet and our study showed that this type of diet increased GDM risk and GWG. Therefore, although the current evidence for healthy eating pattern during pregnancy is weak, the consistency of evidence with non-pregnant populations and a comparison with the alternative diet that is high in energy-dense foods, adherence to a healthy eating pattern may have favourable effects on the health of the women.

A Mediterranean-style diet may offer women protection against GDM, excessive GWG, and dyslipidemia. Although current dietary recommendations for pregnancy do not mention the Mediterranean-style diet, the USDA recommend this dietary pattern for the general population.[226] The diet is characterized by high intakes of whole grains, fruits, vegetables, beans, herbs, spices, nuts, healthy fats such as olive oil, and some intakes of fish, seafoods, and dairy foods. We found that a higher adherence to a Mediterranean-style diet is associated with a 32% (95% CIs: 15, 44%) GDM risk reduction, 2.5-times (95% CIs: 1.77, 3.25) increased likelihood of achieving appropriate GWG, and a 0.10 mmol/L (95% CIs: -0.18, -0.02) LDL-C reduction without increasing the risk of pre-eclampsia and GH. Foods that make up these dietary patterns, including nuts and peanuts, whole grains, higher fibre, and vegetable intake were protective against GDM and pre-eclampsia. Red meat, processed foods and meats, animal protein, and SSBs, foods that characteristically avoided on a Mediterranean-style diet, increased the risk for GDM or pre-eclampsia.

Although the confidence we have in most of the above dietary comparisons is low, the consistency of the effect estimates across food components of the Mediterranean-style diet increases our confidence that diets in high in fruits and vegetables, and whole grains, and low in sugary foods and drinks, and processed and red meat, supports a healthy pregnancy.

Dietary quality (types of foods and beverages consumed) and quantity (total energy) are likely important for a healthy pregnancy. We found that lower energy intake reduced the risk of pre-eclampsia and GDM; however, in RCTs where investigators gave GWG advice in addition to the dietary intervention (i.e. both quality and quantity were addressed), there appeared to be no additional benefit of energy-restriction when quality was good. The reason for this is not clear. It may relate to the small number and size (n<500) of RCTs that targeted energy intake. It may also relate to adherence with dietary interventions. Most RCTs did not report adherence; however, in those that did, often it was poor. Thus, these trials may have achieved an insufficient treatment contrast to detect the desired treatment effect on the primary clinical outcomes. These limitations underscore a major challenge of conducting RCTs in nutrition: achieving high adherence over a long period of time. Even in a highly-motivated population (pregnant women) followed for a relatively short time period (<6 months), this has proven difficult. Indeed, the difficulty in conducting proper RCTs in nutrition is evident in the PREDIMED (Prevención con Dieta Mediterránea) trial that compared the Mediterranean diet vs low-fat diet, which was retracted for inadequate randomization, re-analyzed, and republished

as a less-reliable cohort study.[230] More research is needed to understand effective strategies for behaviour change during pregnancy and identify resources to facilitate adherence to these changes.

2.4.3. Consistency of evidence between cohort studies and RCTs

When findings of cohort studies and RCTs are inconsistent, it makes it more difficult for women and their healthcare providers to identify healthy food choices during pregnancy. We found such discrepant findings to be infrequent. Out of the 12 associations tested with both designs, 4 results from cohort studies were contradicted by RCTs (e.g. low-fat diet and GDM, healthy eating and GDM, energy intake and pre-eclampsia, and DASH-style diet and pre-eclampsia). This overall general consistency of the findings between study designs increases our confidence in the relationship between these dietary factors and health outcomes, because each study design corrects the methodological limitations of the other (e.g. exposure misclassification, length of follow-up, adherence, control of confounding, etc.).[231]

We identified discrepant findings between cohort studies and RCTs in our analysis. In reviewing each of these, methodological limitations of both designs made it difficult for us to conclude with certainty which of the estimate (cohort studies or RCT) was more reliable. For example: 1) of the low-fat diet and GDM analysis, the pooled cohort study reported extreme fat intake that is atypical of diets studied in RCTs and suffered from confounding by other nutrients. Bower et al.,[112] which had the most weight on the pooled effect estimate (84.2%), reported that median fat intake in the highest quintile was

75.05% of total energy intake compared to the reference group which consumed 48.30%. Further, those in the highest quintile of fat intake also consumed a high amount of red meat and a low amount of fruits and vegetables, which was not accounted for in the multi-variable analyses. The single included RCT suffered from both an insufficient dietary contrast and a comparator arm that was healthier than typical. The comparator arm was a Mediterranean diet that promoted intakes of healthy fats (participants received olive oil (≥40mL/d) and pistachios (25-30 g/d).[174] This type of dietary pattern, however, has previously shown to reduce T2DM incidence in the PREDIMED trial.[232] 2) Of the energy intake and PE analysis, the cohort study reported extreme intakes of energy that is atypical of diets studied in RCTs and also suffered from confounding. The cohort study reported that the highest energy intake quantile was >3000 kcal/d versus the reference group which was reported <2000 kcal/d, and the analysis did not adjust for energy expenditure (e.g. physical activity) which may have confounded the findings.[118] The included RCTs assessed lower energy intake compared to the cohort study and also suffered from poor dietary contrast. Of the three RCTs included in the pooled analysis, two reported an adequate energy intake contrast (average contrast= 700 kcal/day) between the arms;[207,212] however, the RCT that carried the highest meta-analytic weight (Rae et al.; 88.0%) reported similar energy intake between the intervention and comparator arms (1566 kcal/d vs 1630 kcal/d).[210] 3) Of the DASH-style diet and pre-eclampsia, the differences in findings between the cohort studies and RCTs may be due to differences in participant characteristics. The one included cohort study enrolled

nulliparous White-Caucasians living in Norway and the pooled RCTs included women from Iran and China, with a combination of nulliparous and multiparous women. Both ethnicity and parity have differential association with pre-eclampsia risk.[233] Further, although both the cohort study and RCTs assessed "DASH-style diet", the actual foods that make up each of the major food groups of the DASH-style diet maybe very different. For example, commonly consumed vegetables in Norway are root vegetables (e.g. carrots, rutabaga, onions), cabbages, and potatoes,[234] whereas commonly consumed vegetables in China are green beans, bok choy, and bitter melon. Thus, the dietary label (e.g. DASH-style diet) may be the same across these studies but the foods that make up the diet may be different in different settings, which may influence the association of the dietary factor and pre-eclampsia risk.

Of the healthy eating diet and GDM analysis, we were also less certain of the findings reported in the RCTs than the cohort studies assess a healthy eating diet because of smaller than planned achieved dietary contract between the "healthy" and the low GI diet. In this study, the achieved GI difference was 3 units (55.8 vs 52.8).[53]

2.4.4. Limitations

We often downgraded the quality of the cohort studies for the use of single and/or short-term measures of dietary intakes (e.g. 24-hour dietary recalls) or an interviewer-based FFQ as well as a failure to completely adjust for important confounders (e.g. age, gestational age, and history of diabetes or hypertension). RCTs of low quality often suffered from poor dietary adherence and low statistical power. In addition to these

methodological limitations, most of the data came from women living in North American and Europe, which may limit the generalizability of these findings to women living in other parts of the world. The most highly-rated evidence to inform dietary guidelines is that from both prospective cohort studies and RCTs. Larger and higher-quality RCTs in multi-ethnic population in moderate and low-income countries are needed to confirm the role of diet on the health of the women during pregnancy.

A significant limitation of our study was the small number of reports (<10) that were included for any given dietary comparisons. For this reason, we were unable to conduct subgroup analyses or assess publication bias with acceptable reliability. Second, most RCTs included in our analysis reported on biomarkers of metabolic disorders of pregnancy (e.g. weight change, fasting glucose, and blood pressure) rather than on the clinically-important outcomes (e.g. excessive GWG, GDM, and HDP). As the conduct of RCTs is feasible in this population and a well-designed, conducted trial with high follow-up and adherence represents the highest level of evidence for causal inference, higher quality RCTs examining and reporting on clinical outcomes are needed. Third, we only considered metabolic outcomes experienced during the index pregnancy. Although a dietary factor may not affect metabolic complications in women during pregnancy, it may still predict or serve as a marker for poor post-partum health outcomes in woman and/or her infant. Thus, readers should consider our results in the context of the effects that may occur post-partum. Last, the generalizability of our findings is limited because most of the cohort studies and RCTs included relatively healthy women in high-income North

American or European countries. We need more research into how diet may affect pregnancy outcomes in more ethnically-diverse populations in moderate and low-income countries.

2.5. Conclusions

Diet choices may increase or decrease a woman's risk of developing metabolic disorders of pregnancy. The use of rigorous methodology is essential to identify, appraise, and synthesize the evidence used to support guidelines for healthy eating during pregnancy. Our systematic review and meta-analysis found high quality evidence that red meat increases the risk of GDM and low-quality evidence that a healthy diet and a Mediterranean-style diet support metabolic health during pregnancy. The evidence base from cohort studies and RCTs is sparse and mostly of low-quality. More high-quality cohort studies (where important confounding variables are adjusted and validated FFQs are used to ascertain food intakes) and RCTs (where sufficient dietary contrast is achieved with adequate statistical power) are needed to better understand the relationship between dietary factors and metabolic diseases of pregnancy.

CHAPTER 3. THE EFFECTS OF VARIOUS DIETS ON GLYCEMIC OUTCOMES DURING PREGNANCY

3.1. Introduction

The need for implementation of effective dietary strategies in GDM prevention and management has been emphasized by diabetes organizations.[10,17,18] Most women also prefer to not use medications to manage their diabetes risk during pregnancy.[235]

One method of managing GDM risk is the use of dietary strategies. Data from individual randomized trials suggest benefits of dietary strategies in diabetes control.[53,55,61] The success of diet and lifestyle changes in managing T2DM, some of its etiology shared with GDM, in high-risk patients further emphasize the importance of dietary strategies in GDM management.[236] Nonetheless, the evidence to support the application of dietary strategies to the treatment of GDM is lacking.[10,17,18] Further, a clear benefit for dietary strategies have not been demonstrated in recent meta-analyses.[237,238] However, these analyses have usually been limited to single pair-wise dietary comparisons with a small number of participants. Furthermore, single pair-wise comparisons do not lend itself easily to determine if it is the most effective strategy amongst all the possible dietary strategies for GDM control.

The above concerns are reflected in current dietary guidelines for GDM prevention and management. Recommendations by the DC have not been updated in almost a decade and most are based on expert consensus, despite that dietary interventions are recommended as the first-line of therapy.[18] This has been echoed by the ADA and the

NICE in the UK, both of which claim no evidence-based recommendations can be made given the lack of high-quality research in this area.[10,17] Although the importance of diet is acknowledged in GDM prevention and management, current dietary recommendations for GDM are sparse, and where it exists, is outdated or based on experts' opinion.[10,17,18]

Our goal in this study was to conduct a systematic review and network meta-analysis (NMA) of randomized trials to compare and rank the relative efficacy of various diets on glycemic outcomes in pregnant women with or without diabetes. Our analysis was stratified based on whether GWG advice was given in addition to the dietary interventions so that the effects of diet can be isolated.

3.2. Methods

3.2.1. Protocol and registration

The Cochrane Handbook for Systematic Reviews of Interventions (version 5.2) and the PRISMA for network meta-analyses was followed for analysis and reporting of results, respectively.[98,239] The protocol was registered with PROSPERO (CRD42015026008).

3.2.2. Data source

MEDLINE, EMBASE, and Cochrane were searched up until April 2017 (**Appendix Table 3.1.**). A manual search of the references of the included studies was also conducted to identify additional eligible studies.

3.2.3. Study selection and eligibility criteria

Each study identified by the electronic or manual search was screened by title and abstract to assess for inclusion by one reviewer (VH). Studies that passed the title/abstract

screening were retrieved for full-text review. Eligible studies were randomized trials that examined the effect of one dietary intervention compared to another dietary intervention or routine care on glycemic outcomes in pregnant women with or without diabetes and who were followed for at least two-weeks. A minimum of two-weeks of follow-up duration was chosen in accordance with diabetes guidelines which recommend that dietary therapy should be given for at least two-weeks before the use of insulin therapy.[10,17,18] FG and fasting insulin (FI), hemoglobin-A1c (Hb_{A1c}), and homeostatic model assessment for insulin resistance (HOMA-IR) were glycemic outcomes of interest. No restriction was placed on language.

3.2.4. Data extraction

Study characteristics and data from eligible studies were independently extracted by two reviewers (VH and JKJ). Extracted data included article citation, study design, participant characteristics, dietary interventions and macronutrient composition, level of feeding control, institution and country at which the study was conducted, study results, and statistical tests used. To ensure accuracy, extracted data were compared between the two reviewers and any discrepancies were resolved through consensus.

3.2.5. Quality assessment

The quality of evidence for each dietary comparison was assessed using the GRADE approach.[240] The overall quality of evidence for each dietary comparison was rated as high, moderate, low, or very low. Depending on the type of evidence in question, the starting point for GRADE assessment differed. Direct comparisons, where head-to-head

comparisons from randomized trials were available, started at high quality of evidence and were downgraded based on the degree of study limitation, imprecision of pooled effect estimates, inconsistency of results, indirectness, and publication bias. First-order indirect comparisons, where two interventions had been individually compared against one common comparator but not with each other, started at the lower rating of the two dietary comparisons that made up the link and were downgraded based on evidence of intransitivity. Second and higher order indirect comparisons, where ≥2 common comparators were found between the two interventions being compared, were always rated as very low because of the distance between the two dietary interventions being compared.

3.2.6. Statistical analysis

The network meta-analysis was conducted using R (version 3.2.0, R Project for Statistical Computing) with the *gemtc* and *rjags* packages, which interface with Just Another Gibbs Sampler (JAGS) software (version 3.4.0).

A NMA for FG was performed. Relative effect estimates from the NMA are expressed as median differences (MeD) with 95% credible intervals (CrIs). MeD and their CrIs can be interpreted in the same manner as traditional MD with 95% CIs. The FG achieved at the end of each dietary intervention for each included trial was extracted and pooled using the Bayesian fixed effects model, with a minimally informative prior distribution for relative treatment effects. A fixed effects model was chosen because it had a lower deviance information criterion (DIC) compared to the random effects model,

suggesting a better model fit. Non-informative prior distributions were chosen for model parameters so that results were driven entirely by the reported data. Analyses were performed using Markov-Chain Monte-Carlo methods, a method that estimates the effect of each dietary comparison by simulation, using four chains with 200,000 iterations and thinning interval of ten, after a burn-in of 100,000. Convergence of the chains was assessed using the Gelman plot and diagnostic test.[241] Consistency of direct and indirect sources of evidence within the network was assessed using the node-splitting method.[242] Statistical significance was considered when the CrIs did not cross the line of no effect.

Surface Under the Cumulative Ranking (SUCRA) values were calculated to assist in determining the probability of a given dietary intervention as being the best overall among the interventions compared, but this does not necessarily reflect that the dietary intervention is good to treat with as other important clinical factors are not considered in the calculation (e.g. patient preferences, cost-effectiveness, etc.). The closer SUCRA is to 100, the more certain we are that it is the best overall and the closer it is to zero, the more certain we are that it is worst.[243] Ranks, cumulative ranks, and SUCRA values were considered as supplementary measures to the primary effect estimates for each dietary comparison because the former three measures are known to have substantive uncertainty.[244]

Standard pair-wise meta-analyses for FI, Hb_{A1c}, and HOMA-IR were performed because they lacked a common dietary comparator that connected them to a network plot. Results were expressed as MD with 95% CIs. The glycemic outcome achieved at the

end of each dietary intervention for each included trial was extracted and pooled using the fixed effects model as there were <10 studies included per analysis. Significance was considered when $p<0.05$.

Analyses were stratified by whether advice regarding optimal weight gain during pregnancy was given in addition to the dietary intervention ("GWG advice"). Trials were considered to have given participants GWG advice if the investigators established energy requirements so that women would achieve appropriate GWG. Trials were grouped into "trials with GWG advice provided in both dietary arms" if the study was designed to include GWG advice in addition to the dietary interventions. In contrast, trials were grouped into "trials with no GWG advice" if no GWG advice was given at all. Finally, studies were grouped into "trials with GWG advice provided in one of the dietary arms" if only one of the dietary interventions included GWG advice but not the other. Studies, where GWG advice was given in only one of the dietary arm but not in the comparator, were not included in the NMA. Further, studies were not included in the NMA if they did not connect to the network plot due to a lack of a common comparator. A standard pairwise meta-analysis was performed for these types of studies.

3.2.7. Network assumptions

Prior to conducting the network meta-analysis, the assumptions of homogeneity and transitivity were assessed. Homogeneity, which reflects the degree of similarity between the effect estimates of each trial within the same dietary comparison, was assessed using Higgins criteria for I^2.[98] The I^2 was chosen because it quantifies the degree of variation

between trials that is due to inter-study heterogeneity and not by chance. Transitivity, which reflects the distribution of effect modifiers between trials, was assessed by examining the distribution of *a priori* effect modifiers for both direct and indirect dietary comparisons including stage of pregnancy (first, second, or third trimester), diagnosis of GDM (yes or no), pre-pregnancy body weight (as a continuous variable), and ethnicity (Europeans, Asians, Africans, or others).

3.3. Results

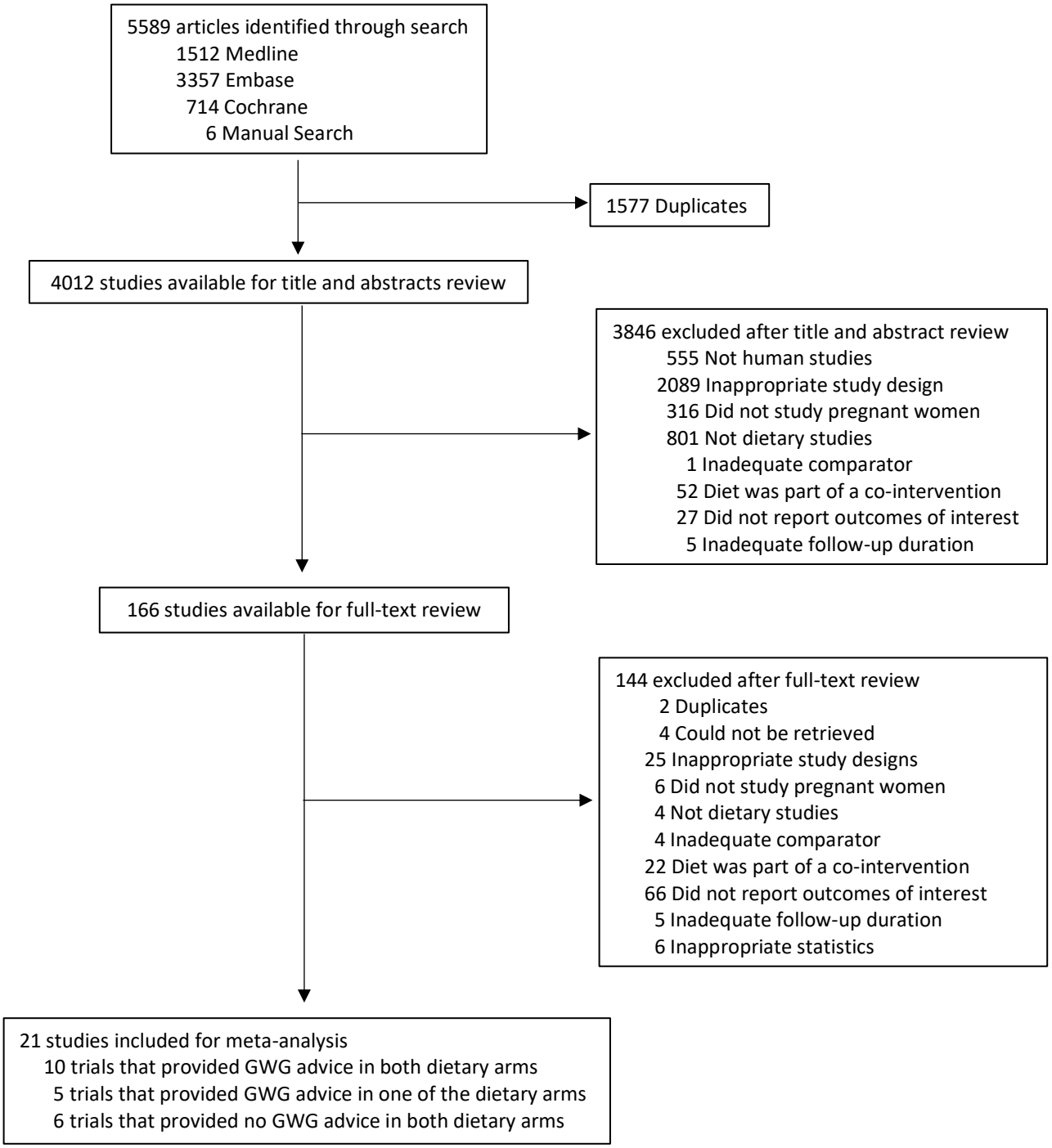
3.3.1. Literature search and study characteristics

Of the 5589 studies that were identified, twenty-one studies were included (**Figure 3.1.**).[52,55,61,172,173,179,184,186,187,189,191,195,203-205,210,212,245-248] Ten trials were designed to include GWG advice in addition to the dietary intervention, five trials included GWG advice in only one of the dietary arms, and seven trials did not report giving any GWG advice in either arm.

Participants were predominantly young women (median= 30.6 years [interquartile range (IQR): 29.5 to 30.9 years]) in their second trimester at the start of the study (median= 24.4 weeks [IQR: 20.8 to 28.5 weeks]) with some degree of glucose intolerance (**Appendix Table 3.2.**). Most participants were considered overweight based on their pre-pregnancy BMI (median= 26.6 kg/m^2 [IQR: 23.5, 27.7]). Smokers were included in one trial only (20% of included participants).

Overall, the baseline FG (median= 4.9 mmol/L [IQR: 4.7 to 5.0]) and Hb_{A1c} (median= 5.7% [IQR: 4.9 to 5.4%]) were within the normal range. The median baseline FI was 99.8

Figure 3.1. Flow of the literature search.



pmol/L (IQR: 63.8 to 135.2 pmol/L) and the median baseline HOMA-IR was 2.2 (IQR: 1.3 to 2.5).

Macronutrient composition was targeted in twenty-three dietary arms. CHO intake was the focus of fifteen dietary arms (a low- GI or GL diet in six arms, a high-fibre diet in three, a low-GI/GL and high-fibre in one, a low-CHO and low GI diet in two, and a low-CHO diet in three). Fat intake was the focus of four dietary arms (low fat in one arm, high MUFA intake in one, and high unsaturated fat intake in two), a low-CHO and high fat diet in three dietary arms, and a high-fibre and low-fat diet in one dietary arm. Diets that targeted whole patterns of food consumption were the focus of fourteen dietary arms. The DASH-style diet was used in three dietary arms, healthy eating was used in two dietary arms, calorie restriction only was used in nine dietary arms. Routine care, which were dietary arms with no dietary advice given or a standard macronutrient distribution (45-64% of energy from CHO: 10-35% of energy from protein: 20-35% of energy from fat) was followed, was used in seven dietary arms.

Six trials were conducted in North America (Canada two, US three, and Mexico one), seven trials were conducted in Europe (Italy and Denmark two each, and Finland, Ireland, and Poland had one each), three trials were conducted in Australia, and six were conducted in Asia (Iran and China had three trials each). The median follow-up duration was 11.0 weeks (IQR: 7.1 to 14.8 weeks).

3.3.2. Network assumptions

The assumptions of homogeneity and transitivity for NMAs were reasonably met. No

evidence of inter-study heterogeneity was found between trials of dietary comparisons that did not provide GWG advice (I^2= 0%). Within trials that offered GWG advice, inter-study heterogeneity was low (range: 0 to 45.5%). Further, too few studies reported pre-pregnancy BMI (n=8 trials) to assess whether the transitivity assumption was violated due to an imbalance on this characteristic across trials, but there was no evidence of an imbalanced distribution of effect modifiers for GDM diagnosis, ethnicity, and pregnancy stage.

3.3.3. Trials with GWG advice provided in both dietary arms

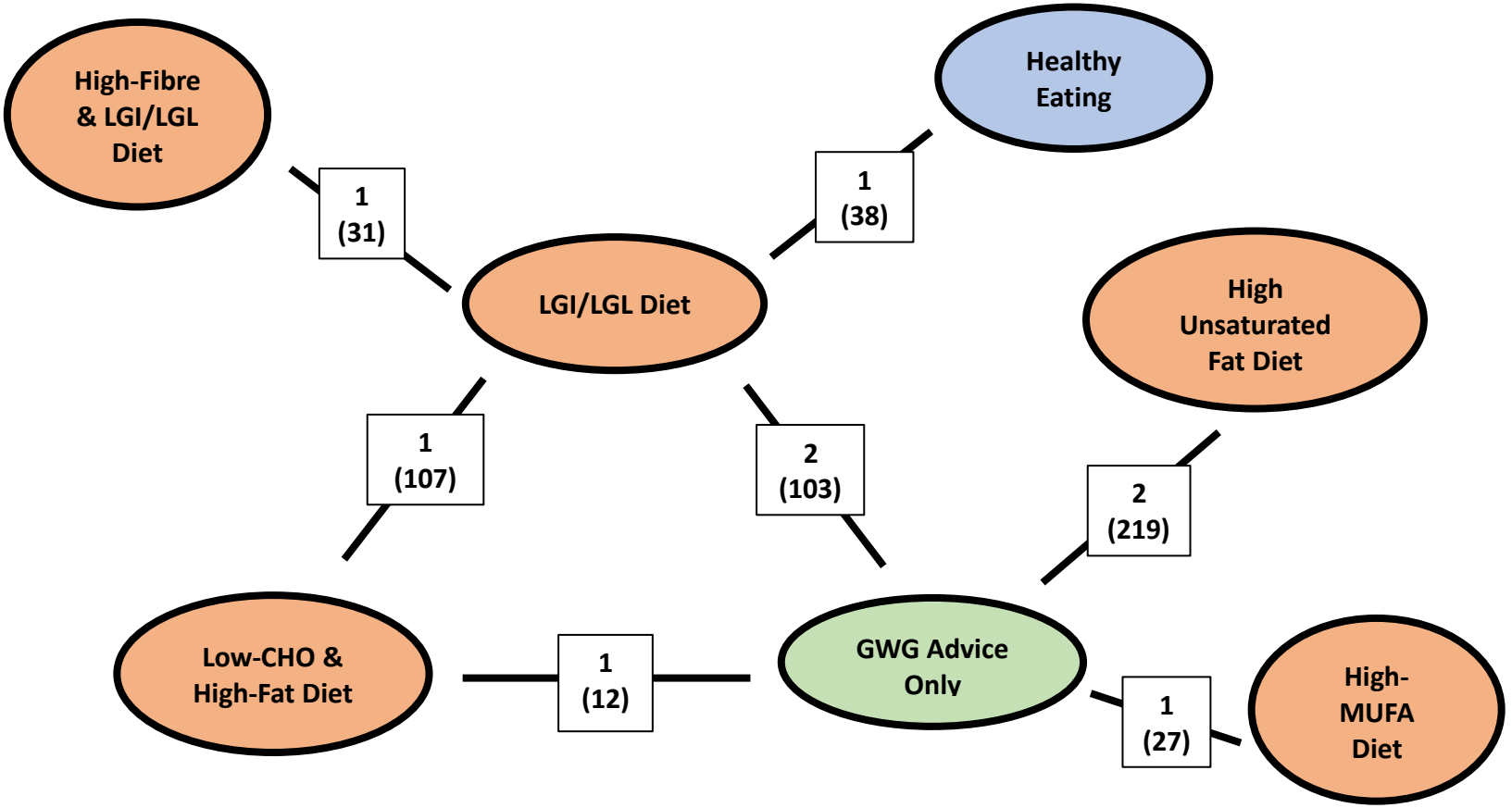
3.3.3.1. Fasting glucose

GWG advice was given in addition to dietary interventions and had FG reported in nine trials (**Figure 3.2.**).[61,179,184,186,189,191,195,203,204,247]

Where direct comparisons were available, no between diet differences were observed (high unsaturated fat diets vs GWG advice only and high-MUFA diet vs GWG advice) (**Figure 3.3.**). Using indirect comparisons, in general, FG increased in diets that modified fat quality intake compared with other diets. FG increase was observed in four out of the six dietary comparisons that prescribed a high unsaturated fat diet and three out of four dietary comparisons that involved a high-MUFA diet.

FG was improved when appropriate GWG advice was given alongside dietary advice compared with GWG advice only. FG reduction was observed in four of the six dietary comparisons, two of which were derived from mixed comparisons (low GI/GL diets vs GWG advice only and low CHO & high-fat diet vs GWG advice only) and the other two

Figure 3.2. Network plot of trials that reported fasting glucose and provided gestational weight gain advice in both dietary arms.



Abbreviations: CHO, carbohydrate; LGI, low-glycemic index; LGL, low-glycemic load; GWG, gestational weight gain; MUFA, monounsaturated fatty acids. The colors of each node correspond to a different diet class: orange node represents diets that targeted macronutrient intake, blue nodes represent diets that targeted overall healthy eating, and green nodes represent diets that targeted GWG. The numbers above each line joining two comparators correspond to the number of trials that compare the treatments with the number of included participants expressed in brackets. Thickness of line represent the number of studies included for that dietary comparison. Distances between nodes are not meaningful.

Figure 3.3. Effect of fasting glucose between diets in trials that provided gestational weight gain advice in both dietary arms.

	High Unsaturated Fat Diet						
High Unsaturated Fat Diet	-	**LGI/LGL Diet**					
LGI/LGL Diet	0.33 (0.08, 0.57)	-	**High-MUFA Diet**				
High-MUFA Diet	-0.44 (-1.15, 0.29)	-0.77 (-1.49, -0.02)	-	**High-Fibre & LGI/LGL Diet**			
High-Fibre & LGI/LGL Diet	0.88 (0.16, 1.60)	0.55 (-0.13, 1.24)	1.32 (0.32, 2.33)	-	**Low-CHO & High-Fat Diet**		
Low-CHO & High-Fat Diet	0.41 (0.10, 0.71)	0.08 (-0.18, 0.34)	0.85 (0.08, 1.60)	-0.47 (-1.20, 0.25)	-	**Healthy Eating**	
Healthy Eating	0.83 (0.20, 1.46)	0.50 (-0.08, 1.08)	1.27 (0.33, 2.20)	-0.05 (-0.95, 0.85)	0.42 (-0.21, 1.06)	-	**GWG advice only**
GWG advice only	0.06 (-0.07, 0.19)	-0.27 (-0.47, -0.06)	0.50 (-0.22, 1.20)	-0.82 (-1.53, -0.11)	-0.35 (-0.62, -0.07)	-0.77 (-1.38, -0.16)	-

Abbreviations: CHO, carbohydrate; LGI, low-glycemic index; LGL, low-glycemic load; GWG, gestational weight gain; MUFA, monounsaturated fatty acids. The value in each cell expresses the median difference and its 95% credible intervals between the dietary pattern in the column and the dietary pattern in the row (e.g. the median difference of the high-unsaturated fat diet compared to LGI/LGL diet is 0.33 mmol/L (95% CrIs= 0.08, 0.57 mmol/L).

were derived from indirect comparisons (high-fibre & low GI/GL vs GWG advice only and healthy eating vs GWG advice only).

The most effective diet to reduce FBG was the low GI, high-fibre diet (SUCRA= 89.33%), followed by healthy eating (SUCRA= 88.17%), and then a low CHO with a high-fat diet (SUCRA= 65.05%) (**Appendix Figure 3.1.**).

3.3.3.2. Other glycemic outcomes

A high-MUFA diet compared to GWG advice only increased HbA1c (MeD= 0.40% [95% CrIs: 0.12, 0.68]) (**Appendix Figure 3.2.**). No significant differences in Hb_{A1c}, FI, and HOMA-IR were seen between pairs of any other diets (**Appendix Figures 3.2.** to **3.4**).

3.3.3.3. Insulin therapy

In a *post-hoc* NMA analysis, based on an indirect comparison, the odds of progressing to insulin therapy to manage hyperglycemia during pregnancy was greater for a low GI diet than to a combined low GI and high-fibre diet (OR= 5.92 [95% CrI: 1.20, 36.41]). No other diets were associated with the use of insulin therapy (data not shown).

3.3.4. Trials with GWG advice provided in one of the dietary arms

A significant FI reduction was observed when comparing GWG advice to routine care (MD= -25.00 pmol/L [95% CIs: -46.50, -3.50]) (**Appendix Figure 3.7.**). No significant FG or Hb_{A1c} effect was observed in any of the dietary comparisons (**Appendix Figure 3.5.** and **3.6.**).

3.3.5. Trials with no GWG advice provided in both dietary arms

3.3.5.1. Fasting glucose

Dietary interventions given with no GWG advice and had FG reported were identified in six trials (**Figure 3.4.**).[52,172,173,187,245,248]

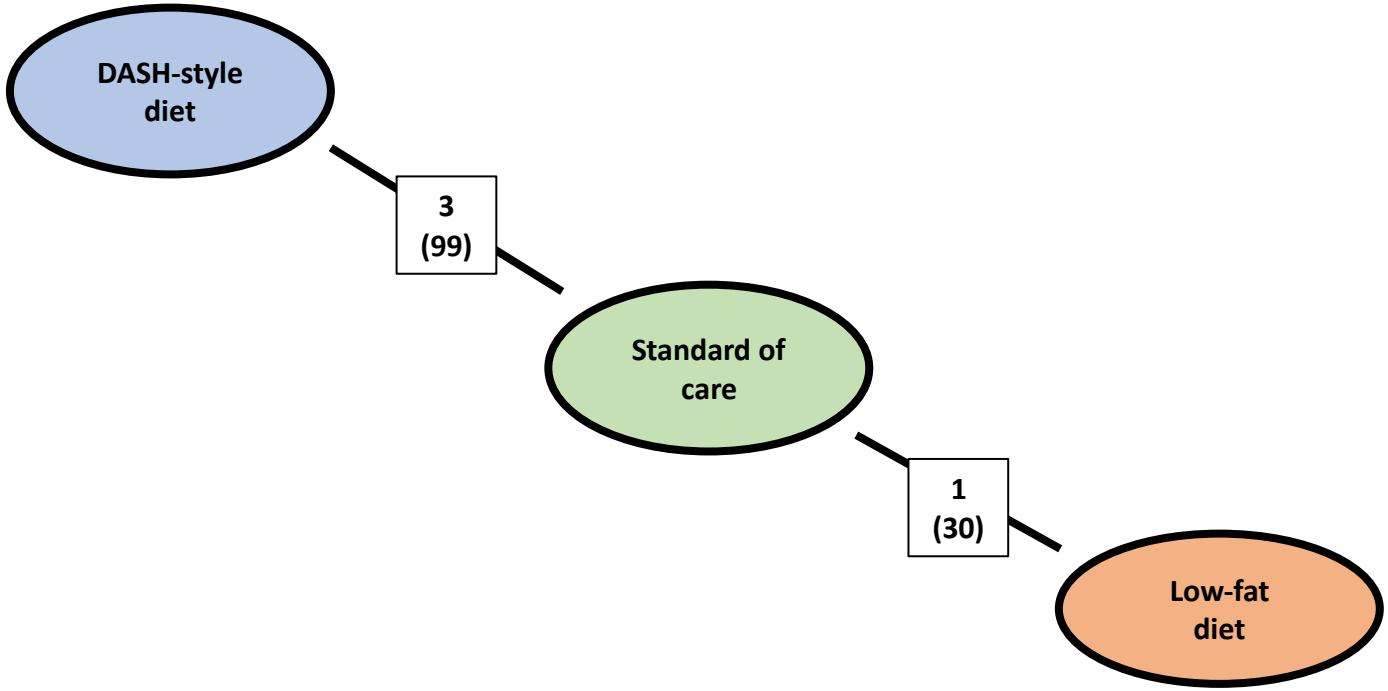
In the absence of GWG advice, an improvement in FG was found in DASH-style diet compared to other diets (**Figure 3.5.**). FG was reduced for the DASH-style diet in an indirect comparison with low-fat diet (MeD= -0.74 mmol/L [95% CrIs: -1.12, -0.36]) and in a direct comparison with routine care (MeD= -0.47 mmol/L [95% CrIs: -0.73, -0.21]). Further, a non-significant FG-effect was observed in a low GI diet compared to a high-fibre diet in a study that was not analyzed as part of the NMA due to a lack of a common comparator (MD= -0.10 mmol/L [95% CIs: -0.38, 0.18]; p= 0.48).[187]

The most effective diet to reduce FG in the absence of GWG advice was the DASH-style diet (SUCRA= 66.7%), followed by routine care (SUCRA= 32.5%), and low-fat diet (SUCRA= 0.88%).

3.3.5.2. Other glycemic outcomes

There were no significant differences on HbA1c (**Appendix Figure 3.8.**), FI (**Appendix Figure 3.9.**), and HOMA-IR (**Appendix Figure 3.10.**) between diets with the exception of an insulin-reducing effect (MD= -47.60 pmol/L [95% CIs: -77.34, -17.86]; p=0.002) and a HOMA-IR-reducing effect (MD= -1.90 [95% CIs: -3.08, -0.72]; p=0.002) in a DASH-style diet compared to routine care in the absence of GWG advice.

Figure 3.4. Network plot of trials that reported fasting glucose and did not provide gestational weight gain advice in both dietary arms.



Abbreviations: DASH, Dietary Approach to Stop Hypertension. The colors of each node correspond to a different diet class: orange node represents diets that targeted macronutrient composition, blue represents diets that targeted food consumption, and green on weight gain advice. The number above each line correspond to the number of trials that compared the two diets with the number of included participants expressed in brackets.

Figure 3.5. Dietary comparisons of trials that did not provide gestational weight gain advice in both dietary arms.

	DASH-style diet		
DASH-style diet	-	**Low-fat diet**	
Low-fat diet	-0.74 (-1.12, -0.36)	-	**Standard of care**
Standard of care	-0.47 (-0.73, -0.21)	0.27 (-0.002, 0.55)	-

Abbreviations: DASH, Dietary Approach to Stop Hypertension. Fasting glucose is expressed in mmol/L. The value in each cell expresses the median difference (MeD) in fasting glucose with the 95% credible intervals (CrIs) in brackets between the diet in the column and the diet in the row (e.g. the MeD in fasting glucose between DASH-style diet compared to low-fat diet is -0.74 mmol/L (95% CrIs: -1.12, -0.36).

3.3.6. Insulin therapy

None of the dietary comparisons showed a significant association to start insulin therapy to manage hyperglycemia during pregnancy in our post-hoc NMA analysis (data not shown).

3.3.7. Quality of evidence assessment

The quality of the evidence ranged from moderate to very low (**Appendix Table 3.3.** to **Appendix Table 3.8.**). Most comparisons were downgraded because of serious concerns regarding indirectness and/or imprecision.

3.4. Discussion

We have systematically reviewed and conducted a network meta-analysis of randomized trials to assess the relative effectiveness of various diets on glycemic outcomes in women during pregnancy. Alongside with gestational weight gain advice, most diets, with the exception of a high unsaturated or a high monounsaturated fatty acid diet, demonstrated a fasting glucose improvement compared with gestational weight gain advice only. When gestational weight gain advice was not given, the DASH-style diet appeared optimal on fasting glucose. Similar trends were observed in the other glycemic outcomes.

The benefits of diets given in addition to GWG advice or routine care on FG appeared modest, but we believe that these have important clinical relevance. Reductions in FG of 0.1 mmol/L in the Metformin in Gestational Diabetes Trial and 0.3 mmol/L in a large RCT were observed when insulin was compared to anti-hyperglycemic medications in pregnant women.[249,250] Similar magnitudes of FG reductions were observed in our

analysis, ranging from -0.27 to -0.77 mmol/L in trials with GWG advice and -0.47 to -0.74 mmol/L in trials with no GWG advice. This is particularly important during pregnancy as most women prefer dietary approaches to manage FG levels than the use of insulin therapy.[235] Furthermore, our findings build on existing dietary approaches for management of GDM which mostly focus on CHO-counting or limiting caloric intake to manage GDM risk.[10,17,18] All our dietary comparisons that demonstrated a FG improvement emphasized on the consumption of high-quality (e.g., unrefined, minimally processed foods such as vegetables and fruits, whole grains), healthy foods, and minimizing low-quality foods (e.g., highly processed snack foods, refined grains, fried foods, and high GI foods). Providing high-quality diets may be more effective to manage FG than GWG advice or routine care only.

Both the quantity and quality of diet have been emphasized as equally important in the management of cardiometabolic risk.[251] Pregnancy is a time of heightened sensitivity and attention to food intake in most women,[235] so the ability of healthcare providers to provide accurate and evidence-based advice increases the relevance of our findings. Although most diets that were given in addition to GWG advice demonstrated an FG reduction in our NMA, these same findings were not found in trials that had been specifically designed to assess if diets in addition to GWG advice would affect FG. Instead, a null FG-effect had been reported by these trials. This may, however, be due to the small number trials of such trials identified and included in our analysis.

High unsaturated fat intake has been found to be cardio-protective but there is

uncertainty concerning its relationship with diabetes risk. Although meta-analyses have shown non-significant findings, a trend for increased T2DM risk have been noted for polyunsaturated fatty acid intakes (PUFAs), omega-3's, and foods that are a source of these fatty acids such as fish and other seafood.[252,253] High fat intake is linked to increased hepatic glucose production by reducing the ability of insulin to suppress endogenous glucose production.[254] Trials that were included in our analysis showed a positive correlation between unsaturated fat or MUFA intakes with PUFA intakes.[186,204] Consistent with the above findings between PUFAs and T2DM, our analysis found that FG increased in diets that increased unsaturated or MUFA intakes.

Insulin therapy is usually initiated after two weeks if women cannot manage their GDM using diet therapy alone.[10,18] No difference in the use of insulin therapy was found between diets in our analysis except for low GI diets compared to low GI with high-fibre diets. One interpretation of this finding is that the examined interventions (diets, GWG advice, and routine care) were equally effective in preventing the use of insulin. We cannot, however, rule out the more likely possibility that trials achieved suboptimal dietary compliance (as reflected in our GRADE assessment) or that the dietary contrasts were not large enough to detect effects on insulin therapy use.

Several limitations were noted in the present study. First, our network meta-analysis included only RCTs which may have limited the number of available dietary comparisons. We had, however, decided not to include non-randomized studies because of concerns that these types of studies are more likely to introduce bias into the effect

estimates because of confounding arising from the lack of randomization. A specific barrier to including both randomized and non-randomized studies in a network meta-analysis is that this practice would compromise the validity of our network by possibly violating two key assumptions: transitivity (the distribution of patient and study characteristics that are modifiers of treatment effect be sufficiently similar across studies) and as such, could possibly affect the consistency of the evidence (agreement of direct and indirect evidence for a given pair of treatments). Second, our certainty in the pooled effect estimates for each dietary comparison was moderate to very low. For our FG analysis, the quality of evidence was downgraded mostly due to poor (indirect) network connectivity between diets, small sample sizes, or both. For other glycemic outcomes, a lack of similar dietary comparisons precluded us from conducting a useful NMA. Furthermore, most dietary comparisons were under-powered to detect a difference in FG, HbA1c, FI, or HOMA-IR as we had found in our *post-hoc* analysis (data not shown). Third, most of our findings were derived from indirect comparisons rather than direct comparisons. Although we concluded that the assumption of transitivity was reasonably met for indirect comparisons within our study, we were not able to use the less-reported BMI to guide our assessments and as always, the case with indirect comparisons, minor, immeasurable effect-modifying characteristics could bias these estimates. Fourth, the generalizability of our results is limited. Most of the included trials were predominantly in young women in their second trimester who were already diagnosed with GDM. Therefore, it is unclear if the studied diets can prevent GDM per se. Certainly, however,

based on our results, some diets appeared to be more effective in managing glycemic outcomes than others. Notwithstanding these limitations, many of the dietary comparisons in our analyses were designed to assess two dietary interventions that may benefit glycemic control; as such comparisons to a usual diet (e.g. typical North American/European non-therapeutic diet) were few and in this regard, a maintenance in glycemic control after intervention may be noteworthy.

3.9. Conclusions

Alongside with gestational weight gain advice, most diets, except for a high unsaturated or a monounsaturated fatty acid diet, demonstrated a fasting glucose improvement compared with gestational weight gain advice only. When gestational weight gain advice was not given, the DASH-style diet appeared optimal on fasting glucose. However, the number of trials is small, and most were underpowered to detect differences in FG. To clarify the role of diets in glycemic management during pregnancy, data from larger, high-quality, and well-powered feeding trials of dietary approaches and high-quality prospective cohort studies are required. Nonetheless, diets, with the exception of the ones that modify fat intake, may be useful as part of a strategy to improve FG.

CHAPTER 4. GENETIC RISK, DIETARY CARBOHYDRATE QUALITY, AND GESTATIONAL DIABETES RISK

4.1. Introduction

The prevalence of GDM, a condition in which women without diabetes develop high blood glucose levels (hyperglycemia) during pregnancy, is increasing worldwide.[25,255] Maternal hyperglycemia places a continuous stress on the woman and her infant to produce more insulin to handle the increased glucose load. This increased and persistent demand for insulin can cause pancreatic β-cell dysfunction,[256] which may predispose a woman and her offspring to chronic diseases later in life. Women with GDM have an increased risk for T2DM,[30,31] and infants of women with GDM have a greater amount of body fat at birth, are of higher birth weight, and are at increased risk of obesity and glucose intolerance in childhood and early adulthood.[257,258] Observational studies have linked GDM with several downstream consequences, but the etiology of GDM is not well-characterized and little attention has been paid to the prevention of the disease in major diabetes guidelines including ADA, DC, and NICE.[10,17,18]

Meta-analyses of candidate gene studies confirm many genetic susceptibility loci related to β-cell function are conserved between GDM and T2DM, including SNPs in TCF7L2, MTNR1B, KCNJ11, IGF2BP2, CDKAL1, GCK, and KCNQ1.[259,260] These findings are largely from studies of White Caucasians and a small number of East Asians and Hispanics.[259,260] Previous analyses have shown that the association of selected genetic loci and GDM risk may differ between Asians and White-Caucasians.[259] Diet also likely plays a

role in the development of the disease. In the NHS II, total CHO intake prior to pregnancy does not increase the risk of GDM development, but markers of CHO quality including lower GL, higher dietary fibre, and higher whole grains were shown to be protective against GDM.[58] However, in RCTs reported that low GI diets do not prevent GDM (pooled RR= 0.87 [95% CIs: 0.60, 1.26]), but these trials typically do not achieve the planned contrast in the GI between diets, leaving them underpowered to show a clinical effect.[53,55,61] Despite the recent r identification of novel genetic contributors to GDM, it is not known whether these SNPs interact with the environment and what role such interactions play in the development of disease. Prospective cohort studies including the European Prospective Investigation into Cancer and Nutrition (EPIC) and Health Professional Follow-up Study (HPFS) showed that dietary factors such as CHO, fat, dietary fibre, whole grains, and the Western diet modify the genetic susceptibility to T2DM.[261-263] Such studies are lacking for gene-diet interaction and GDM risk.

Previous gene-diet interaction studies of GDM are limited by a small sample size and low statistical power, a focus on a single genetic locus (MTNR1B or HLA-DRB1), within homogenous population of either European or Asian ancestry.[65,66] In this study, we assessed the associations between genetic risk scores (GRS) on GDM and also dietary components of GI, GL, total sugars, and added sugars on GDM, and tested the interaction between genetic and dietary factors on GDM and markers of glycemia including FG, area-under-the-curve glucose ($AUC_{glucose}$) in White-Caucasians and South Asians from two Canadian birth cohort studies.

4.2. Methods

4.2.1. Study population

START is a prospective birth cohort study designed to identify cardiometabolic risk factors in 1,012 South Asian women with singleton pregnancies living in the province of Ontario, Canada recruited between 2011 and 2015.[105] CHILD is a multi-ethnic prospective cohort study designed to identify risk factors for atopic diseases which enrolled 3,624 women with singleton pregnancies in the provinces of British Columbia, Alberta, Manitoba, Ontario, Canada between 2008 and 2012.[103]

For the genetic risk analysis, 3,456 women had genotype data available (2,589 women in the CHILD and 867 in the START study). We excluded women whose blood samples did not pass genotype quality control (n= 158), or who self-reported pre-gestational diabetes or had this value missing (n= 140), high blood sugar at initial visit (n= 42), or an ethnicity other than White-Caucasian in the CHILD study (n= 567), or did not report GDM diagnosis for the GDM genetic risk analysis (n= 20), or did not have a FG measurement for the FG genetic risk analysis (n= 6), or did not have an $AUC_{glucose}$ measurement for the $AUC_{glucose}$ risk analysis (n= 15); thus, we included 2,529 women in the GDM genetic risk analysis (1,730 in the CHILD and 799 in the START study), 805 women in the FG genetic risk analysis, and 796 women in the $AUC_{glucose}$ genetic risk analysis. For the dietary analysis, 4,636 women were available for us to screen for eligibility. We excluded women who withdrew from the study (n= 131), with duplicate IDs (n=13), or who did not complete a FFQ (n= 507), or who did but had >10-items missing (n= 21), an

implausible energy intake of <500 or ≥6,500 kcal/day (n=18), self-reported pre-gestational diabetes or had this value missing (n= 90), reported high blood sugar at initial visit (n= 81), or did not report GDM diagnosis (n= 41); thus, we included 2,810 women from the CHILD and 924 women from the START cohort. For the gene-diet interaction analysis, we included 1730 women from CHILD and 774 women from the START cohorts (**Appendix Figure 4.1.**). We limited our genetic analyses to White-Caucasians only in the CHILD cohort because White-Caucasians had >50 and all other ethnic groups had <12 incident GDM cases.

4.2.2. Dietary assessment

In the START cohort, the investigators administered a previously validated ethnic-specific food frequency questionnaire (FFQ) at the baseline visit, which took place between 24 and 28 weeks of gestation.[264] The 163-item FFQ asked about food intakes in the past 12 months. We obtained the GI values for a single food items from the ESHA database (version 11.3.285, Salem, OR) or from publications using glucose as the reference food.[265-269] To calculate the average daily GI and GL for each participant, we used the following formulae:[270]

$$DietaryGI = \left(\frac{DietaryGL}{\sum_{j=1}^{n} CHO_j \times FPD_j} \right) \times 100$$

and

$$DietaryGL = \sum_{i=1}^{n} \frac{GI_i \times CHO_i \times FPD_i}{100}$$

,

where CHO is the carbohydrate content (g) per serving and FPD is the average frequency per standard portion size of servings of food per day.

We obtained total sugars and added sugars using ESHA Food Processor (version 11.3.285, Salem, OR). Total and added sugar values were not tracked in the original 1996 analysis, so we updated the database to the 2017 ESHA version, supplemented with published values from the 2015 Canadian Nutrient File (CNF) and 2015 USDA nutrient database (release SR-28) and includes estimates of total and added sugars. We only updated foods known to have a high added sugar content, defined as foods where the added sugar contributes ≥25% of total calories per standard serving of that food (e.g. doughnuts, pies, cakes, sugar-coated cereals, yogurt, creamy salad dressing, ketchup, etc.). When sugar values were available in both the CNF and USDA nutrient database, we preferred the values in the CNF because it is more reflective of the nutrient compositions of the foods available in Canada given the dissimilar manufacturing and fortification practices between Canada and US. If foods that were available in the 1996 ESHA database were no longer available in the 2017 ESHA database or if multiple food items in the 2017 ESHA database matched that of the original food in the 1996 ESHA database, we kept the food from the 2017 ESHA database that most closely matched the calories per standard serving of the original 1996 food item as the replacement. Total energy and CHO changed by <10% between the 1996 and 2017 versions of the database. We manually entered the nutrient profile of ethnic-specific foods (e.g. rasmali, chumchum, gulab jamun, etc.) based on the available home-made recipes.

In the CHILD cohort, investigators administered a previously validated FFQ developed at the Fred Hutchinson Cancer Center at baseline visit of 6-39 weeks of gestation.[103] The FFQ asked about 151 food and beverage group intakes during pregnancy and included Canadian ethnic foods. The database used to analyze nutrient intakes was the University of Minnesota Nutrition Data Systems for Research (NDSR) software, updated to include Canadian food products. All dietary exposures were energy adjusted using the residual method.[271]

4.2.3. Genotyping

Personnel at the Genetic and Molecular Epidemiology Laboratory (Population Health Research Institute, Hamilton, Ontario, Canada) performed buffy coat DNA extractions and genotyping in batches using the Illumina Human Core Exome (12 v1.1. and 24 v1.0.) and Infinium Core Exome (24 v1.1.) Beadchip. Genotyping was successful for 2,589 and 867 women in the CHILD and the START cohorts, respectively. AL performed genetic imputation to predict single nucleotide polymorphism (SNPs) that were not directly available for genotyping using SHAPEIT (version 2.0.) and IMPUTE2 software with the 1000 Genomes Phase III as a reference panel (**Appendix Tables 4.1.** and **4.2.**).[272,273] The imputation used SNPs that had a high call rate (>95%) in its calculations.

4.2.4. Gene scores

To build a gene score for GDM (GDM-GRS) and FG (FG-GRS), we identified eligible SNPs from the DIAbetes Genetics Replication And Meta-analysis (DIAGRAM) Consortium and the Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC),

respectively.[274,275] Eligible SNPs were previously associated with T2DM or FG in non-pregnant populations at genomic wide significance (i.e. $5x10^{-8}$) in White-Caucasians. Based on this eligibility criteria, the GDM-GRS included 102 SNPs,[275] and the FG-GRS included 77 SNPs,[274] all of which were available in the CHILD and START cohorts.

We created a weighted gene score to increase precision and power. Previous studies reported that a weighted gene score was more predictive of T2DM than an unweighted gene score.[276,277] We defined the risk allele as the GDM-risk-elevating allele in the GDM-GRS and FG-elevating allele in the FG-GRS. We weighted each included risk allele according to its relative effect size (β-coefficient) (i.e. multiplied each risk allele with its β-coefficient) and summed these cross-products.[278] The sum of the cross-products was divided by the maximum weighted gene score and the quotient was multiplied by the number of risk alleles in each gene score (e.g. 204 for GDM-GRS and 154 for FG-GRS). Thus, each point on the gene score corresponded to one risk allele.

4.2.5. Outcomes

GDM was the main outcome of this analysis and FG and $AUC_{glucose}$ were the secondary outcomes.

4.2.5.1. GDM ascertainment

The CHILD and START cohorts used different methods to assess GDM status. In the CHILD cohort, the study personnel assessed GDM status via: 1) a self-administered questionnaire, given at baseline and 1-year postpartum visits, which asked women to recall if they had ever been diagnosed with GDM (yes or no) and 2) a review of each

woman's medical history file or electronic record to see if a healthcare provider had ever recorded a GDM diagnosis. If either of these inquiries were positive, the study personnel recorded the participant with a positive GDM status. In the START cohort, study personnel assessed GDM status via: 1) the same approaches as the CHILD cohort and 2) a 75-g OGTT test after an ≥8-hour overnight fast at the baseline visit (gestational age: 20.30 to 33.70 weeks). To avoid ascertainment bias, our primary analysis considered only self-reported (or medical chart review) GDM in both cohorts. In START, the sensitivity of self-reported GDM status versus GDM diagnosis by IADPSG (FG ≥5.1 mmol/L, 1-hr plasma glucose ≥10.0 mmol/L, or 2-hr plasma glucose ≥8.5 mmol/L) was 61.88% and specificity was 99.00%.[15]

In a sensitivity analysis, we used the GDM diagnostic threshold based on the results of the 75-g OGTT derived from the Born in Bradford (BiB) cohort to assess if an ethnic-specific GDM diagnosis would modify the association of the gene-diet interaction and GDM.[28] This analysis included only women in the START cohort because the BiB criteria: 1) is an ethnic-specific criteria targeted at South Asian women and 2) requires results from a 75-g OGTT which women in the START cohort received but not women in the CHILD cohort. Using the BiB definition, the cut-offs for GDM diagnosis are: 1) FG ≥5.2 mmol/L or 2) 2-hr plasma glucose ≥7.2 mmol/L. Previous studies showed that these cut-off values increase the odds of a high birthweight and adiposity.[28] The sensitivity of Bibs-defined GDM versus IADPSG cut-offs was 37.0% and the specificity was 97.8%.

4.2.5.2. FG and $AUC_{glucose}$

Only the START cohort assessed FG and $AUC_{glucose}$ because women in the CHILD cohort did

not receive a 75-g OGTT. Personnel measured FG after an overnight fast. We calculated $AUC_{glucose}$ using the trapezoidal method:

$$AUC_{glucose} = \left(\frac{FG + 1hr_{glucose}}{2} \times 60\right) + \left(\frac{1hr_{glucose} + 2hr_{glucose}}{2} \times 60\right),$$

where FG is the blood glucose measured at fasting, $1hr_{glucose}$ is the blood glucose measured 1 hour after the OGTT, and $2hr_{glucose}$ is the blood glucose measured 2 hours after the OGTT.

4.2.6. Statistical analysis

We used R Studio (v1.0.136, R Foundation) and PLINK (http://pngu.mgh.harvard.edu/~purcell/plink/), as appropriate, to perform statistical analysis. Logistic regression performed association testing within each cohort (for main effect analysis) or ethnicity (for main effect of genetic risk score and genetic risk score x diet interaction), adjusting for potential confounders. Confounders included previously established risk factors for GDM in South Asians: age (continuous), height (continuous), pre-pregnancy BMI (continuous), and diet quality (low, or reference= high),[44] or strongly suspected risk factors of GDM: energy intake (continuous) and social disadvantage (continuous). We assessed diet quality using consumption patterns of 6 food groups. Each participant received a point for consuming more than the study population median of 1) green vegetables, 2) raw vegetables, 3) cooked vegetables and 4) fruits, and less than the study population median of 5) fried foods and 6) meat. The highest possible score on the diet index was 6 and the lowest was 0. A low-quality diet scored 0 to 2, a medium quality

diet scored 3 to 4, and high-quality diet was 5 to 6. We assessed social disadvantage using the social disadvantage index (SDI), which included employment status, income, and marital status. The SDI was developed in a Canadian multi-ethnic cohort to study its association with CVD risk but has not been externally validated.[279] The maximum score on the SDI was 5 and the lowest was 0. The least social disadvantage received a score of 0 to 1, moderate was 2 to 3, and high was 4 to 5.

The mean or mode replaced missing values if the missingness was <10%. Only income (10.25% in CHILD and 13.74% in START cohorts) and pre-pregnancy weight (13.17% in CHILD and 0.00% in START cohorts) had missing values ≥10%. For these variables, we used a regression model to predict the missing value. The variables included in these models were from previously established predictors of income in Canada[280] or previously constructed multivariable model.[281]

To test for a gene-diet interaction, the regression model contained terms for each main effect--diet (quintile) and gene score (per 10-risk-allele increment), their cross-product, along with potential confounders. An interaction is significant when the cross-product term reached statistical significance, defined as $p< 0.10$. We assessed the OR of GDM for a 10-risk allele increase in the GRS within each quintile of the CHO quality marker as well as performed a stratified analysis to examine the joint classification of CHO quality marker (in quartiles) and genetic risk scores (in tertiles). The p-value for significance in our interaction analysis is higher than the usual $p<0.05$ because our analysis is likely underpowered as the number of cases was <45 n the CHILD cohort and <150 in the START

cohort. Within each ethnicity, we derived the quintiles of the CHO quality marker and tertile of the GRS separately.

4.3. Results

4.3.1. Baseline characteristics

Most social, clinical, and dietary characteristics were different between the CHILD and START cohorts (**Tables 4.1. and 4.2.**). Compared to women in the CHILD cohort, women from the START cohort were younger (mean ± SD: 31.62 ± 4.62 years vs 30.12 ± 3.98 years), weighed less (median (interquartile range [IQR)]: 63.50 kg (56.92, 72.57) vs 61.00 kg (54.00, 69.00))), had a higher proportion of participants with high SDI (15.57% vs. 1.73%), had a higher CHO intake (53.38 ± 6.35% of total energy vs 59.60 ± 5.53% of energy) but lower GI (49.90 ± 3.15 vs 45.66 ± 3.65), GL (121.71 ± 17.10 vs 109.49 ± 15.41), total sugars (142.63 ± 29.86 g/d vs 100.19 ± 30.05 g/d) and added sugars intake (58.14 g/d (47.21, 71.30) vs 25.92 (17.63, 37.28)). The mean GDM-GRS was 85 in the CHILD (range: 58 to 115) and 101 in the START (range: 66 to 133) cohorts. The mean FG-GRS was 81 in the START cohort (range: 63 to 101).

4.3.2. Association of genetic risk score and gestational diabetes mellitus risk, fasting glucose, and $AUC_{glucose}$

As the GDM-GRS increased, the number of GDM cases also increased in both cohorts (**Appendix Figures 4.2.** and **4.3.**). The GDM-GRS increased the odds of GDM in both cohorts (p-trend< 0.05), and the association is significant in the extreme tertiles of the GDM-GRS (**Appendix Table 4.3.**). When we modelled the gene score as a continuous

Table 4.1. Study characteristics at baseline*

	mean ± SD		
	CHILD (n= 1730)	**START (n= 774)**	**p-value†**
Age, years	31.62 ± 4.62	30.12 ± 3.98	<0.0001
Gestational age at study enrollment, weeks	25.78 ± 6.91	26.50 ± 1.51	<0.0001
Married or in a common law relationship, n(%)	1656 (95.89)	774 (100.0)	<0.0001
Completed post-secondary education, n(%)	2159 (77.52)	647 (83.59)	0.0005
Currently employed, n(%)	1459 (85.42)	419 (54.42)	<0.0001
Annual household income, n(%)			
<$30,000	57 (3.61)	171 (25.48)	<0.0001
$30,000 to 60,000	209 (13.25)	270 (40.24)	
≥$60,000	1311 (83.13)	230 (34.28)	
SDI, n(%)‡			
High	27 (1.73)	104 (15.57)	<0.0001
Moderate	219 (14.06)	251 (37.57)	
Low	1312 (84.21)	313 (46.86)	
Living with partner, n(%)	1659 (96.73)	753 (97.54)	0.312
Length of time in Canada, years	31.00 (27.00, 34.00)	6.00 (3.00, 10.00)	<0.0001
Smoker during pregnancy, n(%)	129 (7.49)	2 (0.26)	<0.0001
Mainly sedentary, n(%)	-	174 (22.51)	-
Pre-pregnancy weight, kg	63.50 (56.92, 72.57)	61.00 (54.00, 69.00)	<0.0001
Height, metres	1.66 ± 0.08	1.62 ± 0.06	<0.0001
Nulliparity, n(%)	860 (50.38)	290 (39.35)	<0.0001
Family history of diabetes, n(%)	-	139 (39.15)	-
Gestational diabetes mellitus- self-reported and chart review, n(%)	44 (2.54)	107 (13.82)	<0.0001
Gestational diabetes mellitus- BiB, n(%)	-	254 (33.29)	-
Genetic risk score- weighted T2DM§	85 ± 10	101 ± 11	<0.0001
Genetic risk score- weighted FG§	-	81 ± 7	-

Abbreviations: BiB, Born in Bradford; CHILD, Canadian Healthy Infant Longitudinal Development; FG, fasting glucose; SDI, social disadvantage index; START, South Asian Birth Cohort.

*Data are reported as mean ± standard deviation if normally distributed and as median (interquartile range) if non-normally distributed. Count data are reported as n(%).

† P-value were derived from t-test for continuous and normally distributed data, Mann-Whitney U test for continuous and non-normally distributed data, Fisher's Exact test for count data of 2 levels, and Chi-square test for count data of 3+ levels.

‡ SDI was scored using employment status, income, and marital status. The highest score on the SDI was 5 and the lowest was 0. The least social disadvantage was reflected in a score of 0 or 1, moderate was 2 to 3, and high was 4 to 5.

§ per one risk allele increase.

variable, each 10-risk allele increase in the GDM-GRS increased the risk of GDM by 38% in the START cohort and increase the risk of GDM by 57% in the CHILD cohort. Higher tertiles of GDM-GRS associated with higher levels of FG and $AUC_{glucose}$, but when expressed as a continuous variable, the GDM-GRS only positively associated with $AUC_{glucose}$.

The FG-GRS increased FG in the START cohort (**Appendix Table 4.4.**). When we modelled FG-GRS as a continuous variable, each 10-risk allele increased FG by 0.09 mmol/L.

4.3.3. Association of CHO quality and gestational diabetes mellitus

A higher GI increased GDM risk in the CHILD cohort (p-trend= 0.064) and in the pooled analysis of the CHILD and START cohorts (p-trend= 0.083) but not in the START cohort alone (**Appendix Table 4.5.**). Total sugar intake reduced GDM risk in the CHILD cohort (p-trend= 0.014) and we observed a similar trend in the START cohort (p-trend= 0.101). When we pooled both cohorts, the trend was significant (p-trend = 0.003). Added sugar intake

Table 4.2. Dietary characteristics at baseline*

	mean ± SD		
	CHILD (n= 1730)	**START (n= 774)**	**p-value†**
Total energy, kcal/day	1946.00 (1567.00, 2365.00)	1718.90 (1356.70, 2195.60)	<0.0001
Total carbohydrates, %E	53.38 ± 6.35	59.60 ± 5.53	<0.0001
Total sugars, g/d	142.63 ± 29.86	100.19 ± 30.05	<0.0001
Added sugars, g/d	58.14 (47.21, 71.30)	25.92 (17.63, 37.28)	<0.0001
Dietary fibre, g/d	25.02 ± 6.51	22.12 ± 5.19	<0.0001
Glycemic index	49.90 ± 3.15	45.66 ± 3.65	<0.0001
Glycemic load	121.71 ± 17.10	109.49 ± 15.41	<0.0001
Total fats, %E	32.53 ± 5.48	28.94 ± 4.10	<0.0001
MUFA, %E	11.68 ± 2.32	10.23 ± 1.92	<0.0001
PUFA, %E	6.79 (5.81, 7.72)	5.48 (4.81, 6.20)	<0.0001
SFA, %E	11.19 ± 2.32	9.57 ± 2.11	<0.0001
trans fat, %E	1.04 (0.89, 1.25)	0.13 (0.08, 0.21)	<0.0001
Cholesterol, mg/d	243.47 (203.46, 293.57)	141.54 (98.12, 205.66)	<0.0001
Protein, %E	16.96 ± 2.64	15.10 ± 2.09	<0.0001
Alcohol consumption, %E	0.008 (0.004, 0.02)	0.004 (0.002, 0.007)	<0.0001
Low diet quality‡	356 (20.58)	154 (19.90)	0.707
Multivitamin use, n(%)	-	738 (95.47)	-

*Data are reported as mean ± standard deviation if normally distributed and as median (interquartile range) if non-normally distributed. Count data are reported as n(%).

† P-value were derived from t-test for continuous and normally distributed data, Mann-Whitney U test for continuous and non-normally distributed data, and Fisher's Exact test for count data of 2 levels.

‡Diet quality was scored using 6 domains reflecting the intake of green vegetables, raw vegetables, cooked vegetables, fruits, fried foods, and meat. The highest score on the diet quality was 6 and the lowest was 0. Low diet quality was reflected in a score of 0 to 1, moderate was 2 to 3, and high diet quality was 4 to 6.

reduced GDM in the START cohort (p-trend= 0.009) and in the pooled analysis (p-trend= 0.060) but not in the CHILD cohort alone. We did not observe significant association between GL and GDM risk in either cohort alone or in the pooled analysis.

4.3.3. Interaction between genetic risk score and CHO quality on gestational diabetes mellitus

In the START cohort, the GDM-GRS significantly interacted with GL (p-interaction= 0.047) but not in the CHILD cohort (**Table 4.3.**). For every 10-risk allele increase in the GDM-GRS, the OR of GDM within quintiles of GL was 0.96 (95% CIs: 0.61, 1.50), 1.14 (95% CIs: 0.68, 1.94), 1.74 (95% CIs: 1.09, 2.90), 1.70 (95% CIs: 0.97, 3.18), 1.87 (95% CIs: 1.14, 3.23), from first to fifth quintile (lowest to highest). When classified into tertiles of GDM-GRS, the OR

Table 4.3. P-values for interaction between the genetic risk scores and CHO quality on GDM and markers of glycemia*

	GDM		**Fasting glucose**		**$AUC_{glucose}$**
Cohort	CHILD	START	START		START
Type of GRS	GDM-GRS		GDM-GRS	FG-GRS	GDM-GRS
n cases of GDM	44	107	-	-	-
n participants	1,730	774	769	769	760
Glycemic index	0.409	0.307	0.129	0.334	0.407
Glycemic load	0.220	0.047	0.179	0.756	0.090
Total sugars	0.211	0.006	0.003	0.780	0.066
Added sugar	0.220	0.451	0.514	0.620	0.263

Abbreviations: AUC, area under the curve; CHILD, Canadian Healthy Infant Longitudinal Development; FG, fasting glucose; GDM, gestational diabetes mellitus; GRS, genetic risk score; START, South Asian Birth Cohort.

*P-values were obtained from models that adjusted for age, pre-pregnancy weight, height, low diet quality, energy intake, social disadvantage index.

of GDM increased across tertiles of GDM-GRS and quintiles of GL. Those in the highest quantiles of GDM-GRS and GL had an OR of 6.08 (95% CIs: 1.06, 42.19) for GDM (**Figure 4.1.**).

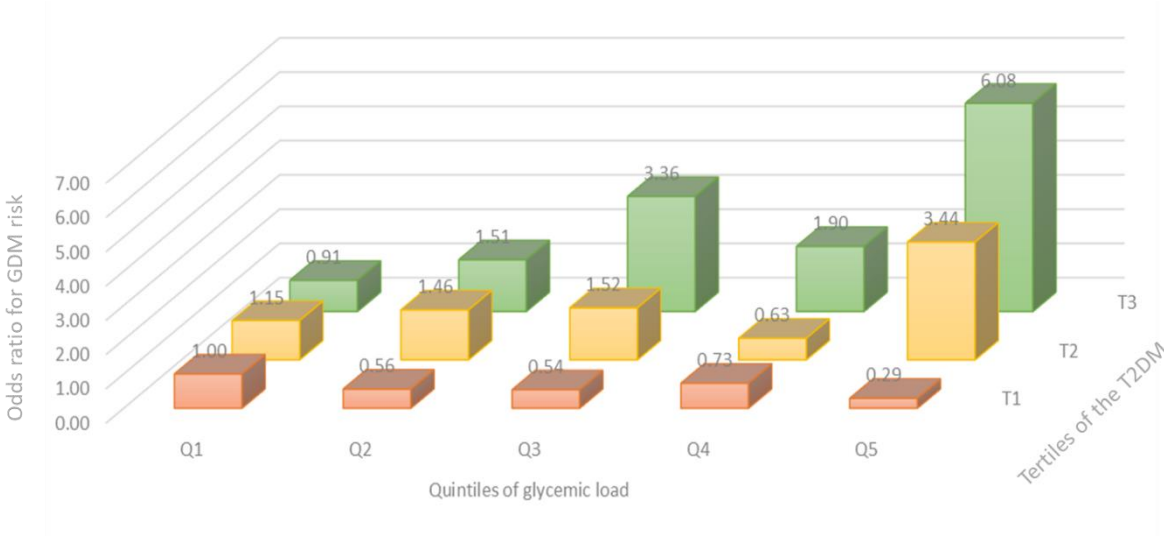
We found an interaction between GDM-GRS and total sugars in the START cohort (p-interaction= 0.006) but not in the CHILD cohort. For every 10-risk allele increase in the GDM-GRS, the OR of GDM within quintiles of total sugars was 2.14 (95% CIs: 1.32, 3.67), 1.71 (95% CIs: 1.05, 2.90), 1.67 (95% CIs: 0.97, 2.99), 0.94 (95% CIs: 0.56, 1.58), and 1.11 (95% CIs: 0.70, 1.79) from first to fifth quintile (lowest to highest). The associations between GDM-GRS and total sugars was not significant among higher quintiles of total sugar intake. When classified into tertiles of GDM-GRS, the OR of GDM increased across tertiles of GDM-GRS and quintiles of total sugars. Those in the highest quantiles of GDM-GRS and total sugars have an OR of 0.36 (95% CIs: 0.07, 1.77) for GDM (**Figure 4.2.**). We did not observe significant interactions between GDM-GRS and other CHO quality.

4.3.4. Interaction between genetic risk score and CHO quality on markers of glycemia

Within each quintile of total sugar intake in the START cohort, every 10-risk allele increase reduced FG (p-trend= 0.003). At the most extreme quintile of total sugar intake, a 10-risk allele increase reduced FG by 0.003 mmol/L. We did not observe significant interaction between the FG-GRS and any of the other CHO quality measures on FG.

We found significant interactions between the GDM-GRS and GL (p-interaction= 0.090) and GDM-GRS and total sugars (p-interaction= 0.066) on $AUC_{glucose}$. Within the highest quintile of GL, $AUC_{glucose}$ increased by 37.51 mmol/hr for a 10-risk allele increase

Figure 4.1. Interaction between genetic predisposition to T2DM and glycemic load on GDM risk in START study.*



*Odds ratios of GDM risk according to joint classification of glycemic load (in quartiles; Q) and genetic risk scores (in tertiles; T). The analyses were adjusted for age, prepregnancy weight, height, diet quality, calories, social disadvantage index.

Abbreviations: GDM, gestational diabetes mellitus; START, South Asian Birth Cohort; T2DM, type 2 diabetes mellitus.

on the GDM-GRS. Within the highest quintile of total sugar intake, $AUC_{glucose}$ was reduced by 3.79 mmol/L for every 10-risk allele increase.

4.3.5. Correlation of food intakes with CHO quality

To understand the unexpected finding of apparent protection against GDM, and lower fasting and $AUC_{glucose,}$ for high total sugar intake and a high genetic risk score, we conducted a correlation analysis in the START cohort to identify foods correlated with higher total sugar intake. Overall, total sugars were positively correlated with higher fruit, cooked vegetables, and better diet quality, but inversely correlated with raw vegetables, meat, fried foods, starch, total fibre, and whole grains (**Table 4.4.**).

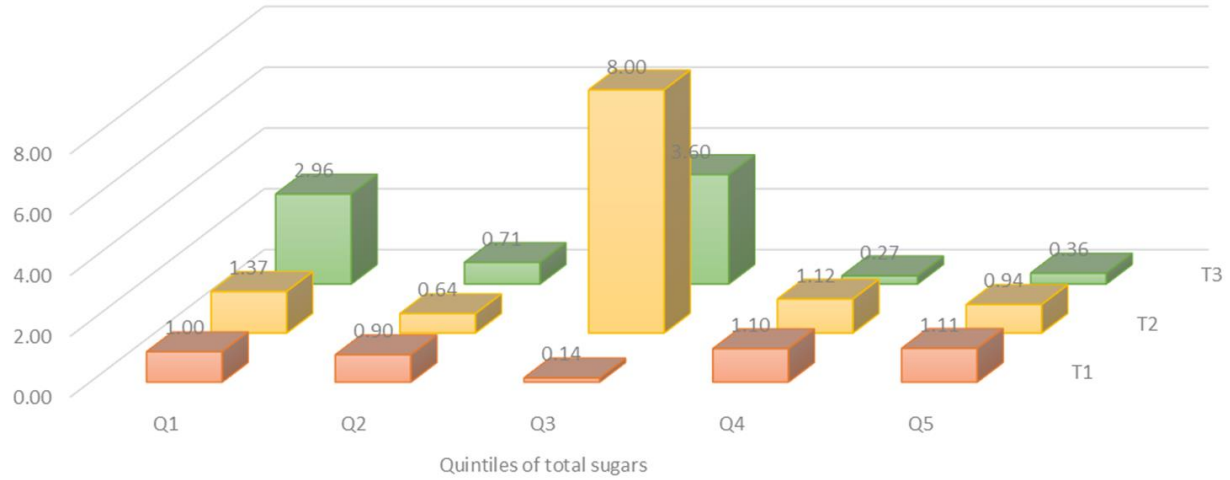
4.3.6. Sensitivity analysis

In a sensitivity analysis, we tested the interaction of the GDM-GRS and each dietary carbohydrate quality measure on GDM as defined by the BiB criteria. Only the interaction between GDM-GRS and GL remained significant (p-interaction= 0.070). For every 10-risk allele increase, the OR of GDM across the quintiles of GL was 0.92 (95% CIs: 0.66, 1.27), 0.88 (95% CIs: 0.61, 1.26), 1.58 (95% CIs: 1.12, 2.28), 0.94 (95% CIs: 0.66, 1.34) and 1.56 (95% CIs: 1.09, 2.28).

4.4. Discussion

We found significant interactions between a genetic risk score for GDM and GL and total sugars on GDM and markers of glycemia in South Asian women living in Ontario, Canada. In those with a greater genetic risk score, a higher GL increased GDM risk and $AUC_{glucose}$ more than what genetics or GL alone predicted. Contrary to our hypothesis, we found that

Figure 4.2. Interaction between genetic predisposition to T2DM and total sugars on GDM risk in START study.*



*Odds ratios of GDM risk according to joint classification of total sugars (in quartiles; Q) and genetic risk scores (in tertiles; T). The analyses were adjusted for age, prepregnancy weight, height, diet quality, calories, social disadvantage index.

Abbreviations: GDM, gestational diabetes mellitus; START, South Asian Birth Cohort; T2DM, type 2 diabetes mellitus.

Table 4.4. Correlation of total sugar intake and other dietary variables in the START study.*

	Total sugars	
	Correlation	**p-value**
Energy	0.02 (-0.04, 0.08)	0.540
Legumes	-0.06 (-0.12, 0.005)	0.070
Nuts and seeds	0.001 (-0.06, 0.06)	0.973
Fruits	0.34 (0.28, 0.40)	<2.2E-16
Leafy vegetables	0.01 (-0.05, 0.08)	0.669
Cooked vegetables	-0.13 (-0.19, -0.06)	7.81E-05
Raw vegetables	-0.10 (-0.16, -0.04)	0.002
Meat	-0.15 (-0.21, -0.09)	4.38E-06
Fried foods	-0.15 (-0.21, -0.09)	4.65E-06
Starch (estimated)	-0.70 (-0.73, -0.67)	<2.2E-16
Fibre	-0.08 (-0.14, -0.01)	0.017
Whole grains	-0.24 (-0.30, -0.18)	2.59E-13
Diet quality	0.13 (0.06, 0.19)	8.15E-05

*Data are reported as correlation with its 95% CIs.

†Diet quality was calculated based on servings of fruits, leafy vegetables, cooked vegetables, raw vegetables, meat, and fried foods. A higher score means a higher quality diet.

women with higher total sugar intake have lower GDM risk in the presence of a higher genetic predisposition. However, higher total sugar intake correlated with higher intakes of fruit, cooked vegetables, and lower intakes of meat, fried foods, raw vegetables, starch, and whole grains, suggesting protection against GDM. We did not identify significant any interactions between genetic predisposition and carbohydrate quality in White-Caucasians.

We only observed significant interactions between the genetic risk score and carbohydrate quality on GDM risk in South Asians in our cohort. This may reflect differences in clinical characteristics between South Asians and White-Caucasians in our study such as smoking, social disadvantage, parity, and dietary intakes. South Asians have a higher risk of GDM than White-Caucasians and may be more susceptible to environmental risk factors. It may also relate to the differences in study design and methodology. For example, food and nutrients intakes were assessed using different instruments and databases. The CHILD study [White-Caucasians] used an FFQ designed by the Fred Hutchinson Cancer Research Centre and analyzed using the University of Minnesota NDSR software.[103] The START study [South Asians] used an ethnic-specific FFQ designed by the START investigators and analyzed using ESHA.[264] Further, the number of study centres in each cohort varied in geographical locations (i.e. the CHILD cohort included 4 major study centres [British Columbia, Alberta, Manitoba, and Ontario],[103] whereas the START cohort included 3 study centres, spread across Peel Region, Ontario).[105] More likely, however, the small number of cases of GDM (n=44 cases)

provided insufficient power to detect an interaction between the GDM-GRS and total sugars analysis on GDM in White-Caucasians. In the GDM-GRS and the total sugars analysis, we achieved 10% power in the White-Caucasian cohort compared to 67% in South Asians. The GDM-GRS and GL analysis achieved 72% power in the White-Caucasian cohort (n=44 cases) but only 22% in the South Asian cohort (n=107 cases), implying that the significant association observed in the South Asian cohort may be a false positive.

Among South Asians, a high GL or low total sugar intake resulted in a higher risk of GDM in those with a high genetic risk score for T2DM. Emerging evidence suggests that healthy lifestyle choices can reduce GDM risk. The RADIEL trial in White-Caucasian women with a history of GDM and BMI≥ 30kg/m^2 found that women homozygous for the C-allele of rs10830963 of the gene MTNR1B responded better to the lifestyle intervention than the control group, resulting in a lower risk of GDM (OR= 0.16 [95% CIs: 0.03, 0.85], p= 0.014).[65] The MTNR1B is a protein-coding gene for the melatonin receptor 1B.[282] Individuals with T2DM have higher expressions of MTNR1B in the pancreas and high MTNR1B levels may antagonize insulin release.[282] Other studies have also reported significant gene-diet interactions in T2DM risk.[263] Our findings are consistent with these previous reports and for the first time indicate that high quality carbohydrate sources may modify the genetic predisposition on GDM. Our study showed that GL and total sugars strongly interacted with GRS, but not GI nor added sugars. GL and total sugars are carbohydrate quality markers that are broader than GI and added sugars, respectively. As such, these metrics may allow for a more comprehensive measure of dietary carbohydrate

quality and may account for the differences in association for GL and GI, and in the presence of different levels of total sugars and added sugars intake.

We found that women with a higher genetic risk score for T2DM and higher intake of total sugars had the lowest GDM risk. Higher total sugar intake was correlated with intakes of healthy foods (e.g. fruits and vegetables) and inversely correlated with intakes of unhealthy foods (e.g. fried foods, meat, starch), suggesting that sugar positively associated with a high-quality diet. This finding lends support to directing public health practice and research in GDM prevention to consider dietary patterns and foods more so than specific foods or macronutrients.

Our study has several limitations. First, both our GDM-GRS and FG-GRS consists of SNPs that showed GWAS significance with T2DM or FG, respectively. Some investigators have suggested that GWAS-level significance (i.e. $5x10^{-8}$) is too restrictive and have called for a higher significance cut-off;[283] thus, we may have missed other SNPs that predicted diabetes. Further, we could not build a GRS made up of SNPs associated with GDM because only one study has examined this relationship and the investigators of this study reported only two SNPs that predicted GDM risk at GWAS-level significance. Instead, we built our GRS consisting of SNPs associated with T2DM.[49] However, these SNPs were studied in non-pregnant and White-Caucasian populations. Second, both cohorts measured food intake using self report with a retrospective semiquantitative FFQ.[103,264] As such, we cannot rule out that dietary misclassification biased our analyses towards the null. Furthermore, the FFQ used in the CHILD cohort captured food intake during

pregnancy,[103] while the FFQ in the START cohort captured food intake in the previous 12 months.[264] This may partially explain some of the differences in food and nutrient intake at baseline. Third, GDM diagnosis was self-reported and we may have missed potential GDM cases in the CHILD and START cohorts. Fourth, some women in the CHILD cohort had completed the FFQ after the 24-28 weeks of gestation, which typically is when women are diagnosed with GDM using an OGTT. Thus, it cannot be ruled out that women made changes to their lifestyle in the recent past, which could bias associations and interactions observed.

4.5. Conclusion

In this study, South Asian women with a higher genetic predisposition to GDM were more susceptible to the detrimental effect of GL on GDM risk. Counter-intuitively, in women with a higher genetic predisposition for GDM, a higher total sugar intake was protective against GDM; however higher total sugar intake correlated with higher diet quality. Thus, for women of South Asian ancestry who are genetically predisposed to T2DM risk, adopting a healthy low GL diet may help reduce GDM risk. However, our study had some important limitations, and there is often a high potential for false positive findings in gene-diet interaction studies,[261] thus larger and higher quality studies are needed to confirm our findings.

CHAPTER 5. EPILOGUE AND CONCLUSIONS

5.1. Discussion

During pregnancy, glucose metabolism undergoes extraordinary changes in preparation for fetal development and growth. By the third trimester, all women experience some degree of insulin resistance, which helps shunt glucose and other nutrients to the feto-placental unit; however, when this insulin insensitivity becomes too extreme, it acts as a stressor on pancreatic β-cells to produce more insulin.[1] This may lead to pancreatic dysfunction that harms both the woman and infant. It is likely that this pathological state results from the interplay of genetics and environmental factors.

In this thesis, I attempted to comprehensively summarize the association between dietary factors and GDM risk and assess if CHO quality can modify women's genetic predisposition to GDM. Diets lower in energy intake, and higher in fruits and vegetables, and whole grains reduced GDM risk, while diets higher in SSBs, red meat, and refined grains increased the risk of GDM. In our network meta-analysis, we found that most dietary patterns when given alongside GWG advice, reduced fasting glucose. However, these same dietary patterns did not consistently reduce GDM risk. Possible explanations include that the fasting glucose reduction maybe too small to influence GDM risk and/or differences in the study sample result in different responses to the same dietary exposure. Finally, the findings from our cohort analysis suggest that CHO quality can modify genetic predisposition to T2DM on GDM risk in a cohort of pregnant Canadian South Asian women. We found that women with a high genetic predisposition to T2DM who ate a

higher GL diet were at the highest risk for GDM, but surprisingly, women in the highest quantile of genetic predisposition to T2DM and total sugar intake were at the lowest risk for GDM. Although these findings are unexpected, it may be that total sugar intake is a marker of a healthy eating pattern. We observed positive correlation between total sugar intake and other putatively protective foods including fruits (r= 0.34), and negative correlation with meat (r= -0.15) and fried foods (r= -0.15). However, we also reported that the power for the gene and GL interaction analysis was 22% and for the gene and total sugars interaction analysis, it was 67%, which implies that these significant associations observed in the South Asian cohort may be a false positive. We also observed that diet and foods can modify the likelihood of appropriate GWG, HDP risk, and blood lipids in women. Taken together, these findings suggest that food intake likely influences the development of GDM and other metabolic disorders of pregnancy. However, the quality of most of the evidence for the association of diet, foods, and nutrients and metabolic disorders of pregnancy is low.

5.2. Clinical and health policy implications

Most major diabetes organizations with the exception of DC do not include dietary recommendations for GDM prevention.[10,17] DC recommends that women follow a healthy diet to prevent GDM and excessive GWG.[18] The findings from our systematic review and meta-analysis makes us less confident in this dietary recommendation for three reasons: 1) cohort studies and RCTs showed divergent findings regarding the relationship between healthy diet and GDM prevention. The pooled analysis in cohort studies showed a

protective association, while RCTs showed a null effect; 2) the evidence is rated low quality in cohort studies and very low quality in RCTs, indicating low confidence in the effect estimates as being the true effect; 3) healthy diet even when combined with GWG advice did not show significant protection against GDM. Having noted this, pre-pregnancy body weight is a strong predictor of GDM and accounts for almost 30% of GDM.[43,44] As such, we believe that health policies and healthcare providers should explore other dietary interventions and lifestyle modifications including physical activity aimed at achieving optimal body weight to prevent GDM.

We found high-quality evidence to suggest that red meat intake increases GDM risk. However, none of the current dietary guidelines have emphasized this relationship.[10,17,18] Each serving of red meat (e.g. 3-oz) increases GDM risk by 74% (95% CIs: 1.46, 2.08),[108,159] and red meat intake may account for 7% of all GDM cases. The substitution of red meat intake with other protein sources including poultry, seafood, nuts, and legumes have shown to reduce T2DM and GDM risk.[108,214] Thus, from a clinical and public health point of view, reduction of red meat consumption and its replacement with other healthy dietary protein should be considered to reduce GDM risk.

5.3. Methodological considerations

Our findings have implications for nutrition epidemiology methodology. Our cohort analysis highlights the importance of considering dietary patterns, rather than single nutrients as an exposure in elucidating the association between “diet” and complex health outcomes. We found that total sugars may be a marker of a high-quality diet. Total sugars

do not differentiate between food sources of sugars. Sugars can come from "healthy" food sources such as fruits, vegetables, and grain products, and it can also come from "unhealthy" food sources such as SSBs and refined grains. Eating more or less of healthy or unhealthy food sources of sugars may change the amount of total sugars consumed but its association of GDM risk would differ. Our meta-analyses found that fruits and vegetables reduce GDM risk, while a higher adherence to the Western diet, which includes high intakes of SSBs and refined grains, increased GDM risk. Future analyses should consider sources of sugar, to better understand the relative contribution of different food sources. Second, individuals do not eat nutrients in isolation. We found that higher total sugar intake was correlated with higher intakes of fruit and cooked vegetable and lower intakes of meat, fried foods, raw vegetables, starch, and whole grains. A healthy eating pattern identified in our meta-analyses to be protective against GDM and may explain the protective GDM association we found in South Asian women with the highest genetic predisposition to T2DM and total sugar intake. Our findings suggest that future policies and research efforts to prevent GDM should consider patterns of eating as potentially relevant dietary metrics.

In order to progress, nutritional sciences must improve both the quality and quantity of evidence they generate. Although some argue that improvement in our understanding of nutrition can only come from well-conducted RCTs, others have argued that this is not necessarily true.[231] Prospective cohort studies and RCTs have different strengths and limitations. It is by viewing the totality of the evidence from prospective

cohort studies and RCTs and assessing their consistency, and the methodological underpinnings of each study designs, we can best build an evidence-based nutrition platform. Indeed, in our meta-analyses we found that where evidence from both cohort studies and RCTs were available for the same exposure and outcome, concordance is usually reported. Diverse types of evidence, when considered together, best support causal inference.[231]

5.4. Limitations of this thesis

There are several limitations to the projects found in this thesis. First, the generalizability of results of our studies is uncertain. Most of the cohort studies and RCTs included in our systematic reviews and meta-analyses enrolled in White-Caucasians living in high-income countries, and the CHILD and START analyses we conducted included White-Caucasians and South Asians living in Canada only. Interventions that work in some settings may not work in others, because of social, economic, and cultural forces that influence diet. This is a special concern in Canada, where there is great regional and ethnic diversity in lifestyle patterns and where diabetes is especially frequent in certain racial and ethnic groups, including Indigenous, East Asians, Hispanics, and African Canadians. Second, diet is only one component of a healthy lifestyle pattern. This thesis did not consider other lifestyle tools for GDM prevention including physical activity, vitamins and mineral supplement use, sleep patterns, social connections, and self-monitoring of blood glucose (SMBG). Like dietary patterns, the use of different lifestyle interventions can lead to synergistic effects, providing an even more powerful tool against GDM development. Third, this thesis

considered only the relationship of dietary factors on outcomes in women. These same dietary factors may have differing effects on the infant. For example, although GI did not significantly prevent GDM cases in our meta-analyses and cohort analysis, RCTs have shown women who received a low GI intervention were more likely to deliver infants with a lower birth weight without an increase in numbers of small-for-gestational-age and macrosomia cases.[61] Future studies are needed to study the effects of diets consumed by women on infant outcomes. Finally, we considered the relation of the dietary factors with each of the outcomes separately (GDM, GWG, HDP, and blood lipids) in our meta-analysis. We, however, did not assess the "global" impact of the dietary interventions on this cluster of metabolic risk factors. A previous meta-analysis that evaluated RCTs that were designed to prevent excessive GWG via dietary interventions also found a risk reduction in GDM.[284] Future analyses should consider the global impact of dietary factors so that "optimal" diets to manage the risk of metabolic disorders of pregnancy can be identified.

5.5. Future directions and conclusions

Most women understand the importance of a healthy diet during pregnancy and are motivated to change their diets to support a healthy pregnancy.[285] I saw this first-hand when I was working at an obstetrics clinic during the second-year of my PhD program. Prior to the start of working at the clinic, I expected only to briefly interact with these mothers-to-be. Instead, I heard stories and learnt so much from these women about the state of the dietetic field. I heard the confusion in their voice and saw the desire in their eyes to learn more about nutrition. I felt their frustration in wanting more reliable

information about healthy eating during pregnancy and sensed their unwilling acceptance that they may not get the answers to the questions they have.

*Should I be taking omega-3's? Is it healthy for my baby if I follow a vegetarian diet during pregnancy? How do I use the nutrition label to make healthier choices for my family? What **IS** the optimal diet?*

Their struggle to learn more about nutrition and from a reliable source is real.[286] Their stories grounded me to keep this thesis as relevant to public health use as much as possible. The two biggest take-home messages from my PhD experiences are that: 1) we need more high-quality research to better understand how diet affects women and their infants during their pregnancy and 2) we need to get this information back to the public for women and healthcare providers to be able to use it.

To accomplish this, we must begin with carefully posed, patient-centered research questions and well-designed studies as these serve as the foundation in building our understanding of what healthy eating is during pregnancy. Our meta-analyses showed that the evidence for most dietary factors and their relation to pregnancy outcomes is of low or very low quality. We need larger studies that are conducted to a high standard (e.g. adjust for confounding, blind investigators to treatment groups, have clear a priori study plan etc.). Particularly, we need more RCTs. RCTs are feasible in this population, but most of our understanding of the association of diet with pregnancy outcomes comes from cohort studies, which are challenged by confounding and recall bias. Second, we need to study women from different ethnic backgrounds and countries. Interventions that work

in some societies may not work in others, because social, economic, and cultural forces influence diet. Adherence is always an issue in dietary studies and in clinical practice, particularly when women do not feel advice is relevant or personalized to their dietary needs.[287,288] It is important to understand the cultural context of diet and foods and how this may affect one's ability to put dietary information into practice.

Although this thesis did not examine knowledge translation behaviours and activities, I believe that this is an important component to address because ultimately, the research that we are doing is meant to help influence healthy behaviour in people. We need to provide more nutrition training to physicians. Most women prefer going to their physician for information about nutrition before searching for more information elsewhere (e.g. internet).[289] Yet in survey studies, many healthcare providers reported that barriers to providing nutrition counselling to women include lack of resources and relevant training.[290] Specific changes to how we train clinicians during medical school and residency is needed to increase their confidence and ability to provide dietary counselling. This may include dedication to more time in the curriculum to nutrition training and incorporating more nutrition-related questions in board exam to make the subject area more relevant.[291] Second, more education about healthy eating need to be provided to women. Most women understand the importance of healthy eating during pregnancy, but few know where to start. Some studies have cited barriers to achieving healthy eating include personal food preferences, eating in different social environments where food choice and portions were out of control, and lack of knowledge and skills in dietary

management.[288] Providing credible resources online, which is often cited as one of the common sources of information relating to pregnancy, and offering prenatal workshops that include a dietician may help women overcome some of these barriers.

Taken together, some additional questions that should be addressed in future research include:

1. What is the relationship of diet, foods, and nutrients and metabolic disorders in women from other ethnic groups, where the dietary composition differs from that of North America and Europe?
2. Is there a diet that is optimal for women and infant health that is also environmentally sustainable? Are vegetarian or vegan diets “safe” to adopt during pregnancy?
3. What are some of the approaches to increasing dietary adherence in RCTs? Do these approaches need to consider food cravings and aversions during pregnancy?
4. What are the thoughts and preferences of women on diet, food, and nutrient during pregnancy? What are some of the factors that women face during pregnancy that facilitate or hinder their ability to adopt a healthy eating pattern?
5. Should strategies for the prevention of metabolic disorders of pregnancy consider other lifestyle components including physical activity, social factors, and behavioural factors? If so, what is the relationships of these components

individually and in combination with metabolic disorders of pregnancy?

6. Which genes influence metabolic disorders of pregnancy and what are their functions? How does epigenetics or ethnicity modify these relationships?
7. Can future studies replicate the findings in our gene-diet interaction study (Chapter 4)?

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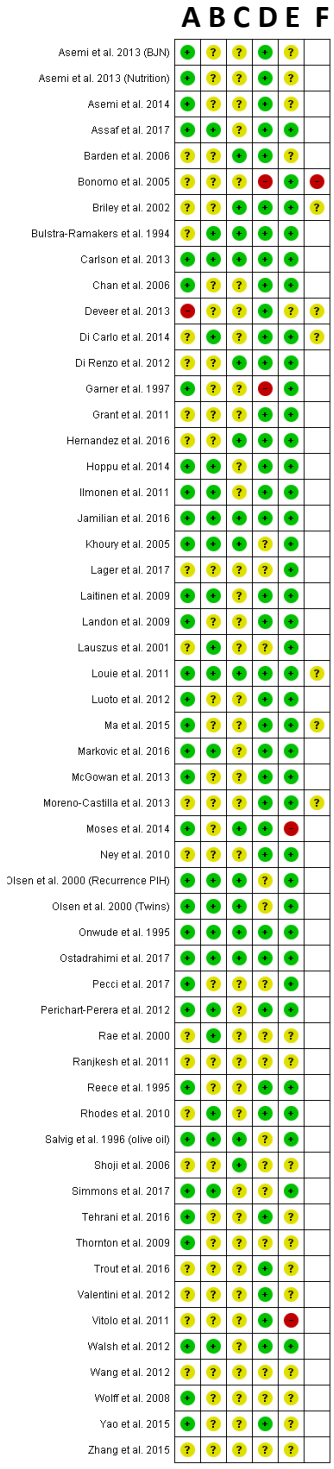
Appendix Figure 2.1. Risk of bias rating for randomized controlled trial.*

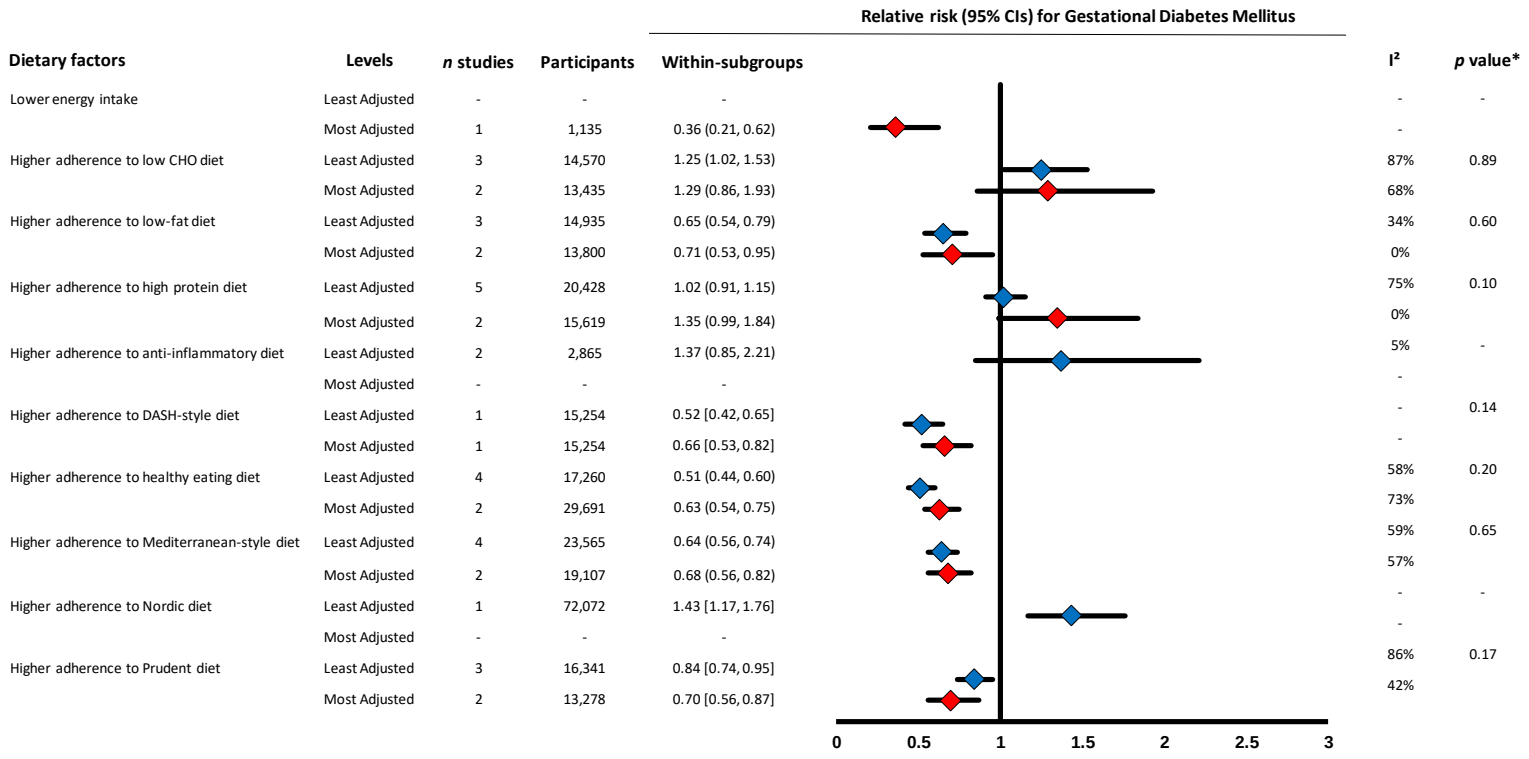


Abbreviations: A, Random sequence generation; B, Allocation concealment; C, Blinding of

participants and personnel; D, Incomplete outcome data; E, Selective reporting; F, Other bias.

* Red dot denotes high risk of bias, yellow for unclear risk of bias, and green for low risk of bias.

Appendix Figure 2.2. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational diabetes mellitus.

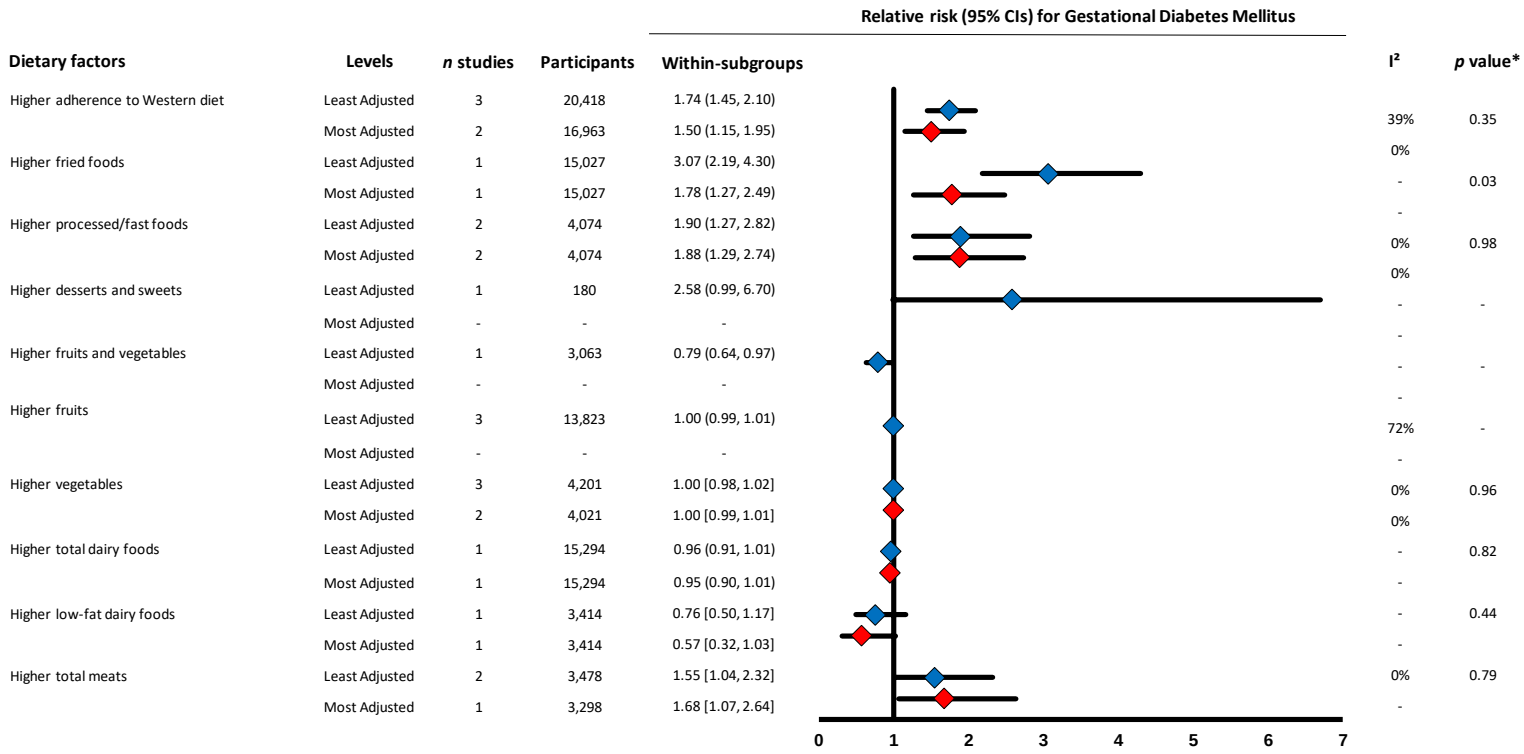


Dietary factors	Levels	*n* studies	Participants	Within-subgroups	I^2	*p* value*
Lower energy intake	Least Adjusted	-	-	-	-	-
	Most Adjusted	1	1,135	0.36 (0.21, 0.62)	-	
Higher adherence to low CHO diet	Least Adjusted	3	14,570	1.25 (1.02, 1.53)	87%	0.89
	Most Adjusted	2	13,435	1.29 (0.86, 1.93)	68%	
Higher adherence to low-fat diet	Least Adjusted	3	14,935	0.65 (0.54, 0.79)	34%	0.60
	Most Adjusted	2	13,800	0.71 (0.53, 0.95)	0%	
Higher adherence to high protein diet	Least Adjusted	5	20,428	1.02 (0.91, 1.15)	75%	0.10
	Most Adjusted	2	15,619	1.35 (0.99, 1.84)	0%	
Higher adherence to anti-inflammatory diet	Least Adjusted	2	2,865	1.37 (0.85, 2.21)	5%	-
	Most Adjusted	-	-	-	-	
Higher adherence to DASH-style diet	Least Adjusted	1	15,254	0.52 [0.42, 0.65]	-	0.14
	Most Adjusted	1	15,254	0.66 [0.53, 0.82]	-	
Higher adherence to healthy eating diet	Least Adjusted	4	17,260	0.51 (0.44, 0.60)	58%	0.20
	Most Adjusted	2	29,691	0.63 (0.54, 0.75)	73%	
Higher adherence to Mediterranean-style diet	Least Adjusted	4	23,565	0.64 (0.56, 0.74)	59%	0.65
	Most Adjusted	2	19,107	0.68 (0.56, 0.82)	57%	
Higher adherence to Nordic diet	Least Adjusted	1	72,072	1.43 [1.17, 1.76]	-	-
	Most Adjusted	-	-	-	-	
Higher adherence to Prudent diet	Least Adjusted	3	16,341	0.84 [0.74, 0.95]	86%	0.17
	Most Adjusted	2	13,278	0.70 [0.56, 0.87]	42%	

Abbreviations: CHO, carbohydrate; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

Appendix Figure 2.2. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational diabetes mellitus.



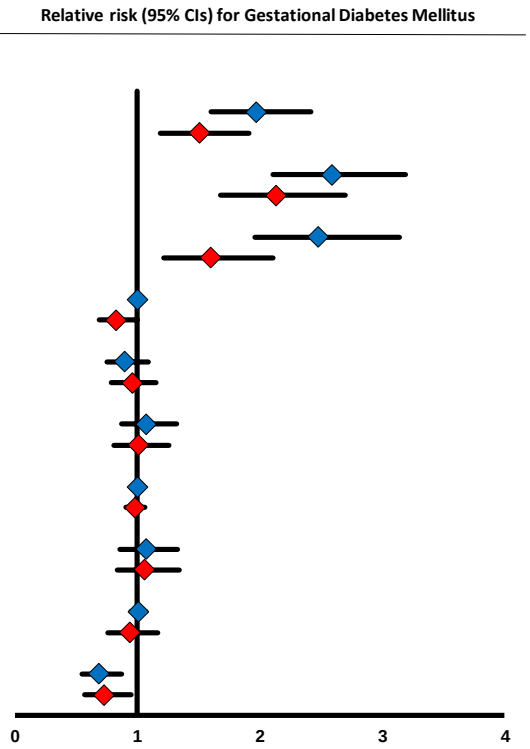
Dietary factors	Levels	*n* studies	Participants	Within-subgroups	I^2	*p* value*
Higher adherence to Western diet	Least Adjusted	3	20,418	1.74 (1.45, 2.10)	39%	0.35
	Most Adjusted	2	16,963	1.50 (1.15, 1.95)	0%	
Higher fried foods	Least Adjusted	1	15,027	3.07 (2.19, 4.30)	-	0.03
	Most Adjusted	1	15,027	1.78 (1.27, 2.49)	-	
Higher processed/fast foods	Least Adjusted	2	4,074	1.90 (1.27, 2.82)	0%	0.98
	Most Adjusted	2	4,074	1.88 (1.29, 2.74)	0%	
Higher desserts and sweets	Least Adjusted	1	180	2.58 (0.99, 6.70)	-	-
	Most Adjusted	-	-	-	-	
Higher fruits and vegetables	Least Adjusted	1	3,063	0.79 (0.64, 0.97)	-	-
	Most Adjusted	-	-	-	-	
Higher fruits	Least Adjusted	3	13,823	1.00 (0.99, 1.01)	72%	-
	Most Adjusted	-	-	-	-	
Higher vegetables	Least Adjusted	3	4,201	1.00 [0.98, 1.02]	0%	0.96
	Most Adjusted	2	4,021	1.00 [0.99, 1.01]	0%	
Higher total dairy foods	Least Adjusted	1	15,294	0.96 (0.91, 1.01)	-	0.82
	Most Adjusted	1	15,294	0.95 (0.90, 1.01)	-	
Higher low-fat dairy foods	Least Adjusted	1	3,414	0.76 [0.50, 1.17]	-	0.44
	Most Adjusted	1	3,414	0.57 [0.32, 1.03]	-	
Higher total meats	Least Adjusted	2	3,478	1.55 [1.04, 2.32]	0%	0.79
	Most Adjusted	1	3,298	1.68 [1.07, 2.64]	-	

Abbreviations: CIs, confidence intervals; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

Appendix Figure 2.2. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational diabetes mellitus.

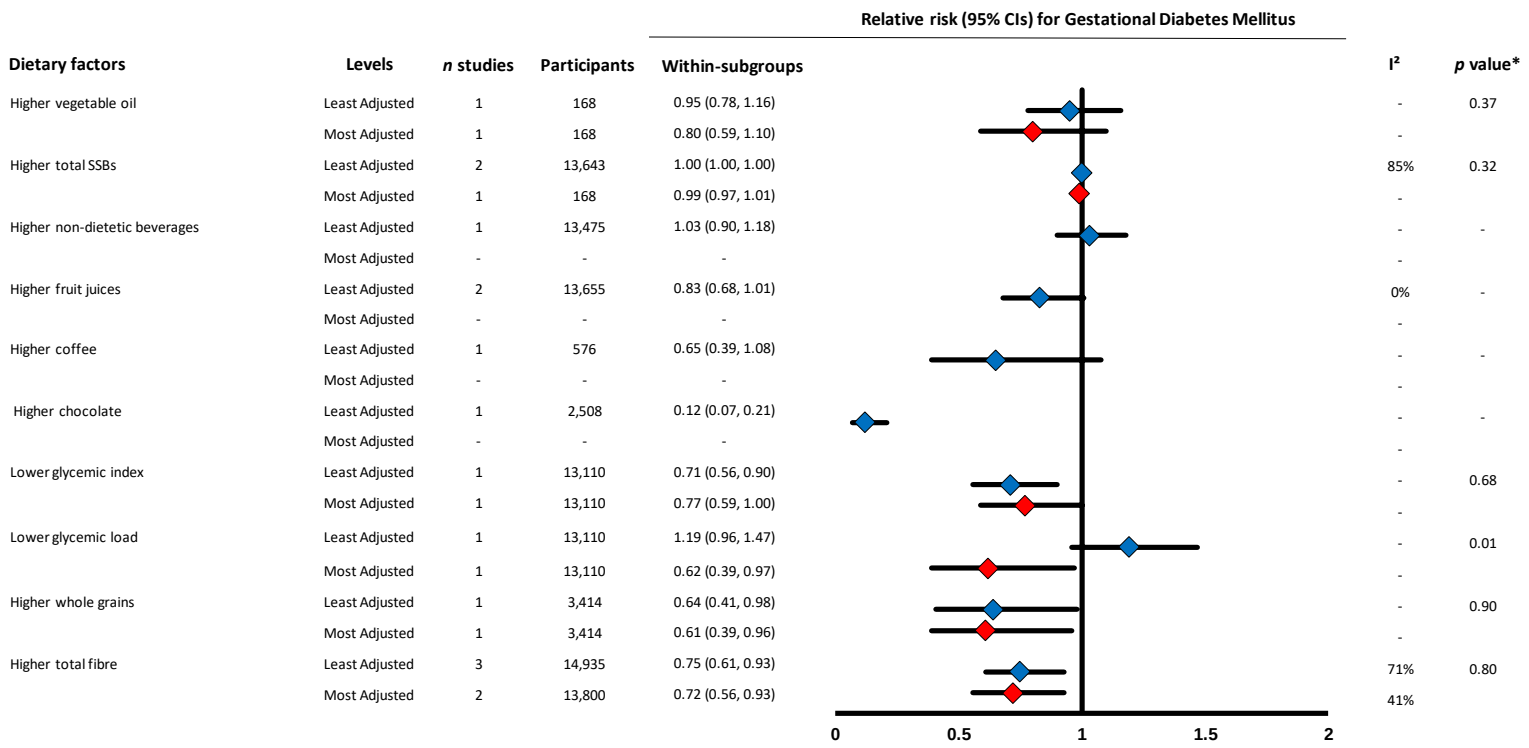
Dietary factors	Levels	*n* studies	Participants	Within-subgroups	I^2	*p* value*
Higher processed meats	Least Adjusted	2	18,592	1.97 (1.60, 2.42)	0%	0.09
	Most Adjusted	2	18,592	1.51 (1.19, 1.91)	49%	
Higher red meats	Least Adjusted	2	18,592	2.59 (2.11, 3.19)	0%	0.22
	Most Adjusted	2	18,592	2.13 (1.68, 2.70)	0%	
Higher unprocessed meats	Least Adjusted	1	15,294	2.48 (1.96, 3.14)	-	0.02
	Most Adjusted	1	15,294	1.60 (1.22, 2.11)	-	
Higher seafoods	Least Adjusted	2	3,447	1.00 (0.96, 1.04)	0%	0.06
	Most Adjusted	2	3,447	0.83 (0.69, 1.00)	0%	
Higher fish	Least Adjusted	2	18,708	0.90 (0.75, 1.09)	42%	0.67
	Most Adjusted	2	18,708	0.96 (0.79, 1.15)	0%	
Higher poultry	Least Adjusted	2	18,592	1.07 (0.87, 1.32)	30%	0.69
	Most Adjusted	2	18,592	1.01 (0.81, 1.26)	0%	
Higher eggs	Least Adjusted	3	18,620	1.00 (0.96, 1.04)	82%	0.71
	Most Adjusted	3	18,620	0.98 (0.91, 1.06)	63%	
Higher legumes	Least Adjusted	1	15,294	1.07 (0.86, 1.33)	-	0.96
	Most Adjusted	1	15,294	1.06 (0.84, 1.34)	-	
Higher nuts and seeds	Least Adjusted	1	168	1.01 (0.95, 1.07)	-	0.54
	Most Adjusted	1	168	0.94 (0.76, 1.17)	-	
Higher nuts and peanuts	Least Adjusted	1	15,294	0.69 (0.55, 0.87)	-	0.73
	Most Adjusted	1	15,294	0.73 (0.57, 0.95)	-	



Abbreviations: CIs, confidence intervals; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

Appendix Figure 2.2. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational diabetes mellitus.

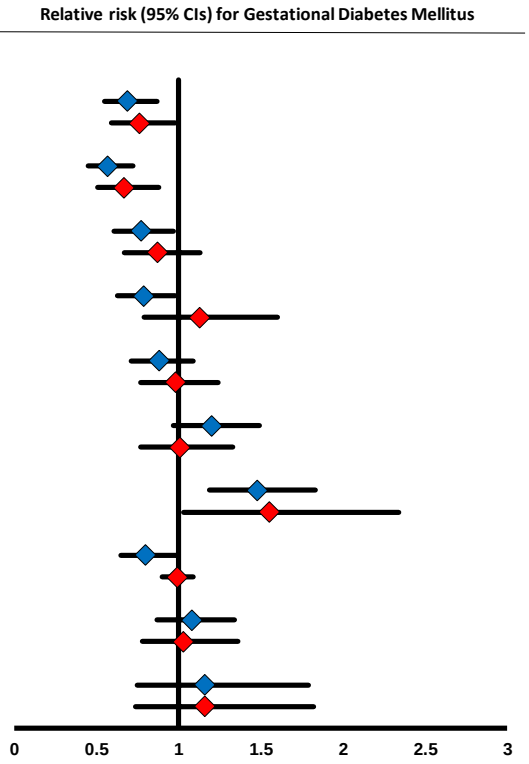


Abbreviations: CIs, confidence intervals; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

Appendix Figure 2.2. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational diabetes mellitus.

Dietary factors	Levels	*n* studies	Participants	Within-subgroups	I^2	*p* value*
Higher cereal fibre	Least Adjusted	1	13,110	0.69 (0.55, 0.87)	-	0.57
	Most Adjusted	1	13,110	0.76 (0.59, 0.98)	-	
Higher fruit fibre	Least Adjusted	1	13,110	0.57 (0.45, 0.72)	-	0.38
	Most Adjusted	1	13,110	0.67 (0.51, 0.88)	-	
Higher vegetable fibre	Least Adjusted	1	13,110	0.77 (0.61, 0.97)	-	0.49
	Most Adjusted	1	13,110	0.87 (0.67, 1.13)	-	
Lower saturated fat	Least Adjusted	1	13,475	0.79 (0.63, 0.98)	-	0.09
	Most Adjusted	1	13,475	1.13 (0.79, 1.60)	-	
Higher PUFA-to-SFA ratio	Least Adjusted	1	13,475	0.88 (0.71, 1.09)	-	0.50
	Most Adjusted	1	13,475	0.98 (0.77, 1.24)	-	
Higher PUFA	Least Adjusted	1	13,465	1.20 [0.97, 1.49]	-	0.34
	Most Adjusted	1	13,475	1.01 [0.77, 1.33]	-	
Higher MUFA	Least Adjusted	1	13,475	1.48 [1.19, 1.83]	-	0.83
	Most Adjusted	1	13,475	1.55 [1.03, 2.34]	-	
Lower trans fat	Least Adjusted	1	13,475	0.80 [0.65, 1.00]	-	0.08
	Most Adjusted	1	13,475	0.99 [0.90, 1.09]	-	
Higher n-3	Least Adjusted	1	13,475	1.08 [0.87, 1.34]	-	0.78
	Most Adjusted	1	13,475	1.03 [0.78, 1.36]	-	
Higher fish oil/DHA & EPA	Least Adjusted	1	3,279	1.16 [0.75, 1.79]	-	1.00
	Most Adjusted	1	3,279	1.16 [0.74, 1.82]	-	

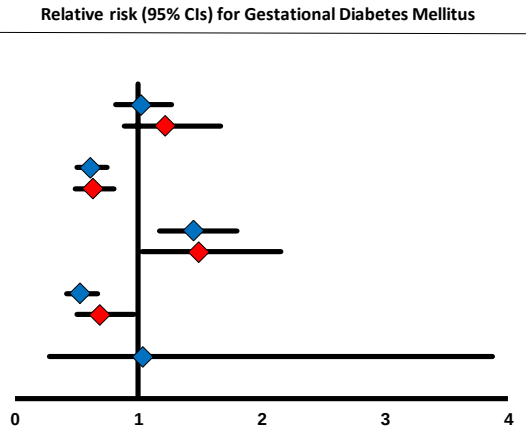


Abbreviations: CIs, confidence intervals; DHA, Docosahexaenoic acid; EPA, eicosapentaenoic acid; MUFA, monounsaturated fatty acids; *n,* number of; n-3, omega-3; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

Appendix Figure 2.2. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational diabetes mellitus.

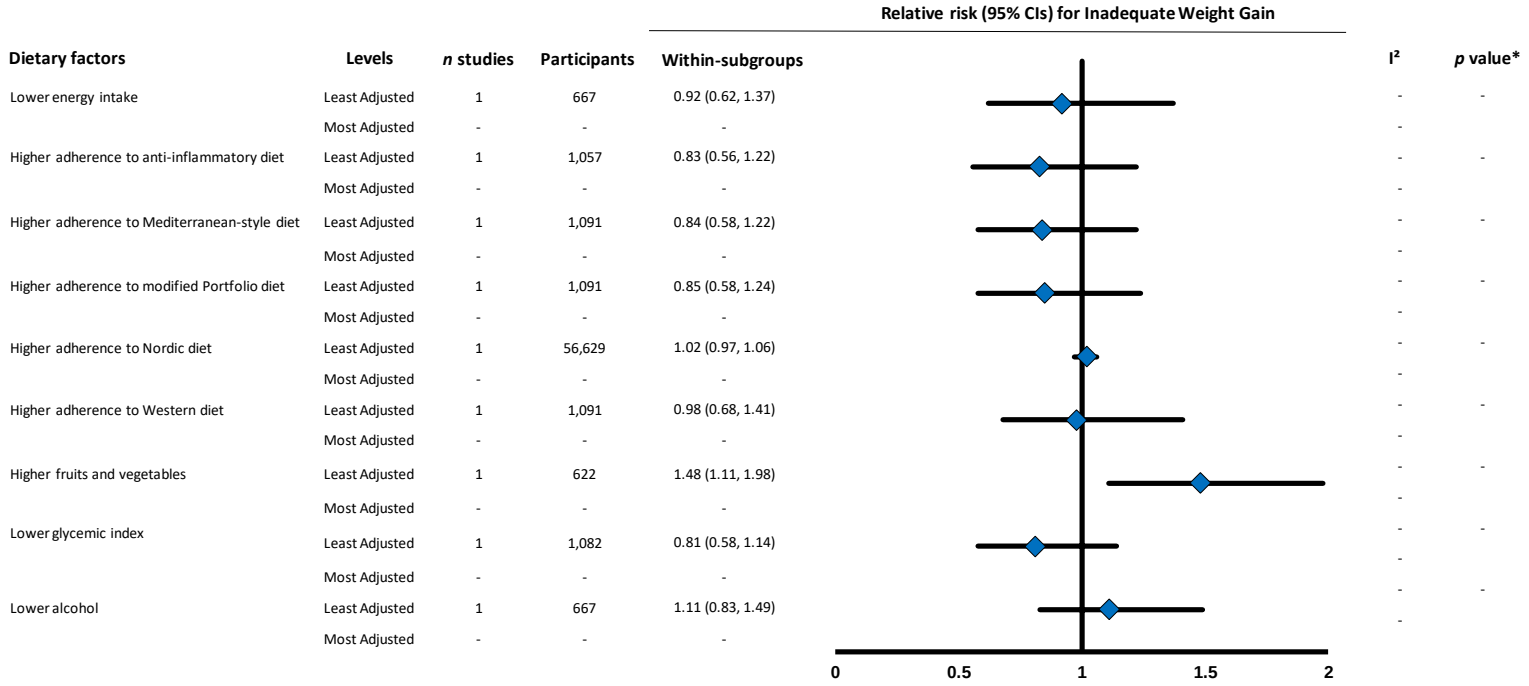
Dietary factors	Levels	*n* studies	Participants	Within-subgroups	I²	*p* value*
Lower n-6	Least Adjusted	1	13,475	1.02 (0.82, 1.27)	-	0.35
	Most Adjusted	1	13,475	1.22 (0.89, 1.67)	-	
Lower dietary cholesterol	Least Adjusted	2	16,633	0.61 (0.50, 0.75)	80%	0.87
	Most Adjusted	2	16,633	0.63 (0.49, 0.80)	58%	
Higher animal protein	Least Adjusted	1	15,294	1.45 (1.17, 1.80)	-	0.89
	Most Adjusted	1	15,294	1.49 (1.03, 2.16)	-	
Higher vegetable protein	Least Adjusted	1	15,294	0.53 [0.42, 0.67]	-	0.21
	Most Adjusted	1	15,294	0.69 [0.50, 0.96]	-	
Lower alcohol	Least Adjusted	1	1,135	1.04 [0.28, 3.87]	-	-
	Most Adjusted	-	-	-	-	



Abbreviations: CIs, confidence intervals; *n,* number of; n-6, omega-6.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

Appendix Figure 2.3. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on inadequate gestational weight gain.

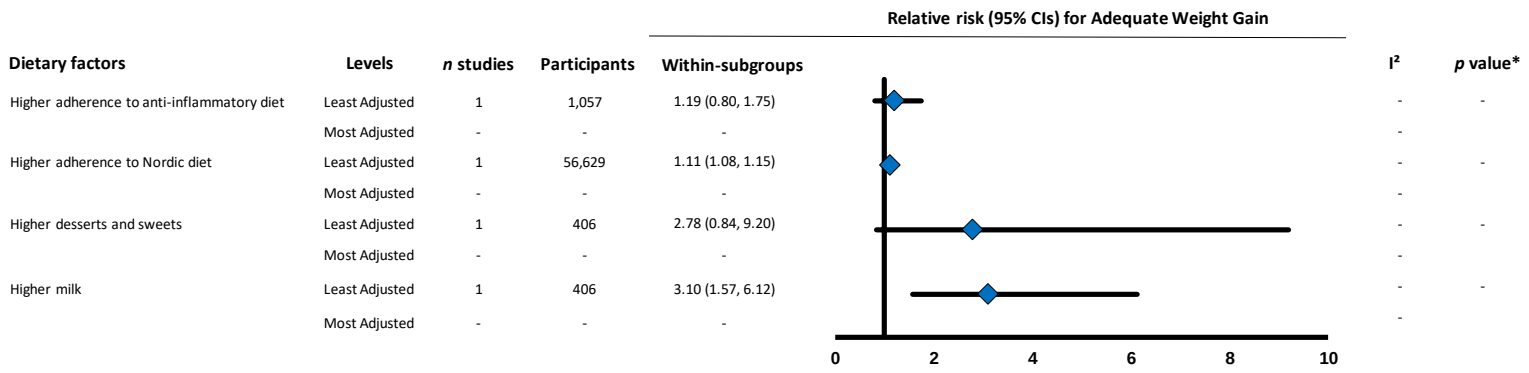


Dietary factors	Levels	*n* studies	Participants	Within-subgroups	I^2	*p* value*
Lower energy intake	Least Adjusted	1	667	0.92 (0.62, 1.37)	-	-
	Most Adjusted	-	-	-	-	
Higher adherence to anti-inflammatory diet	Least Adjusted	1	1,057	0.83 (0.56, 1.22)	-	-
	Most Adjusted	-	-	-	-	
Higher adherence to Mediterranean-style diet	Least Adjusted	1	1,091	0.84 (0.58, 1.22)	-	-
	Most Adjusted	-	-	-	-	
Higher adherence to modified Portfolio diet	Least Adjusted	1	1,091	0.85 (0.58, 1.24)	-	-
	Most Adjusted	-	-	-	-	
Higher adherence to Nordic diet	Least Adjusted	1	56,629	1.02 (0.97, 1.06)	-	-
	Most Adjusted	-	-	-	-	
Higher adherence to Western diet	Least Adjusted	1	1,091	0.98 (0.68, 1.41)	-	-
	Most Adjusted	-	-	-	-	
Higher fruits and vegetables	Least Adjusted	1	622	1.48 (1.11, 1.98)	-	-
	Most Adjusted	-	-	-	-	
Lower glycemic index	Least Adjusted	1	1,082	0.81 (0.58, 1.14)	-	-
	Most Adjusted	-	-	-	-	
Lower alcohol	Least Adjusted	1	667	1.11 (0.83, 1.49)	-	-
	Most Adjusted	-	-	-	-	

Abbreviations: CIs, confidence intervals; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

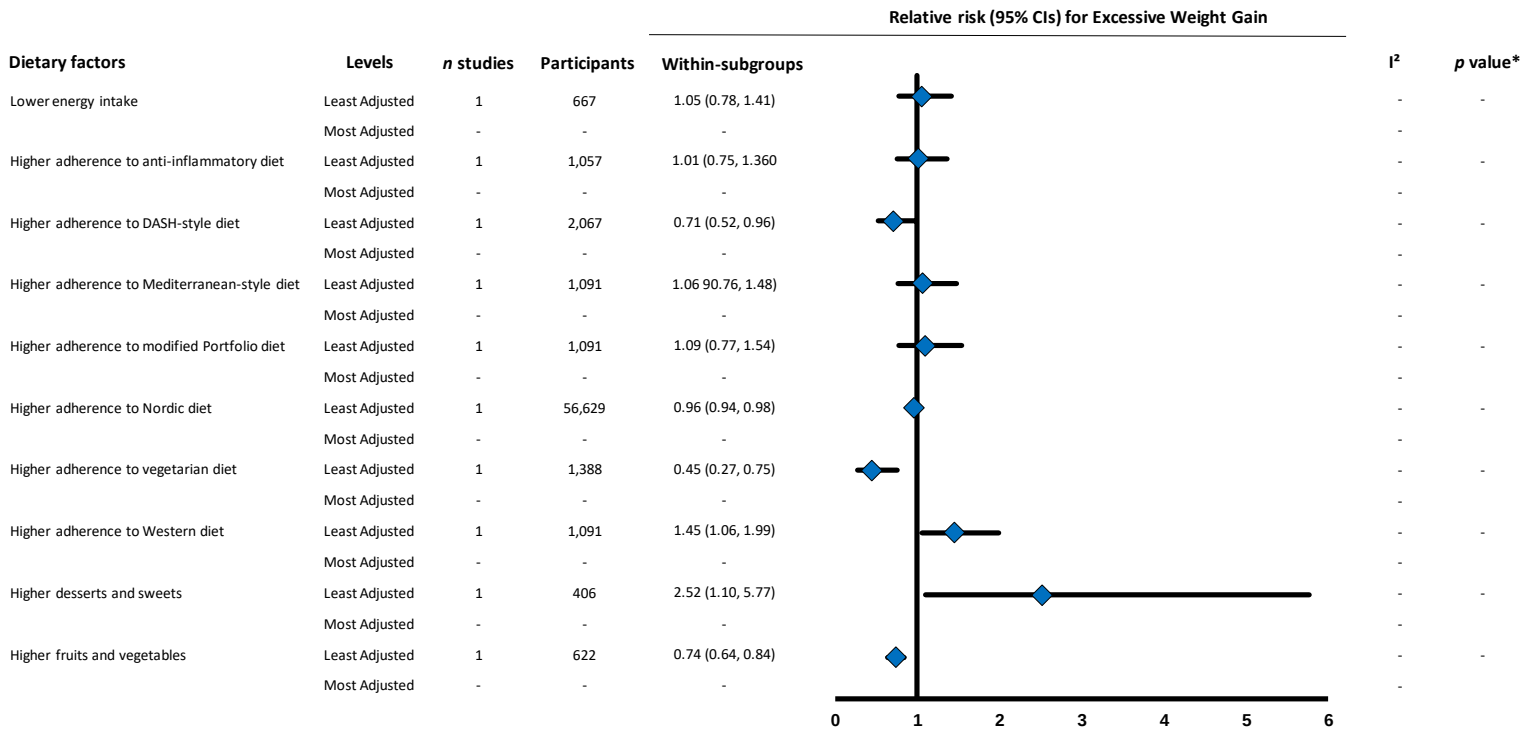
Appendix Figure 2.4. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on adequate gestational weight gain.



Abbreviations: CIs, confidence intervals; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

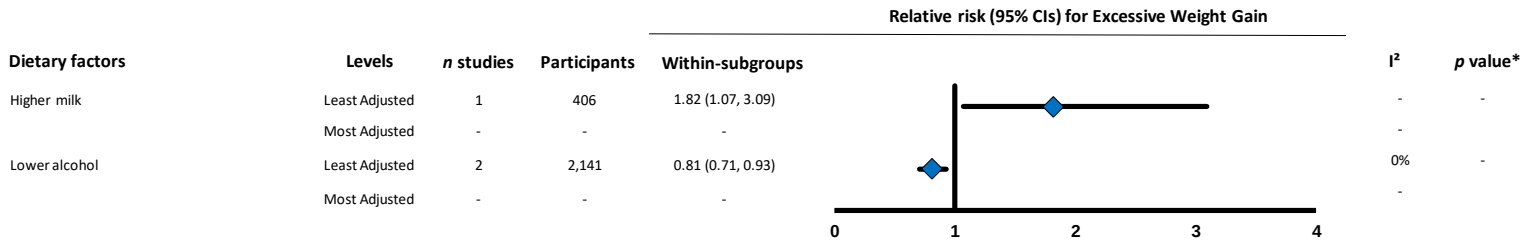
Appendix Figure 2.5. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on excessive gestational weight gain.



Abbreviations: CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

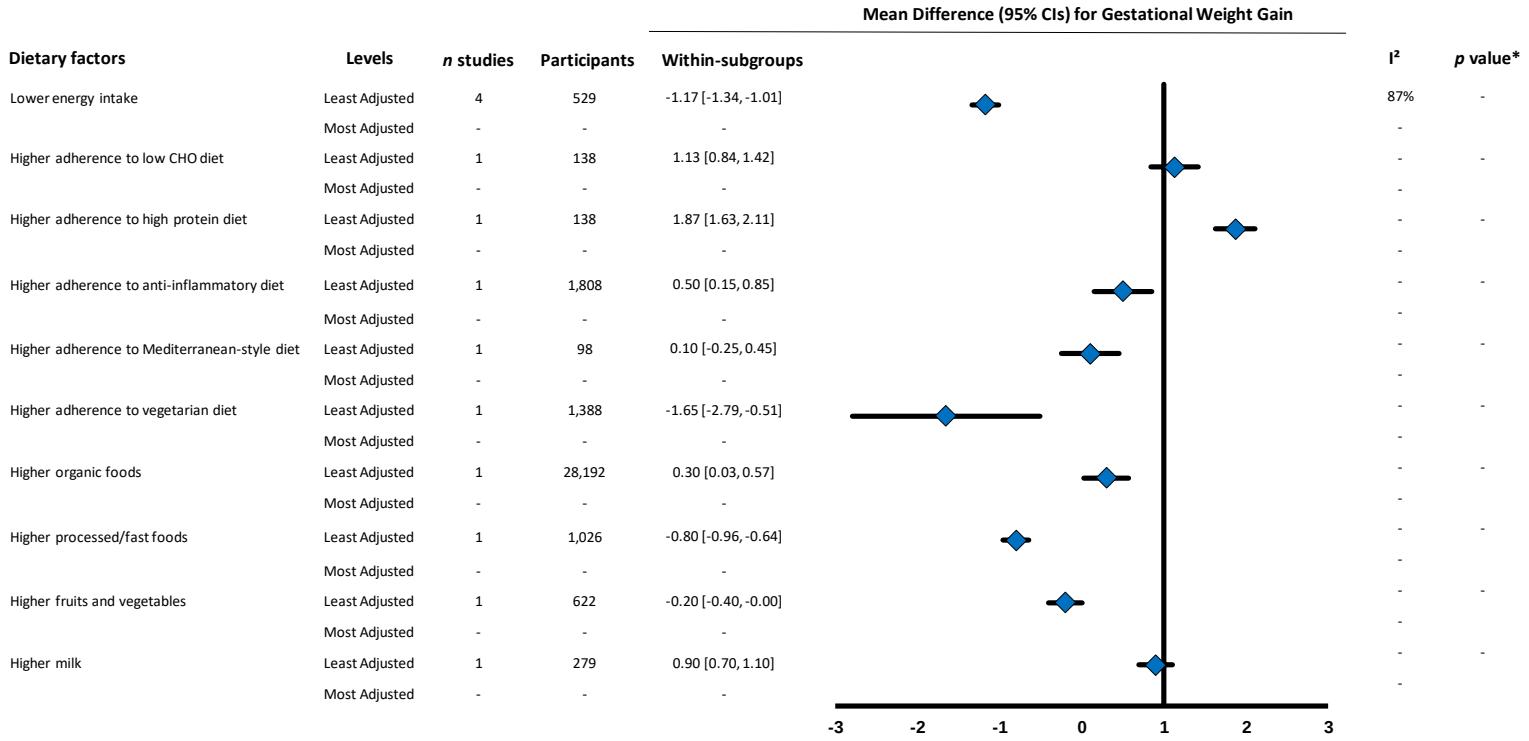
Appendix Figure 2.5. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on excessive gestational weight gain.



Abbreviations: CIs, confidence intervals; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

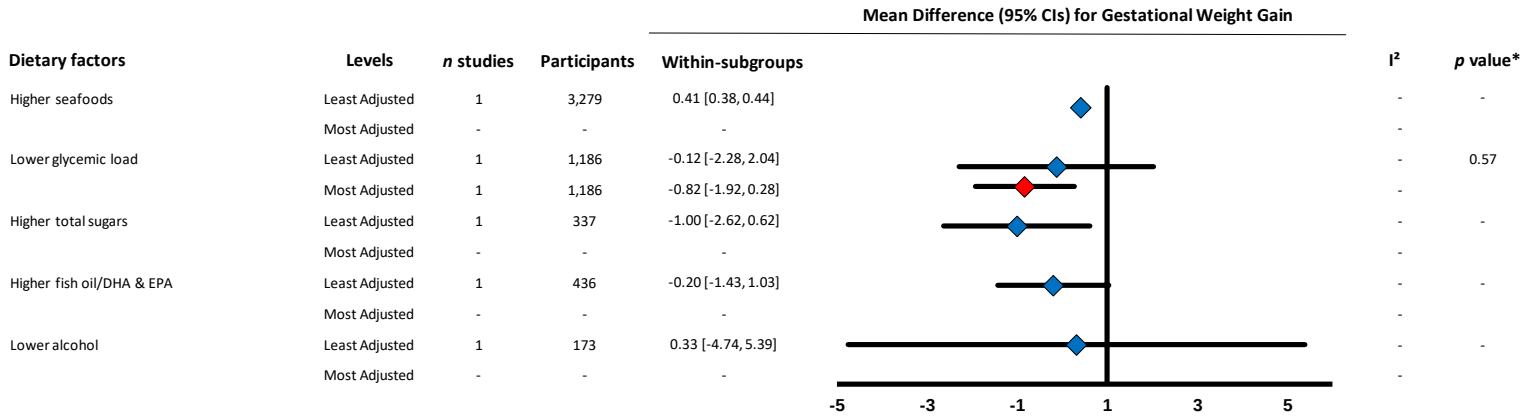
Appendix Figure 2.6. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational weight gain.



Abbreviations: CHO, carbohydrate; CIs, confidence intervals; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

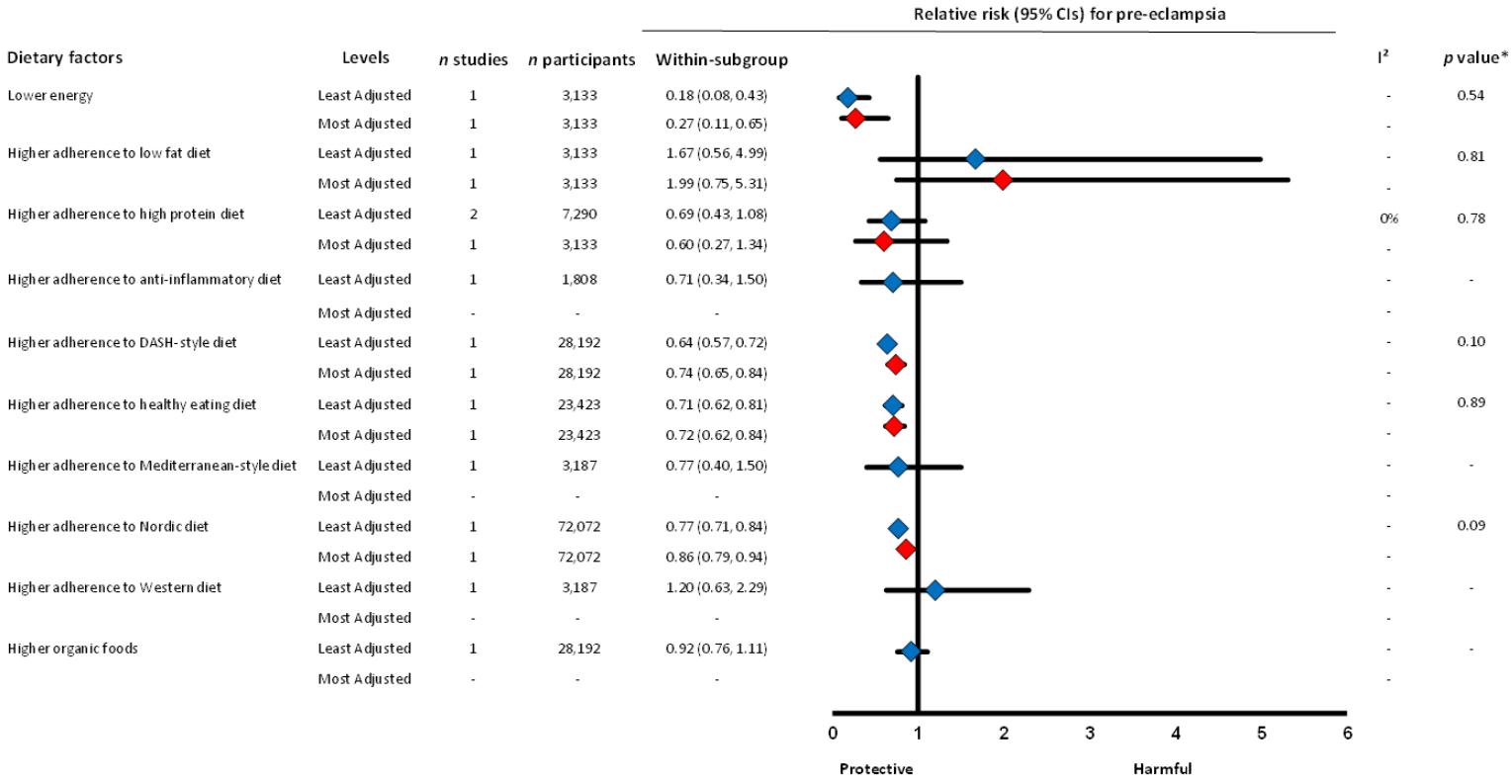
Appendix Figure 2.6. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational weight gain.



Abbreviations: CIs, confidence intervals; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor

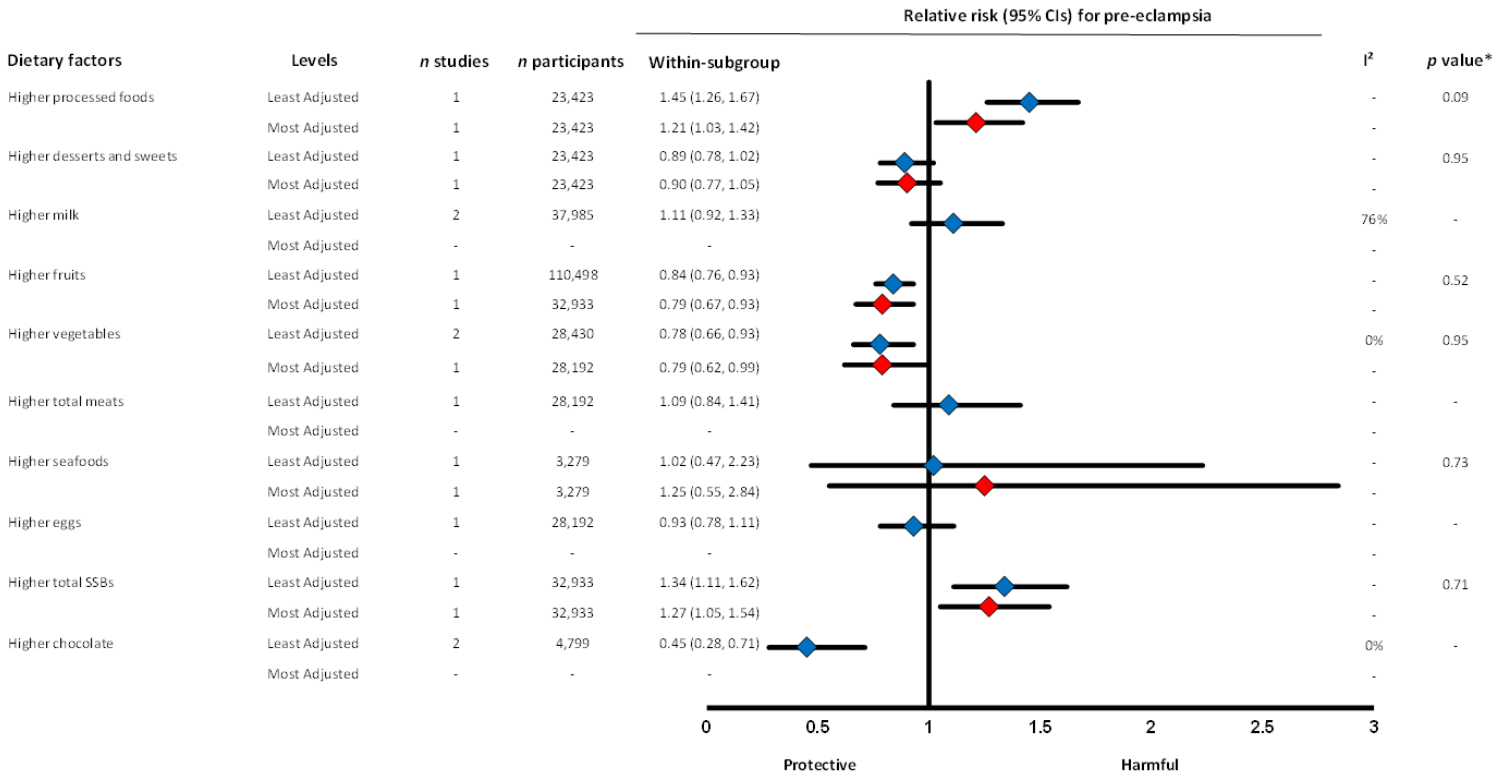
Appendix Figure 2.7. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on pre-eclampsia.



Abbreviations: CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

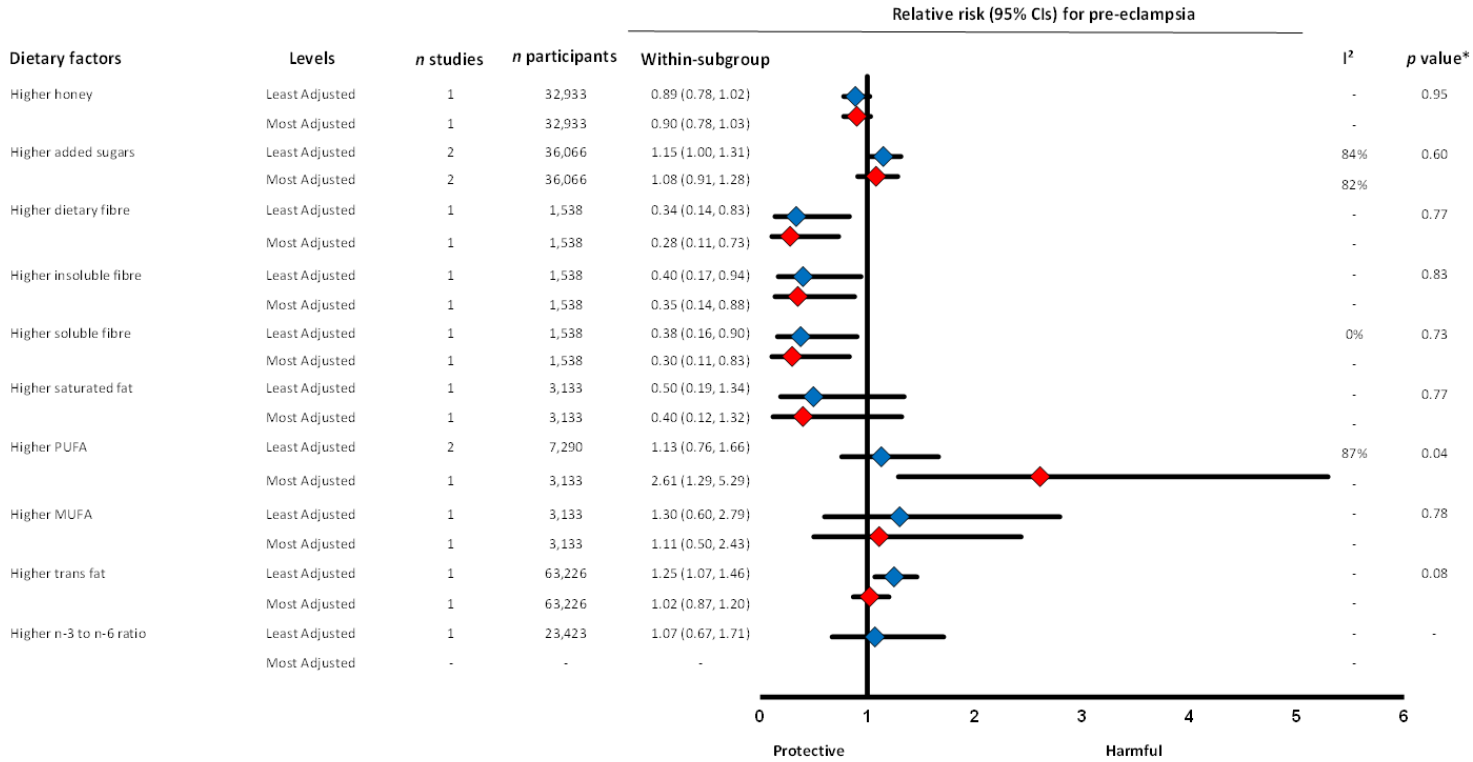
Appendix Figure 2.7. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on pre-eclampsia.



Abbreviations: CIs, confidence intervals; *n,* number of; SSBs, sugar-sweetened beverages.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

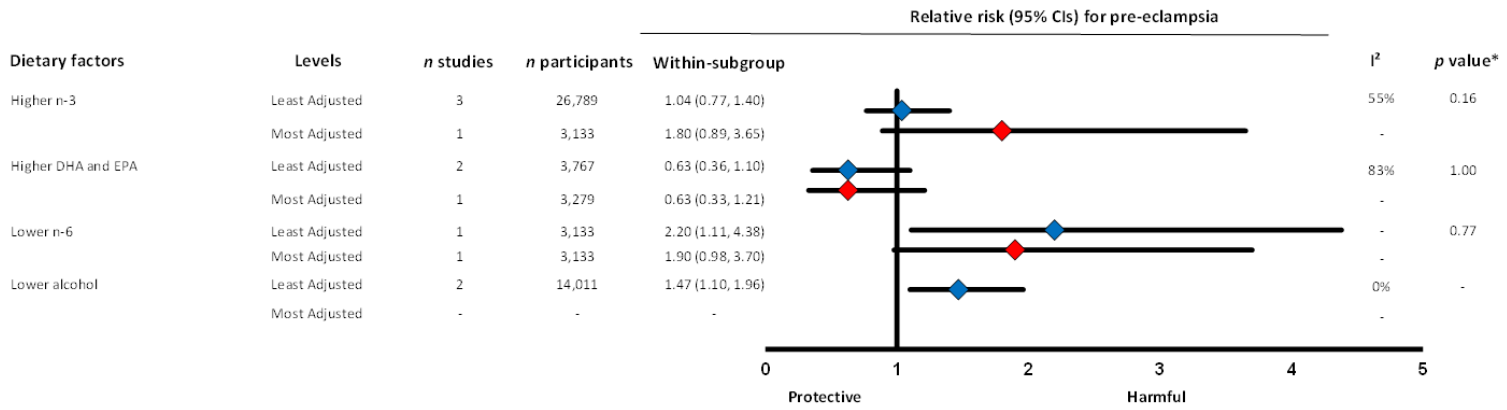
Appendix Figure 2.7. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on pre-eclampsia.



Abbreviations: CIs, confidence intervals; MUFA, monounsaturated fatty acids; *n,* number of; n-3, omega-3; n-6, omega-6; PUFA, polyunsaturated fatty acids.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

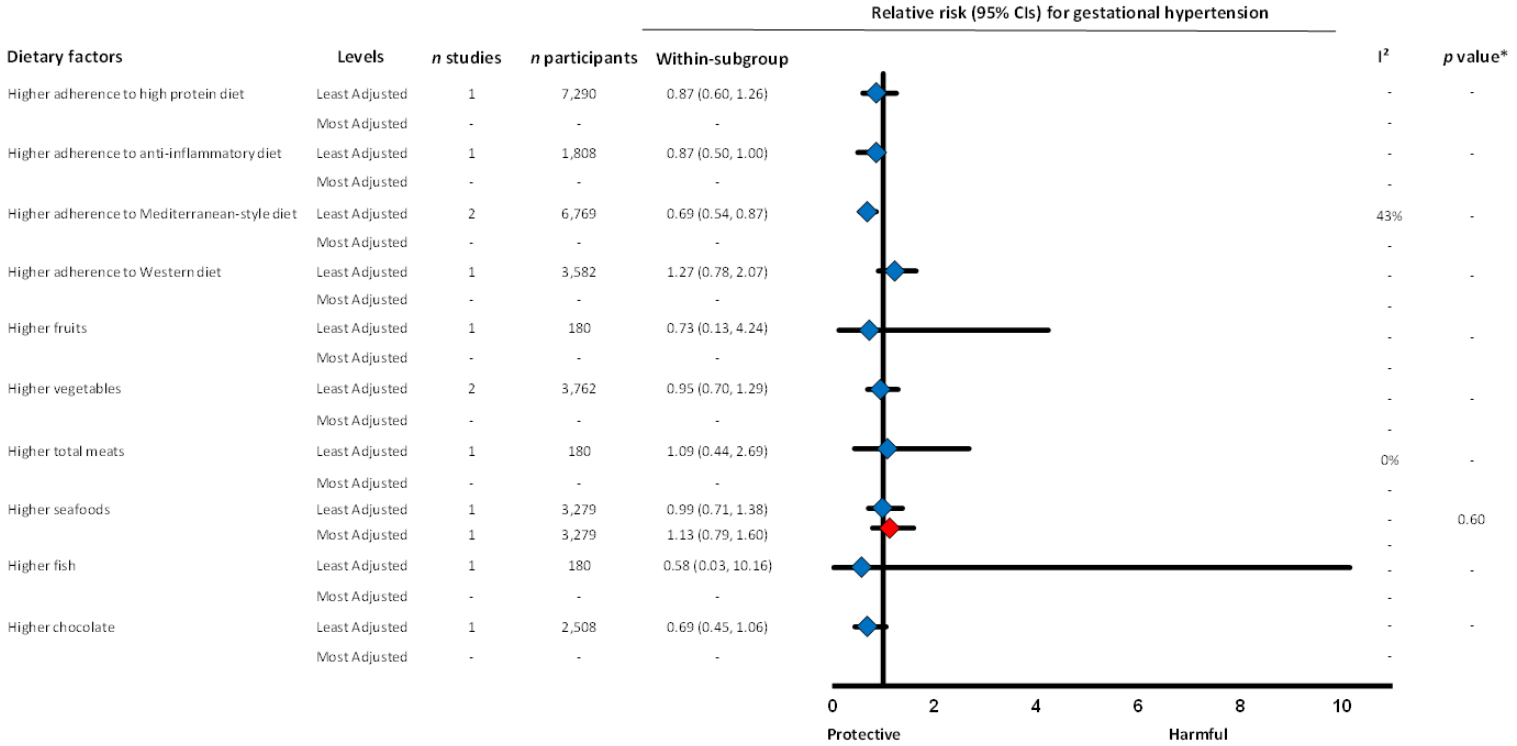
Appendix Figure 2.7. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on pre-eclampsia.



Abbreviations: DHA, docosahexaenoic acid; CIs, confidence intervals; EPA, eicosapentaenoic acid; *n,* number of; n-3, omega-3; n-6, omega-6.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

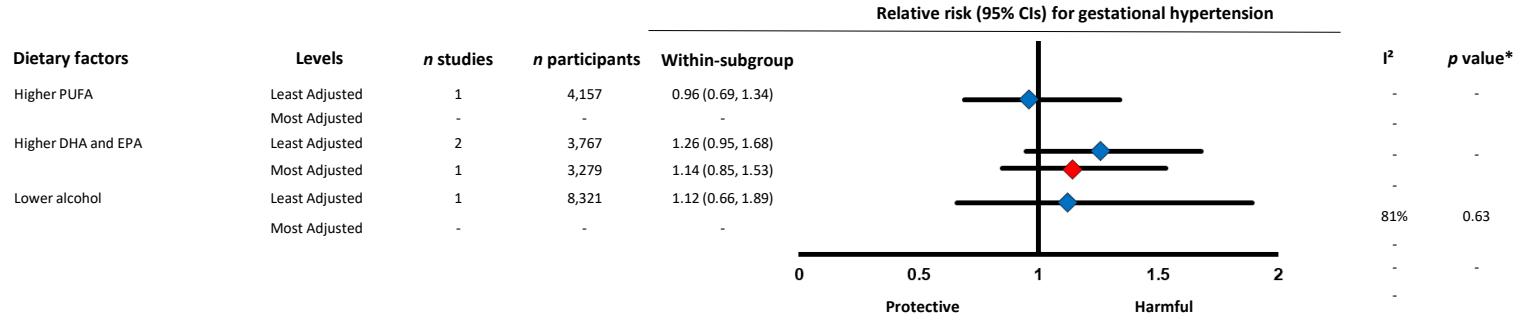
Appendix Figure 2.8. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational hypertension.



Abbreviations: CIs, confidence intervals; *n,* number of.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

Appendix Figure 2.8. CONTINUED. Forest plots comparing the least-adjusted and the most-adjusted models in cohort studies that reported on gestational hypertension.



Abbreviations: DHA, docosahexaenoic acid; CIs, confidence intervals; EPA, eicosapentaenoic acid; *n,* number of; PUFA, polyunsaturated fatty acids.

*p-value reflects the difference between the least and most-adjusted models for the same dietary factor.

Appendix Table 1. Search strategy.*

Database	Search Terms Used
MEDLINE	1 exp Diet/ 2 exp Diet Therapy/ 3 diet*.ti,ab,kf. 4 feeding behavior/ 5 feeding behavio?r.ti,ab,kf. 6 eating behavio?r.ti,ab,kf. 7 exp "diet, food, and nutrition"/ 8 food/ 9 food.ti,ab,kf. 10 vegetables/ 11 vegetable*.ti,ab,kf. 12 fruit/ 13 fruit*.ti,ab,kf. 14 exp Beverages/ 15 "Fruit and Vegetable Juices"/ 16 beverage*.ti,ab,kf. 17 juice*.ti,ab,kf. 18 drink*.ti,ab,kf. 19 vitamin*.ti,ab,kf. 20 mineral*.ti,ab,kf. 21 exp dietary supplements/ 22 exp Dietary Carbohydrates/ 23 carbohydrate*.ti,ab,kf. 24 exp Dietary Proteins/ 25 protein*.ti,ab,kf. 26 exp Dietary Fats/ 27 beta Carotene/ 28 beta carotene.ti,ab,kf. 29 (calor* adj1 restrict*).ti,ab,kf. 30 milk.ti,ab,kf. 31 Milk/ 32 cheese*.ti,ab,kf. 33 dairy product*.ti,ab,kf. 34 butter.ti,ab,kf. 35 egg*.ti,ab,kf. 36 Dietary Fiber/ 37 fiber*.ti,ab,kf. 38 fibre*.ti,ab,kf. 39 Fishes/ 40 fish*.ti,ab,kf. 41 Folic Acid/ 42 folate.ti,ab,kf. 43 folic acid.ti,ab,kf. 44 exp Nutritive Value/ 45 Nutriti* value.ti,ab,kf. 46 (glyc?emic adj2 (load* or ind*)).ti,ab,kf.

	47	healthy eating index.ti,ab,kf.
	48	legume*.ti,ab,kf.
	49	bean*.ti,ab,kf.
	50	pea*.ti,ab,kf.
	51	chickpea*.ti,ab,kf.
	52	lentil*.ti,ab,kf.
	53	meat*.ti,ab,kf.
	54	nuts.ti,ab,kf.
	55	polyunsaturated fat*.ti,ab,kf.
	56	PUFA*.ti,ab,kf.
	57	saturated fat*.ti,ab,kf.
	58	SFA*.ti,ab,kf.
	59	sugar*.ti,ab,kf.
	60	sucrose.ti,ab,kf.
	61	SSB*.ti,ab,kf.
	62	Cola*.ti,ab,kf.
	63	Soda*.ti,ab,kf.
	64	monounsaturated fat*.ti,ab,kf.
	65	MUFA*.ti,ab,kf.
	66	(omega adj2 ("3" or "6")).ti,ab,kf.
	67	trans fat*.ti,ab,kf.
	68	TFA*.ti,ab,kf.
	69	Ascorbic Acid/
	70	ascorbic acid.ti,ab,kf.
	71	exp Vitamin E/
	72	tocopherol*.ti,ab,kf.
	73	Edible Grain/
	74	((edible or whole) adj1 grain*).ti,ab,kf.
	75	Calcium, Dietary/
	76	vitamin D/
	77	Iron, Dietary/
	78	Vitamin B12/
	79	or/1-78
	80	exp Adipose tissue/
	81	adipos*.ti,ab,kf.
	82	body mass index/
	83	body mass ind*.ti,ab,kf.
	84	BMI.ti,ab,kf.
	85	exp Body Weight/
	86	weight.ti,ab,kf.
	87	obesity.ti,ab,kf.
	88	exp Body Fat Distribution/
	89	body fat.ti,ab,kf.
	90	Skinfold Thickness/
	91	skinfold.ti,ab,kf.
	92	exp Diabetes, Gestational/
	93	(diabet* adj2 (pregnan* or gestation*)).ti,ab,kf.
	94	GDM.ti,ab,kf.
	95	Hypoglycemia/
	96	hypoglyc?emi*.ti,ab,kf.

	97 exp Hyperglycemia/ 98 hyperglyc?emi*.ti,ab,kf. 99 Glucose Tolerance Test/ 100 OGTT.ti,ab,kf. 101 glucose tolerance.ti,ab,kf. 102 glucose intolerance.ti,ab,kf. 103 Cholesterol, LDL/ 104 LDL-C.ti,ab,kf. 105 LDL.ti,ab,kf. 106 density lipoprotein*.ti,ab,kf. 107 Cholesterol, HDL/ 108 HDL-C.ti,ab,kf. 109 HDL.ti,ab,kf. 110 exp Apolipoproteins B/ 111 Apo* B.ti,ab,kf. 112 Triglycerides/ 113 triglyceride*.ti,ab,kf. 114 triacylglyceride*.ti,ab,kf. 115 Blood Pressure/ 116 SBP.ti,ab,kf. 117 blood pressure.ti,ab,kf. 118 DBP.ti,ab,kf. 119 exp Hypertension, Pregnancy-Induced/ 120 gestational hypertension.ti,ab,kf. 121 pre-eclampsia.ti,ab,kf. 122 preeclampsia.ti,ab,kf. 123 Maternal Mortality/ 124 maternal mortality.ti,ab,kf. 125 or/80-124 126 exp Maternal Nutritional Physiological Phenomena/ 127 (expect* adj (mother* or wom?n* or female*)).ti,ab,kf. 128 Maternal Exposure/ 129 Maternal exposure.ti,ab,kf. 130 pregnan*.ti,ab,kf. 131 pre-pregnancy.ti,ab,kf. 132 or/126-131 133 cohort studies/ 134 Prospective Studies/ 135 prospective stud*.ti,ab,kf. 136 Prospective cohort stud*.ti,ab,kf. 137 cohort analys?s stud.ti,ab,kf. 138 follow-up Studies/ 139 follow-up stud*.ti,ab,kf. 140 Longitudinal Studies/ 141 longitudinal stud*.ti,ab,kf. 142 or/133-141 143 Randomized Controlled Trial.pt. 144 randomized controlled trial/ 145 clinical trial.pt. 146 experimental trial*.ti,ab,kf.

	147	random*.ti,ab,kf.
	148	rct*.ti,ab,kf.
	149	or/143-148
	150	animals/ not (humans/ and animals/)
	151	149 not 150
	152	79 and 125 and 132 and (142 or 151)

*Original search conducted on August 29, 2016 and updated on December 7, 2017.

Appendix Table 2.2. Definitions of each diet.*

Dietary factors	Definitions	Cohort studies that met this definition	RCTs that met this definition
Energy intake	• daily energy intake was prescribed based on body weight, estimated energy needs, or what the investigators' determined was acceptable, OR • quantile of energy intake	• Bergmann et al. 1997 • Clausen et al. 2001 • Ho et al. 2005 • Rodrigues et al. 2008 • Drehmer et al. 2016 • Xu et al. 2016 • Pathirathna et al. 2017	• Garner et al. 1997 • Rae et al. 2000 • Bonomo et al. 2005 • Wolff et al. 2008 • Deveer et al. 2013 • Zhang et al. 2015
Low-CHO and high-fat diet	• CHO intake ≤40% and fat intake >30% of total energy intake	-	• Ney et al. 2010 • Moreno-Castilla et al. 2013 • Hernandez et al. 2016
Low-CHO diet	• CHO intake ≤40% of total energy intake OR • quantile of CHO intake	• Zhang et al. 2006 • Tajima et al. 2016 • Xu et al. 2016 • Pathirathna et al. 2017	• Trout et al. 2016 • Thornton et al. 2009
Low-fat diet	• fat intake <20% of total energy intake OR • quantile of fat intake	• Clausen et al. 2001 • Bowers et al. 2012 • Tajima et al. 2016 • Xu et al. 2016	• Assaf et al. 2017
High-protein diet	• encouraged higher protein intake OR • quantile of protein intake	• Clausen et al. 2001 • Iqbal et al. 2007 • Morris et al. 2011 • Bao et al. 2013 • He et al. 2015 • Tajima et al. 2016 • Xu et al. 2016 • Pathirathna et al. 2017	• Simmons et al. 2017
Anti-inflammatory diet	• dietary score that captured food intakes associated with inflammation	• Sen et al. 2016 • McCullough et al. 2017	-

Diabetes management diet	• Encouraged adherence to ADA diet	-	• Reece et al. 1995 • Landon et al. 2009
DASH-style diet	• diet rich in fruits, vegetables, low fat or non-fat dairy, and whole grains, while limiting refined grains and sweets, OR • dietary score that captured food intakes associated with higher adherence to the DASH diet	• Tobias et al. 2012 • Torjusen et al. 2014 • Jarman et al. 2016 • Anand et al. 2017	• Asemi et al. 2013 (BJN) • Asemi et al. 2013 (Nutrition) • Asemi et al. 2014 • Yao et al. 2015
Healthy eating diet	• National dietary guideline (e.g. Canada's Food Guide, Australian Guide to Healthy Eating), OR • diet rich in fruits, vegetables, lean meats, and restricted processed foods, OR • dietary score that captured food intakes associated with higher adherence to HEI (Dietary Guidelines for Americans or Icelandic Directorate of Health)	• Brantsaeter et al. 2009 • Tobias et al. 2012 • Sauder et al. 2016 • Tryggvadottier et al. 2016	• Briley et al. 2002 • Moses et al. 2014 • Vitolo et al. 2011 • Zhang et al. 2015 • Pecci et al. 2017
Mediterranean-style diet	• diet rich in fruits, vegetables, low-fat dairy, legumes, nuts, healthy fats, moderate fish/seafoods, and restricted sweets and red meat, OR • dietary score that captured food intakes associated with higher adherence to Mediterranean diet	• Karamanos et al. 2014 • Schoenaker et al. 2015 (AJCN) • Schoenaker et al. 2015 (Diabetologia) • Tielemans et al. 2015 • Timmermans et al. 2011 • Tobias et al. 2012 • Abreu et al. 2016 • Tryggvadottier et al. 2016 • Donazar-Ezcurra et al. 2017	• Khoury et al. 2005 • Di Carlo et al. 2014

Modified Portfolio diet	• High in nuts, fiber, soy, and plant sterols	• Tielemans et al. 2015	-
Nordic diet	• dietary score that captured food intakes associated with higher adherence to Nordic diet	• Hillesund et al. 2014 (Eur J Epi) • Hillesund et al. 2014 (Pub Health Nutr)	-
Prudent diet	• Diet rich in fruits, vegetables, lean meat, legumes and nuts	• Zhang et al. 2006 • He et al. 2015	-
Vegetarian diet	• Investigators' definition	• Stuebe et al. 2009	-
Western diet	• Diet rich in processed foods, refined grains, red and processed meats, high sugary foods	• Zhang et al. 2006 • Timmermans et al. 2011 • Schoenaker et al. 2015 (AJCN) • Schoenaker et al. 2015 (Diabetologia) • Tielemans et al. 2015 • Donazar-Ezcurra et al. 2017	-

Abbreviations: ADA, American Diabetes Association; CHO, carbohydrate; DASH, Dietary Approach to Stop Hypertension

*Studies met >90% of the food components that make up each diet to be categorized under that category.

Appendix Table 2.3. Risk of bias rating for cohort studies using a modified Newcastle Ottawa Scale (NOS).

STUDY	SELECTION				COMPARABILITY		OUTCOME			TOTAL POINTS	RISK OF BIAS†
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Absence of outcome at baseline	Adjusted for pre-pregnancy body weight or BMI	Adjusted for additional factors*	Ascertainment of outcome	Adequacy of follow-up duration	Adequacy of follow-up		
Abreu et al. 2016											
Mediterranean diet	1	1	0	1	0	0	1	1	1	6	Unclear
Dairy foods	1	1	0	1	1	1	1	1	1	8	Low
Adeney et al. 2007	1	1	1	1	1	1	1	1	1	9	Low
Anand et al. 2017	1	1	1	1	1	1	1	1	1	9	Low
Bao et al. 2013	1	1	1	1	1	1	1	1	1	9	Low
Bao et al. 2014 (Diabetologia)	1	1	1	1	1	1	1	1	1	9	Low
Bergmann et al. 1997	0	1	0	1	1	0	1	1	1	6	Unclear
Borgen et al. 2013	1	1	1	1	1	0	1	1	1	8	Low
Bowers et al. 2012	1	1	1	1	1	1	1	1	1	9	Low
Brantsaeter et al. 2009	1	1	1	1	1	1	1	1	1	9	Low
Chavarro et al. 2011	1	1	1	1	1	0	1	1	1	8	Low
Chen et al. 2009	1	1	1	1	1	1	1	1	1	9	Low
Chen et al. 2012	1	1	1	1	1	1	1	1	1	9	Low
Clausen et al. 2001	1	1	1	1	1	1	1	1	0	8	Low
Deierlein et al. 2008	1	1	1	1	1	1	1	1	0	8	Low
Dominguez et al. 2009	1	1	1	1	1	1	0	1	0	7	Low
Donazar-Ezcurra et al. 2017	1	1	1	1	1	1	1	1	1	9	Low
Drehmer et al. 2010	0	1	0	1	0	0	1	1	1	5	Unclear
Egeland et al. 2016	1	1	0	1	0	1	1	1	1	7	Low
Freeman et al. 2014	1	1	0	0	1	0	0	1	0	4	Unclear
Gaillard et al. 2013	1	1	1	0	0	0	1	1	1	6	Unclear
Haugen et al. 2009	1	1	1	1	1	0	1	1	0	7	Low
He et al. 2015	1	1	0	1	1	1	1	1	0	7	Low
Hillesund et al. 2014 (Eur J Epi)	1	1	1	1	1	1	1	1	1	9	Low
Hillesund et al. 2014 (Pub Health Nutr)	1	1	1	1	0	0	1	1	1	7	Low
Ho et al.	1	1	0	1	0	0	0	1	1	5	Unclear
Iqbal et al. 2007	1	1	0	1	1	0	1	1	1	7	Low
Jarman et al. 2016	1	1	0	1	0	0	0	1	1	5	Unclear
Karamanos et al. 2014	1	1	0	1	1	0	1	1	1	7	Low
Klemmensen et al. 2009	1	1	1	1	1	0	1	1	0	7	Low
Lamyian et al. 2017											
GWG	1	1	1	1	0	0	1	1	1	7	Low

GDM	1	1	1	1	1	1	1	1	1	9	Low
Lenders et al. 1995	1	1	0	1	0	0	0	1	0	4	Unclear
Longo-Mbenza et al. 2008	1	1	0	1	0	0	0	1	1	5	Unclear
Mannion et al. 2016	0	1	0	1	0	0	0	1	1	4	Unclear
Mari-Sanchis et al. 2016	1	1	1	1	1	1	1	1	1	9	Low
McCarthy et al. 2013	1	1	0	1	1	0	1	1	1	7	Low
McCullough et al. 2017											
GWG	1	1	0	1	0	0	1	1	1	6	Unclear
GDM	1	1	0	0	0	0	1	1	1	5	Unclear
Mohanty et al. 2017											
GWG	1	1	1	1	0	0	0	1	1	6	Unclear
GDM	1	1	1	1	1	1	1	1	1	9	Low
HDP	1	1	1	1	1	0	1	1	1	8	Low
Morris et al. 2011	1	1	0	0	1	0	1	1	1	6	Unclear
Oken et al. 2007	1	1	1	1	1	1	1	1	1	9	Low
Olafsdottir et al. 2005	1	1	1	1	0	0	0	1	1	6	Unclear
Olafsdottir et al. 2006 (BJOG)	1	1	1	1	1	1	1	1	1	9	Low
Olafsdottir et al. 2006 (Int J Obes)	1	1	1	1	0	0	0	1	1	6	Unclear
Olson et al. 2003	1	1	0	1	0	0	0	1	1	5	Unclear
Osorio et al. 2017	1	1	1	1	1	1	1	1	1	9	Low
Pathirathna et al. 2017	1	1	1	1	1	0	1	1	1	8	Low
Qiu et al. 2008	1	1	0	1	1	0	1	1	0	6	Unclear
Qiu et al. 2011	1	1	0	1	1	1	1	1	1	8	Low
Richardson et al. 1995	1	1	0	1	1	1	1	1	1	8	Low
Rodrigues et al. 2008	1	1	0	1	0	0	0	1	0	4	Unclear
Saftlas et al. 2010											
GDM	1	1	0	1	0	0	0	1	1	5	Unclear
HDP	1	1	0	0	0	0	1	1	1	5	Unclear
Sauder et al. 2016	1	1	0	1	1	1	1	1	1	8	Low
Schoenaker et al. 2015 (AJCN)	1	1	1	1	1	0	1	1	1	8	Low
Schoenaker et al. 2015 (Diabetologia)	1	1	1	1	1	1	1	1	1	9	Low
Scholl et al. 2004	1	1	0	1	0	0	1	1	1	6	Unclear
Sen et al. 2016											
GWG categories	1	1	1	1	1	1	1	1	1	9	Low
GWG	1	1	1	1	0	0	1	1	1	7	Low
GDM	1	1	1	1	1	1	1	1	1	9	Low
Pre-eclampsia	1	1	1	1	1	0	1	1	1	8	Low
GH	1	1	1	0	1	0	1	1	1	7	Low
Soto et al 2015											
Glycemia	1	1	1	1	0	0	1	1	1	7	Low
Blood pressure	1	1	1	1	0	0	1	1	1	7	Low
Stuebe et al 2009	1	1	1	1	1	1	0	1	0	7	Low

Tajima et al. 2016	1	1	0	1	1	1	1	1	1	8	Low
Tielemans et al. 2015	1	1	1	1	1	1	0	0	1	7	Low
Timmermans et al. 2011	1	1	1	0	1	0	1	1	1	7	Low
Tobias et al. 2012	1	1	1	1	1	0	1	1	1	8	Low
Torjusen et al. 2014											
GWG	1	1	1	1	0	0	1	1	1	7	Low
Pre-eclampsia	1	1	1	1	1	1	1	1	1	9	Low
Triche et al. 2008	1	1	0	0	1	0	1	1	1	6	Unclear
Tryggvadottir et al. 2016											
Prudent diet + food groups	1	1	0	0	1	1	1	1	1	7	Low
HEI	1	1	0	0	0	0	1	1	1	5	Unclear
Wrottesley et al. 2011	1	1	0	1	0	0	1	1	1	6	Unclear
Xu et al. 2016	1	1	0	1	1	1	1	1	1	8	Low
Zhang et al. 2006 (Diabetes Care)	1	1	1	1	1	1	1	1	1	9	Low
Zhang et al. 2006 (Diabetologia)	1	1	1	1	1	1	1	1	1	9	Low
Zhang et al 2015	1	1	1	1	0	0	1	1	1	7	Low

Abbreviations: GDM, gestational diabetes mellitus; GH, gestational hypertension; GWG, gestational weight gain; HDP, hypertensive disorders of pregnancy; HEI, healthy eating index

*Additional factors to be adjusted varied by cluster of outcomes. For outcomes relating to GWG, age and gestational age; for GDM and glycemia, age, ethnicity, and pre-gestational diabetes diagnosis; for HDP, age, pre-gestational hypertension, AND history of pre-eclampsia; and for blood lipids, age and history of hypercholesterolemia.

† The NOS was modified so that each star that was awarded was equivalent to receiving a point, for a maximum of 9 points. A total score of 0-3 was considered to be high risk of bias, 4-6 was unclear, and 7-9 was low risk of bias.

Appendix Table 2.4. Table of characteristics of prospective cohort studies that reported on gestational diabetes mellitus.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	GDM ascertainment ‡‡
Lower energy intake													
Xu et al. 2016	-	2012-2013	1,135 healthy	30.64 ± 3.39 (GDM) 29.67 ± 2.97 (NGT)	22.29 ± 3.66 (GDM) 20.81 ± 2.73 (NGT)	28 (2.5)	24-hour dietary recall	second trimester	China	age, BMI, weight	-	Q4 (<1716.1 kcal/d) vs Q1 (>2182.1 kcal/d)	IADPSG
Higher adherence to low-CHO diet													
Zhang et al. 2006 (Diabetes Care)	NHS II	1991-1998	13,110 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI, parity	age, BMI, ethnicity, parity, physical activity, family history of diabetes, smoking status, total energy, alcohol, dietary cereal fiber, fruit and vegetable fiber, protein, saturated fat, PUFA, trans fat, GI	Q5 (40.9 %E) vs Q1 (59.1 %E)	self-reported
Tajima et al. 2016	-	2008-2010	325 healthy	-	19.7 ± 1.9	-	3d food record	first and second trimesters	Japan	none	age, BMI, rate of GWG, family history of diabetes, parity, total energy, dietary fiber	Q3 (49.5%E) vs Q1 (60.6 %E)	IADPSG
Xu et al. 2016	-	2012-2013	1,135 healthy	30.64 ± 3.39 (GDM) 29.67 ± 2.97 (NGT)	22.29 ± 3.66 (GDM) 20.81 ± 2.73 (NGT)	28 (2.5)	24-hour dietary recall	second trimester	China	age, BMI, weight	-	Q4 (<205.4 g/d) vs Q1 (>295.2 g/d)	IADPSG
Higher adherence to low-fat diet													
Bowers et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity, physical activity, family history of diabetes, smoking status, total energy, alcohol, cereal fiber, GL, dietary cholesterol, animal and vegetable fat	Q5 (48 %E) vs Q1 (75 %E)	self-reported
Tajima et al. 2016	-	2008-2010	325 healthy	-	19.7 ± 1.9	-	3d food record	first and second trimesters	Japan	crude	age, BMI, rate of GWG, family history of diabetes, parity, total energy, dietary fiber	Q3 (25.2 %E) vs Q1 (35.2 %E)	IADPSG
Xu et al. 2016	-	2012-2013	1,135 healthy	30.64 ± 3.39 (GDM) 29.67 ± 2.97 (NGT)	22.29 ± 3.66 (GDM) 20.81 ± 2.73 (NGT)	28 (2.5)	24-hour dietary recall	second trimester	China	age, BMI, weight	-	Q4 (<56.72 g/d) vs Q1 (>80.00 g/d)	IADPSG
Higher adherence to high-protein diet													
Iqbal et al. 2007	-	2002-2004	611 healthy	29.4 ± 4.7 (GDM) 26.3 ± 4.3 (NGT)	62.7 ± 9.1 kg (GDM) 58.3 ± 10.5 kg (NGT)	some	85-item FFQ	-	Pakistan	age, BMI, height, body fat percentage, rate of weight gain per week, parity, physical activity, family history of diabetes, education	-	Q2 (higher adherence) vs Q1 (lower adherence)	2004 ADA
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	FFQ	prepregnancy	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, saturated fat, MUFA, PUFA, trans fat, dietary cholesterol, GL, dietary fiber, animal and vegetable protein	Q5 (23.3 %E) vs Q1 (15.2 %E)	self-reported
He et al. 2015	BIGCS	2012-2014	3,063 healthy	28.9 ± 3.2	-	-	FFQ	during pregnancy (in the past wk)	China	Prudent diet, seafood and sweets, vegetables	-	Q3 (higher adherence) vs Q1 (lower adherence)	IADPSG
Tajima et al. 2016	-	2008-2010	325 healthy	-	19.7 ± 1.9	-	3d food record	first and second trimesters	Japan	none	age, BMI, rate of GWG, family history of diabetes, parity, total energy, dietary fiber	Q3 (16.9 %E) vs Q1 (12.9 %E)	IADPSG
Xu et al. 2016	-	2012-2013	1,135 healthy	30.64 ± 3.39 (GDM) 29.67 ± 2.97 (NGT)	22.29 ± 3.66 (GDM) 20.81 ± 2.73 (NGT)	28 (2.5)	24-hour dietary recall	second trimester	China	age, BMI, weight	-	Q4 (>90.20 g/d) vs Q1 (<63.75 g/d)	IADPSG
Higher adherence to anti-inflammatory diet													
Sen et al. 2016	Project Viva	1999-2002	1,808 healthy	32.2 ± 5.0	24.9 ± 5.2	202 (11.2)	FFQ	prepregnancy (first FFQ) + previous 3 mo (2nd FFQ)	USA	none	-	Q4 (more anti-inflammatory diet) vs Q1 (more pro-inflammatory diet)	2008 ADA
McCullough et al. 2017	NEST	2009-2011	1,057 healthy	-	-	165 (16)	interview + FFQ	6 mo prior to enrollment	USA	none	-	Q4 (more anti-inflammatory diet) vs Q1 (more pro-inflammatory diet)	self-reported + confirmed using records

Appendix Table 2.4. CONTINUED. Table of characteristics of prospective cohort studies that reported on gestational diabetes mellitus.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	GDM ascertainment ‡‡
Higher adherence to DASH-style diet													
Tobias et al. 2012	NHS II	1991-2001	15,254 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, total energy	age, BMI, parity, parental history of T2DM, smoking status, physical activity, time spent sitting, total energy, alcohol	Q4 (higher adherence) vs Q1 (lower adherence	self-reported
Anand et al. 2017	START	2011-2015	1,006	31.2 ± 4.0 (GDM)	24.9 ± 4.6 (GDM)	0 (0.0) (GDM)	FFQ	previous 12 mo	Canada	none	-	Q2 (higher adherence) vs	BiB
Higher adherence to healthy eating diet													
Sauder et al. 2016	Healthy Start	2010-2014	832 healthy	29.5 ± 5.8 (dysglycemic) 28.0 ± 6.1 (NGT)	27.6 ± 7.0 (dysglycemic) 25.5 ± 6.2 (NGT)	59 (7.1)	ASA 24-hour dietary recall	first and second trimesters	USA	age, BMI, ethnicity, gestational diabetes history, family history of diabetes		Q2 (≥64 HEI score) vs Q1 (<64 HEI score)	Carpenter and Coustan + unspecified criteria
Tobias et al. 2012	NHS II	1991-2001	15,254 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, total energy	age, BMI, parity, parental history of T2DM, smoking status, physical activity, time spent sitting, total energy, alcohol	Q4 (higher adherence) vs Q1 (lower adherence)	self-reported
Zhang et al. 2015	NHS II	1992-1998	14,437	-	-	1,616 (8.0)	133-item	prepregnancy	USA	-	age, BMI, ethnicity, parity,	Q5 (highest adherence) vs	self-reported
Tryggvadottir et al. 2016	-	2012-2013	168 healthy	-	-	0 (0.0)	4d food record	second trimester	Iceland	none	age, weight, rate of GWG, parity, physical activity, total energy	Q2 (higher adherence) vs Q1 (lower adherence)	2013 WHO
Higher adherence to Mediterranean diet													
Tobias et al. 2012	NHS II	1991-2001	15,254 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, total energy	age, BMI, parity, parental history of T2DM, smoking status, physical activity, time spent sitting, total energy, alcohol	Q4 (higher adherence) vs Q1 (lower adherence)	self-reported
Karamanos et al. 2014	-	2010-2011	1,003	-	-	-	interview +	-	Algeria, France,	age, BMI, family history of	-	Q2 (higher adherence) vs	IADPSG
Schoenaker et al. 2015	ALSWH	2003-2012	3,853 healthy	28.0 ± 1.4 (GDM) 28.0 ± 1.4 (NGT)	25.8 ± 5.8 (GDM) 23.7 ± 4.5 (NGT)	709 (19.8)	Dietary Questionnaire for Epidemiologic Studies version 2 FFQ	previous 12 mo	Australia	age, parity, inter-pregnancy interval, HDP, PCOS, education, total energy	age, BMI, parity, inter-pregnancy interval, HDP, PCOS, education, smoking status, physical activity, total energy	Q3 (higher adherence) vs Q1 (lower adherence	self-reported
Tryggvadottir et al. 2016	-	2012-2013	168 healthy	-	-	0 (0.0)	4d food record	second trimester	Iceland	none	age, weight, rate of GWG, parity, physical activity, total energy	Q2 (higher adherence) vs Q1 (lower adherence)	2013 WHO
Donazar-Ezcurra et al. 2017	SUN	1999-ongoing	3,455 healthy	-	-	861 (24.9)	136-item FFQ	-	Spain	age	-	Q4 (higher adherence) vs Q1 (lower adherence)	self-reported
Higher adherence to Nordic diet													
Hillesund et al. 2014 (Eur J Epidemiol)	MoBa	1999-2008	72,072 healthy	30.1 ± 4.6	24.0 ± 4.3	5,169 (7.8)	MoBa FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q3 (higher adherence) vs Q1 (lower adherence)	Medical Birth Registry of Norway
Higher adherence to Prudent diet													
Zhang et al. 2006 (Diabetologia)	NHS II	1992-1998	13,110 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, total energy, alcohol	Q5 (higher adherence) vs Q1 (lower adherence)	self-reported
He et al. 2015	BIGCS	2012-2014	3,063 healthy	28.9 ± 3.2	-	-	FFQ	during pregnancy (in the past wk)	China	protein, seafood and sweets, vegetables	-	Q3 (higher adherence) vs Q1 (lower adherence)	IADPSG
Higher adherence to Western diet													
Zhang et al. 2006 (Diabetologia)	NHS II	1992-1998	13,110 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, total energy, alcohol	Q5 (higher adherence) vs Q1 (lower adherence)	self-reported
Schoenaker et al. 2015 (Diabetologia)	ALSWH	2003-2012	3,853 healthy	28.0 ± 1.4 (GDM) 28.0 ± 1.4 (NGT)	25.8 ± 5.8 (GDM) 23.7 ± 4.5 (NGT)	709 (19.8)	Dietary Questionnaire for Epidemiologic Studies version 2 FFQ	previous 12 mo	Australia	age, parity, inter-pregnancy interval, HDP, PCOS, education, total energy	age, BMI, parity, inter-pregnancy interval, HDP, PCOS, education, smoking status, physical activity, total energy	Q3 (higher adherence) vs Q1 (lower adherence)	self-reported
Donazar-Ezcurra et al. 2017	SUN	1999-ongoing	3,455 healthy	-	-	861 (24.9)	136-item FFQ	-	Spain	age	-	Q4 (higher adherence) vs Q1 (lower adherence)	self-reported

Appendix Table 2.4. CONTINUED. Table of characteristics of prospective cohort studies that reported on gestational diabetes mellitus.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	GDM ascertainment ‡‡
Higher fried food													
Bao et al. 2014 (Diabetologia)	NHS II	1991-2001	15,027 healthy	25-44	-	some	FFQ	prepregnancy	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, total energy, diet quality, red meat, SSB	Q4 (≥7 servings/wk) vs Q1 (<1 serving/wk)	self-reported
Higher processed foods													
Dominguez et al. 2014	SUN	1999-ongoing	3,048	-	-	760 (24.9)	136-item	-	Spain	age	age, BMI, parity, history of	Q3 (>2 servings/wk) vs	self-reported
Lamyian et al. 2017	-	2010-2011	1,026 healthy	26.7 ± 4.3	25.4 ± 4.5	none	168-item FFQ	previous 12 mo	Iran	none	age, BMI, third trimester GWG, family history of diabetes, history of GDM, education, physical activity, total energy, dietary fibre, dietary cholesterol	Q4 (284.0 g/d) vs Q1 (22.5 g/d)	ADA
Higher desserts and sweets													
Soto et al. 2015	PROTECT	2011-2014	180	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (>1 serving/d) vs	FG >5.3 mmol/L or
Higher fruits and vegetables													
He et al. 2015	BIGCS	2012-2014	3,063	28.9 ± 3.2	-	-	FFQ	during pregnancy	China	age, BMI, parity, education,	-	Q3 (higher intake) vs	IADPSG
Higher fruits													
Chen et al. 2012	NHS II	1991-2001	13,475	-	-	some	133-item	previous 12 mo	USA	age, parity	-	Q5 (2.4 servings/d) vs	self-reported
Soto et al. 2015	PROTECT	2011-2014	180 healthy	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (>1 serving/wk) vs Q1 (<1 serving/mo)	FG >5.3 mmol/L or OGTT >7.8 mmol/L
Tryggvadottir et al. 2016	-	2012-2013	168 healthy	-	-	0 (0.0)	4d food record	second trimester	Iceland	none	age, weight, rate of GWG, parity, physical activity, total energy	Q2 (higher adherence) vs Q1 (lower adherence)	2013 WHO
Higher vegetables													
Schoenaker et al. 2015	ALSWH	2003-2012	3,853	28.0 ± 1.4 (GDM)	25.8 ± 5.8 (GDM)	709 (19.8)	Dietary	previous 12 mo	Australia	age, parity, inter-pregnancy	age, BMI, parity, inter-	Q3 (higher adherence) vs	self-reported
Soto et al. 2015	PROTECT	2011-2014	180 healthy	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (>1 serving/wk) vs Q1 (<1 serving/mo)	FG >5.3 mmol/L or OGTT >7.8 mmol/L
Tryggvadottir et al. 2016	-	2012-2013	168	-	-	0 (0.0)	4d	second trimester	Iceland	none	age, weight, rate of GWG,	Q2 (higher adherence) vs	2013 WHO
Higher dairy foods													
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, fruits, SSB, whole grain, poultry, fish, eggs, red meat, products, nuts, legumes	Q5 (4.2 servings/d) vs Q1 (0.8 serving/d)	self-reported
Higher low-fat dairy foods													
Osorio et al. 2017	Omega	1996-2008	3,414 healthy	32.8	23.5	178 (5.4)	121-item WHI FFQ	3 mo prior to pregnancy + first 3 mo of pregnancy	USA	total energy	age, BMI, ethnicity, family history of diabetes, education, smoking status, physical activity, total energy, alcohol, coffee, SSB, red and processed meats, fatty fish, total fibre, dietary Mg and vitamin D, prenatal vitamin use	Q4 (≥2.92 servings/d) vs Q1 (<0.89 serving/d)	2004 ADA
Higher total meat													
Soto et al. 2015	PROTECT	2011-2014	180 healthy	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (>1 serving/wk) vs Q1 (<1 serving/mo)	FG >5.3 mmol/L or OGTT >7.8 mmol/L
Mari-Sanchis et al. 2017	SUN	1999-2912	3,298 healthy	28	-	825 (25.0)	136-item FFQ	-	Spain	none	age, BMI, family history of diabetes, hypertension, PCOS, parity, multiple pregnancy, smoking status, physical activity, total energy, Mediterranean diet, SSB, dietary fiber, special diet, snacking	Q4 (138.0 g/d) vs Q1 (33.7 g/d)	self-reported + confirmed using medical records

Appendix Table 2.4. CONTINUED. Table of characteristics of prospective cohort studies that reported on gestational diabetes mellitus.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	GDM ascertainment ‡‡
Higher processed meat													
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, fruits, SSB, whole grain, poultry, fish, eggs, dairy products, nuts, legumes	Q5 (0.6 serving/d) vs Q1 (0.1 serving/d)	self-reported
Mari-Sanchis et al. 2017	SUN	1999-2912	3,298	28	-	825 (25.0)	136-item	-	Spain	none	age, BMI, family history of	Q4 (39.3 g/d) vs	self-reported +
Higher red meat													
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, fruits, SSB, whole grain, poultry, fish, eggs, dairy products, nuts, legumes	Q5 (1.5 serving/d) vs Q1 (0.2 serving/d)	self-reported
Mari-Sanchis et al. 2017	SUN	1999-2912	3,298 healthy	28	-	825 (25.0)	136-item FFQ	-	Spain	none	age, BMI, family history of diabetes, hypertension, PCOS, parity, multiple pregnancy, smoking status, physical activity, total energy, Mediterranean diet, SSB, dietary fiber, special diet, snacking	Q4 (260.8 g/d) vs Q1 (106.5 g/d)	self-reported + confirmed using medical records
Higher unprocessed meat													
Bao et al. 2013	NHS II	1991-2001	15,294	-	-	some	133-item	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity,	Q5 (1.0 serving/d) vs	self-reported
Higher seafoods													
Mohanthy et al. 2016	Omega	1996-2008	3,279 healthy	32.7 ± 4.4	23.5 ± 4.8	179 (5.4)	FFQ	3 mo prior to pregnancy + first 3 mo of pregnancy	USA	none	age, BMI, ethnicity, parity, marital status, education, smoking status, physical activity, alcohol, total energy, red and processed meats	Q4 (>1 serving/wk) vs Q1 (<0.2 serving/mo)	ADA
Tryggvadottir et al. 2016	-	2012-2013	168	-	-	0 (0.0)	4d	second trimester	Iceland	none	age, weight, rate of GWG,	Q2 (higher adherence) vs	2013 WHO
Higher fish													
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, fruits, SSB, whole grain, poultry, red meat, eggs, dairy products, nuts, legumes	Q5 (0.5 serving/d) vs Q1 (0.1 serving/d)	self-reported
Osorio et al. 2017	Omega	1996-2008	3,414 healthy	32.8	23.5	178 (5.4)	121-item WHI FFQ	3 mo prior to pregnancy + first 3 mo of pregnancy	USA	total energy	age, BMI, ethnicity, family history of diabetes, education, smoking status, physical activity, total energy, alcohol, coffee, SSB, red and processed meats, fatty fish, total fibre, dietary Mg and vitamin D, prenatal vitamin use	Q4 (≥1.53 serving/d) vs Q1 (<0.35 serving/d)	2004 ADA

Appendix Table 2.4. CONTINUED. Table of characteristics of prospective cohort studies that reported on gestational diabetes mellitus.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	GDM ascertainment ‡‡
Higher poultry													
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, fruits, SSB, whole grain, fish, red meat, eggs, dairy products, nuts, legumes	Q5 (0.86 serving/d) vs Q1 (0.14 serving/d)	self-reported
Mari-Sanchis et al. 2017	SUN	1999-2012	3,298	28	-	825 (25.0)	136-item	-	Spain	none	age, BMI, family history of	Q4 (80.7 g/d) vs	self-reported +
Higher eggs													
Qiu et al. 2011	Omega	1996-2008	3,158 healthy	32.7	23.5	171 (5.4)	121-item WHI FFQ	3 mo prior to pregnancy + first trimester	USA	total energy	age, BMI, ethnicity, physical activity, total energy, meat, dietary fibre, vitamin C, saturated fat	Q6 (≥10 eggs/wk) vs Q1 (0 eggs/wk)	2003 ADA
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, fruits, SSB, whole grain, poultry, red meat, fish, dairy products, nuts, legumes	Q5 (0.4 serving/d) vs Q1 (0.0 serving/d)	self-reported
Tryggvadottir et al. 2016	-	2012-2013	168	-	-	0 (0.0)	4d	second trimester	Iceland	none	age, weight, rate of GWG,	Q2 (higher adherence) vs	2013 WHO
Higher legumes													
Bao et al. 2013	NHS II	1991-2001	15,294	-	-	some	FFQ	prepregnancy	USA	age, parity	age, BMI, ethnicity, parity,	Q5 (0.8 serving/d) vs	self-reported
Higher nuts and seeds													
Tryggvadottir et al. 2016	-	2012-2013	168	-	-	0 (0.0)	4d	second trimester	Iceland	none	age, weight, rate of GWG,	Q2 (higher intake) vs	2013 WHO
Higher nuts and peanuts													
Bao et al. 2013 (Diabetes Care)	NHS II	1991-2001	15,294 healthy	-	-	some	FFQ	prepregnancy	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, fruits, SSB, whole grain, poultry, red meat, fish, dairy products, eggs, legumes	Q5 (0.6 serving/d) vs Q1 (0.0 serving/d)	self-reported
Higher vegetable oils													
Tryggvadottir et al. 2016	-	2012-2013	168	-	-	0 (0.0)	4d	second trimester	Iceland	none	age, weight, rate of GWG,	Q2 (higher intake) vs	2013 WHO
Higher total SSBs													
Chen et al. 2009	NHS II	1992-2001	13,475	-	-	1,186 (8.8)	133-item	previous 12 mo	USA	age, parity	-	Q4 (1 serving/d) vs	self-reported
Tryggvadottir et al. 2016	-	2012-2013	168 healthy	-	-	0 (0.0)	4d food record	second trimester	Iceland	none	age, weight, rate of GWG, parity, physical activity, total energy	Q2 (higher adherence) vs Q1 (lower adherence)	2013 WHO
Higher dietetic beverages													
Chen et al. 2009	NHS II	1992-2001	13,475	-	-	some	133-item	previous 12 mo	USA	age, parity	-	Q4 (1 serving/d) vs	self-reported
Higher fruit juice													
Chen et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	1,186 (8.8)	133-item FFQ	previous 12 mo	USA	age, parity	-	Q5 (1.7 serving/d) vs Q1 (0.1 serving/day)	self-reported
Soto et al. 2015	PROTECT	2011-2014	180 healthy	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (1 serving/d) vs Q1 (<1 serving/wk)	FG >5.3 mmol/L or OGTT >7.8 mmol/L
Higher dark chocolate													
Saftlas et al. 2010	Yale Health in Pregnancy	1988-1991	2,508 healthy	-	-	367 (14.6)	interview	pregnancy	USA	none	-	Q2 (during 1st and 3rd trimester) vs Q1 (infrequent)	-
Higher coffee													
Adeney et al. 2007	Omega	1996-2002	576 healthy	32.1 ± 4.2	-	105 (6.0)	121-item WHI FFQ	3 mo prior to pregnancy + first trimester	USA	none	-	Q2 (before and during pregnancy) vs Q1 (never)	2003 ADA

Appendix Table 2.4. CONTINUED. Table of characteristics of prospective cohort studies that reported on gestational diabetes mellitus.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	GDM ascertainment ‡‡
Lower glycemic index (GI) or load (GL)													
Zhang et al. 2006- GL (Diabetes Care)	NHS II	1991-1998	13,110 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI, parity	age, BMI, parity, ethnicity, family history of diabetes, smoking status, physical activity, total energy, alcohol, dietary cereal fiber, fruit and vegetable fiber, protein, saturated fat, PUFA, trans fat	Q5 (137) vs Q1 (212)	self-reported
Zhang et al. 2006- GI	NHS II	1991-1998	13,110	-	-	some	133-item	previous 12 mo	USA	age, BMI, parity	age, BMI, parity, ethnicity,	Q5 (71) vs	self-reported
Higher whole grains													
Osorio et al. 2017	Omega	1996-2008	3,414 healthy	32.8	23.5	178 (5.4)	121-item WHI FFQ	3 mo prior to pregnancy + first 3 mo of pregnancy	USA	total energy	age, BMI, ethnicity, family history of diabetes, education, smoking status, physical activity, total energy, alcohol, coffee, SSB, red and processed meats, fatty fish, total dietary fibre, dietary Mg and vitamin D, prenatal vitamin use	Q4 (≥0.57 serving/d) vs Q1 (<0.08 serving/d)	2004 ADA
Higher total fibre													
Zhang et al. 2006	NHS II	1991-1998	13,110	-	-	some	133-item	previous 12 mo	USA	age, BMI, parity	age, BMI, parity, ethnicity,	Q5 (25 g/d) vs	self-reported
Tajima et al. 2016	-	2008-2010	325	-	19.7 ± 1.9	-	3d	first and second trimesters	Japan	crude	age, BMI, rate of GWG,	Q3 (10.2 g/1000kcal) vs	IADPSG
Xu et al. 2016	-	2012-2013	1,135	30.64 ± 3.39 (GDM)	22.29 ± 3.66 (GDM)	28 (2.5)	24-hour	second trimester	China	age, BMI, weight	-	Q4 (>16.49 g/d) vs	IADPSG
Higher cereal fibre													
Zhang et al. 2006	NHS II	1991-1998	13,110	-	-	some	133-item	previous 12 mo	USA	age, BMI, parity	age, BMI, parity, ethnicity,	Q5 (9 g/d) vs	self-reported
Higher fruit fibre													
Zhang et al. 2006 (Diabetes Care)	NHS II	1991-1998	13,110 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI, parity	age, BMI, parity, ethnicity, family history of diabetes, smoking status, physical activity, alcohol, total energy, fruit and vegetable fiber, protein, saturated fat, PUFA, MUFA, trans fat, GI	Q5 (6 g/d) vs Q1 (1 g/d)	self-reported
Higher vegetable fibre													
Zhang et al. 2006	NHS II	1991-1998	13,110	-	-	some	133-item	previous 12 mo	USA	age, BMI, parity	age, BMI, parity, ethnicity,	Q5 (11 g/d) vs	self-reported
Lower saturated fat													
Bowers et al. 2012	NHS II	1991-2001	13,475	-	-	some	133-item	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity,	Q5 (16 %E) vs	self-reported
Higher PUFA													
Bowers et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity, physical activity, family history of diabetes, smoking status, alcohol, total energy, dietary cereal fiber, GL, dietary cholesterol, MUFA, saturated fat, trans fat	Q5 (14 %E) vs Q1 (8 %E)	self-reported
Higher MUFA													
Bowers et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, dietary, cereal fiber, GL, dietary cholesterol, PUFA, saturated fat, trans fat	Q5 (29 %E) vs Q1 (18 %E)	self-reported

Appendix Table 2.4. CONTINUED. Table of characteristics of prospective cohort studies that reported on gestational diabetes mellitus.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	GDM ascertainment ‡‡
Higher PUFA-to-saturated fat ratio													
Bowers et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, dietary cereal fiber, GL, dietary cholesterol, PUFA, trans fat	Q5 (0.7) vs Q1 (0.4)	self-reported
Lower trans fats													
Bowers et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, dietary cereal fiber, GL, dietary cholesterol, MUFA, PUFA, saturated fat	Q5 (1.8 %E) vs Q1 (4.5 %E)	self-reported
Higher n-3													
Bowers et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, dietary cereal fiber, GL, dietary cholesterol, MUFA, trans fat, saturated fat, n-6	Q5 (1.6 %E) vs Q1 (0.8 %E)	self-reported
Higher DHA & EPA													
Mohanthy et al. 2016	Omega	1996-2008	3,279 healthy	32.7 ± 4.4	23.5 ± 4.8	179 (5.4)	FFQ	3 mo prior to pregnancy + first 3 mo of pregnancy	USA	none	age, BMI, ethnicity, parity, marital status, education, smoking status, physical activity, alcohol, total energy, red and processed meats	Q4 (12.64 g/mo) vs Q1 (1.02 g/mo)	ADA
Lower n-6													
Bowers et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, dietary cereal fiber, GL, dietary cholesterol, MUFA, trans fat, saturated fat, n-3	Q5 (12.5 %E) vs Q1 (6.9 %E)	self-reported
Lower dietary cholesterol													
Qiu et al. 2011	Omega	1996-2008	3,158 healthy	32.7	23.5	171 (5.4)	121-item WHI FFQ	3 mo prior to pregnancy + first trimester	USA	total energy	age, BMI, ethnicity, physical activity, total energy, meat, dietary fibre, vitamin C, saturated fat	Q4 (<151 mg/d) vs Q1 (≥294 mg/d)	2003 ADA
Bowers et al. 2012	NHS II	1991-2001	13,475 healthy	-	-	some	133-item FFQ	previous 12 mo	USA	age, BMI	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, dietary cereal fiber, GL, dietary cholesterol, MUFA, PUFA, trans fat, saturated fat	Q5 (167 mg/d) vs Q1 (310 mg/d)	self-reported

Appendix Table 2.4. CONTINUED. Table of characteristics of prospective cohort studies that reported on gestational diabetes mellitus.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	GDM ascertainment ‡‡
Higher animal protein													
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	FFQ	prepregnancy	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, GL, dietary fiber, saturated fat, MUFA, PUFA, trans fat, dietary cholesterol, vegetable protein	Q5 (18.6 %E) vs Q1 (12.4 %E)	self-reported
Higher vegetable protein													
Bao et al. 2013	NHS II	1991-2001	15,294 healthy	-	-	some	FFQ	prepregnancy	USA	age, parity	age, BMI, ethnicity, parity, family history of diabetes, smoking status, physical activity, alcohol, total energy, GL, dietary fiber, saturated fat, MUFA, PUFA, trans fat, dietary cholesterol, animal protein	Q5 (6.4 %E) vs Q1 (4.5 %E)	self-reported
Lower alcohol													
Xu et al. 2016	-	2012-2013	1,135 healthy	30.64 ± 3.39 (GDM) 29.67 ± 2.97 (NGT)	22.29 ± 3.66 (GDM) 20.81 ± 2.73 (NGT)	28 (2.5)	24-hour dietary recall	second trimester	China	-	-	Q4 (>5 times/wk) vs Q1 (<1-2 times/wk)	IADPSG

Abbreviations: %E, percentage of daily energy; ADA, American Diabetes Association; ALSWH, Australian Longitudinal Study on Women's Health; ASA, Automated Self-Administered; BiB, Born in Bradford; BIGCS, Born in Guangzhou Cohort Study; BMI, body mass index; CHO, carbohydrate; d, day; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FFQ, food frequency questionnaire; FG, fasting glucose; g/d, grams per day; GDM, gestational diabetes mellitus; GI, glycemic index; GL, glycemic load; GWG, gestational weight gain; HDP, hypertensive disorders of pregnancy; HEI, healthy eating index; IADPSG, International Association of the Diabetes and Pregnancy Study Groups; kcal/d, calories per day; kg, kilogram; mo, month; MoBa, Norwegian Mother and Child Cohort Study; MUFA, monounsaturated fatty acids; n-3, omega-3; n-6, omega-6; NEST, Newborn Epigenetic Study; NGT, normal glucose tolerance; NHS, Nurses Health Study; OGTT, oral glucose tolerance test; PCOS, Polycystic ovary syndrome; PUFA, polyunsaturated fatty acids; PROTECT, Puerto Rico Test-site for Exploring Contamination Threats; Q, quantile; SSB, sugar-sweetened beverage; START, SouTh Asian biRth cohorT; SUN, Seguimiento Universidad de Navarra; T2DM, type 2 diabetes mellitus; WHI, Women's Health Initiative; WHO, World Health Organization; wk, week.

* Values are expressed as mean ± SD unless otherwise noted.

† Zhang et al. 2006 (Diabetes Care) reported the years in which study variables were measured; Iqbal et al. 2007 and Mohanty et al. 2016 reported the study dates; Zhang et al. 2006 (Diabetologia), Tobias et al. 2012 and Schoenaker et al. 2015 reported the years in which data was collected.

‡ Bao et al. 2014 (Diabetologia) reported age as a range.

§ Pre-pregnancy body weight was recorded when BMI was not provided in the original study.

‖ Tajima et al. 2016 reported BMI at first prenatal visit.

¶ Smokers refer to the number of current smokers during pregnancy. Values are reported as count (%) or "some" when the values were not reported but there was information to suggest that smokers were included. Zhang et al. 2015 reported the number of pregnancies where the mother was an active smoker.

** Reflects the period in which the dietary assessment was trying to assess participant's food intake.

†† Setting refers to where the study was conducted.

‡‡ Reflects the criteria that was used to confirm participants' GDM status.

Appendix Table 2.5. Table of characteristics of prospective cohort studies that reported gestational on weight gain.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years	Pre-pregnancy BMI (kg/m^2) or body weight (kg)‡§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	Weight gain classification‡‡
Lower energy intake													
Bergmann et al. 1997	Quedlinburg	1986-1987	156 healthy	-	-	27 (17.3)	7d food record	pregnancy	Germany	BMI	-	Q3 (<2000 kcal/d) vs Q1 (>2400 kcal/d)	-
Ho et al. 2005	-	-	62 GDM	-	-	-	5d food record	pregnancy	China	none	-	Q3 (1384 kcal/d) vs Q1 (1863 kcal/d)	-
Rodrigues et al. 2008	-	2005-2007	173 healthy	25.7 ± 5.7	24.0 ± 4.5	-	81-item FFQ	pregnancy	Brazil	none	-	Q3 (<90 %E requirement) vs Q1 (>110 %E requirement)	1995 WHO
Drehmer et al. 2010	ECCAGE	2006-2007	667 healthy	25.0 ± 6.4	24.2 ± 4.7	138 (20.7)	88-item FFQ	-	Brazil	none	-	Q3 (<2779 kcal/d) vs Q1 (>3099 kcal/d)	2009 IOM
Pathiranthna et al. 2017	-	2015-2016	138 healthy	28.8 ± 6.2	22.1 ± 4.3	-	FFQ	second trimester	Sri Lanka	none	-	Q2 (low intake) vs Q1 (high intake)	-
Higher adherence to low-CHO diet													
Pathiranthna et al. 2017	-	2015-2016	138 healthy	28.8 ± 6.2	22.1 ± 4.3	-	FFQ	second trimester	Sri Lanka	none	-	Q3 (229-429 g/d) vs Q1 (630-829 g/d)	-
Higher adherence to a high-protein diet													
Pathiranthna et al. 2017	-	2015-2016	138 healthy	28.8 ± 6.2	22.1 ± 4.3	-	FFQ	second trimester	Sri Lanka	none	-	Q2 (higher adherence) vs Q1 (lower adherence)	-
Higher adherence to DASH-style diet													
Jarman et al. 2016	APrON	-	2,067 healthy	-	-	-	24-hour dietary recall	second trimester	Canada	not reported	-	Q2 (higher adherence) vs Q1 (lower adherence)	2010 Health Canada
Higher adherence to anti-inflammatory diet													
Sen et al. 2016	Project Viva	1999-2002	1,808 healthy	32.2 ± 5.0	24.9 ± 5.2	202 (11.2)	FFQ	prepregnancy (first FFQ) + previous 3 mo (2nd FFQ)	USA	none	-	Q4 (more anti-inflammatory diet) vs Q1 (more pro-inflammatory diet)	2009 IOM
McCullough et al. 2017	NEST	2009-2011	1,057 healthy	-	-	165 (16)	Interviews + FFQ	6 mo prior to enrollment	USA	none	-	Q4 (more anti-inflammatory diet) vs Q1 (more pro-inflammatory diet)	self-reported + verification via records
Higher adherence to Mediterranean diet													
Tielemans et al. 2015	Generation R	2002-2006	1,091 healthy	31.6 ± 4.3 (healthy weight) 31.0 ± 4.4 (OW)	21.6 (20.4, 23.0) (healthy weight) 27.7 (26.0, 30.5) (OW)	557 (16.5)	293-item FFQ	previous 3 mo	The Netherlands	age, BMI, parity, education, household income, smoking status, stress, fetal sex, alcohol	-	Q4 (higher adherence) vs Q1 (lower adherence)	2009 IOM
Abreu et al. 2016	-	2010-2012	98 healthy	-	-	15 (15.3)	3d food record	first trimester	Portugal	none	-	Q2 (higher adherence) vs Q1 (lower adherence)	hospital records
Higher adherence to modified Portfolio diet													
Tielemans et al. 2015	Generation R	2002-2006	1,091 healthy	31.6 ± 4.3 (healthy weight) 31.0 ± 4.4 (OW)	21.6 (20.4, 23.0) (healthy weight) 27.7 (26.0, 30.5) (OW)	557 (16.5)	293-item FFQ	previous 3 mo	The Netherlands	age, BMI, parity, education, household income, smoking status, stress, fetal sex, alcohol	-	Q4 (higher adherence) vs Q1 (lower adherence)	2009 IOM
Higher adherence to Nordic diet													
Hillesund et al. 2014 (Pub Health Nutrition)	MoBa	1999-2008	56,629 healthy	30.1 ± 4.6	24.0 ± 4.2	5,169 (7.8)	MoBa FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q3 (higher adherence) vs Q1 (lower adherence)	2009 IOM
Higher adherence to vegetarian diet													
Stuebe et al. 2009	Project Viva	-	1,388 healthy	-	-	148 (10.7)	modified NHS FFQ	first trimester	USA	age, BMI, ethnicity, gestational length, nausea, smoking status	-	Q2 (vegetarian during first trimester) vs Q1 (not vegetarian during first trimester)	1990 IOM
Higher adherence to Western diet													
Tielemans et al. 2015	Generation R	2002-2006	1,091 healthy	31.6 ± 4.3 (healthy weight) 31.0 ± 4.4 (OW)	21.6 (20.4, 23.0) (healthy weight) 27.7 (26.0, 30.5) (OW)	557 (16.5)	293-item FFQ	previous 3 mo	The Netherlands	age, BMI, parity, education, household income, smoking status, stress, fetal sex, alcohol	-	Q4 (higher adherence) vs Q1 (lower adherence)	2009 IOM
Higher processed food intake													
Lamyian et al. 2017	-	2010-2011	1,026 healthy	26.7 ± 4.3	25.4 ± 4.5	none	168-item FFQ	previous 12 mo	Iran	none	-	Q4 (284.0 g/d) vs Q1 (22.5 g/d)	-
Higher desserts & sweets													
Olafsdottir et al. 2006 (Int J Obes)	-	1999-2001	406 healthy	-	-	some	Icelandic Nutrition Council FFQ	pregnancy	Iceland	age, gestational length, smoking status	-	Q2 (frequent) vs Q1 (infrequent)	Icelandic studies
Higher fruits & vegetables													
Olson et al. 2003	-	-	622 healthy	-	-	112 (18.0)	questionnaire + FFQ	-	USA	none	-	Q4 (≥5 servings/d) vs Q1 (<1 serving/d)	1990 IOM

Appendix Table 2.5. CONTINUED. Table of characteristics of prospective cohort studies that reported on gestational weight gain.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years	Pre-pregnancy BMI (kg/m^2) or body weight (kg)‡§‖	Active smokers¶	Dietary assessment	Dietary assessment period**	Setting††	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	Weight gain classification‡‡
Higher milk intake													
Olafsdottir et al. 2006 (Int J Obes)	-	1999-2001	406 healthy	-	-	some	Icelandic Nutrition Council FFQ	pregnancy	Iceland	age, gestational length, smoking status	-	Q2 (frequent) vs Q1 (infrequent)	Icelandic studies
Mannion et al. 2016	-	1997-1999	279 healthy	30.0 ± 4.54 (restricted) 31.2 ± 4.3 (usual intake)	22.9 ± 4.61 (restricted) 23.2 ± 3.8 (usual intake)	4 (5.56) (restricted) 12 (5.8) (usual intake)	interview + 24-hr dietary recalls	-	Canada	-	-	Q2 (usual intake) vs Q1 (restricted)	-
Higher seafood intake													
Mohanthy et al. 2016	Omega	1996-2008	3,279 healthy	32.7 ± 4.4	23.5 ± 4.8	179 (5.4)	FFQ	3 mo prior to pregnancy + 3 mo after pregnancy	USA	none	-	Q4 (>1 serving/wk) vs Q1 (<0.2 serving/mo)	-
Higher organic food intakes													
Torjusen et al. 2014	MoBa	-	28,192 healthy	28.6 ± 4.3 (infrequent users) 27.6 ± 4.9 (frequent users)	23.8 ± 4.1 (infrequent users) 23.3 ± 3.9 (frequent users)	1,970 (7.0)	MoBa FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q2 (frequent) vs Q1 (infrequent)	-
Low glycemic index & load													
Scholl et al. 2004	Camden	1996-2002	1,082 healthy	-	-	-	24-hour dietary recall	first + second trimesters	USA	none	-	Q5(<71) vs Q1 (>85)	WIC Program
Deierlein et al. 2008	PIN	2001-2005	1,186 healthy	-	-	118 (10.0)	modified Block-98 FFQ	second trimester	USA	none	age, BMI, ethnicity, education, income, parity, gestational age, total energy	Q4 (93) vs Q1 (222)	-
Higher total sugars													
Lenders et al. 1994	-	1982-1987	337 healthy	-	22.0 ± 4.0 (low-sugars consumers) 21.0 ± 3.0 (high-sugars consumers)	-	24-hour dietary recall	-	USA	none	-	Q2 (≥206 g/d) vs Q1 (<206 g/d)	-
Higher DHA & EPA													
Olafsdottir et al. 2005	-	1999-2001	436 healthy	27.8 ± 4.9 (non-consumers) 29.6 ± 4.6 (consumers)	24.3 ± 4.2 (non-consumers) 24.2 ± 3.2 (consumers)	62 (14.1)	Icelandic Nutrition Council FFQ	pregnancy	Iceland	none	-	Q2 (consumers) vs Q1 (non-consumers)	Icelandic studies
Alcohol user during pregnancy													
Rodrigues et al. 2008	-	2005-2007	173 healthy	25.7 ± 5.7	24.0 ± 4.5	-	81-item FFQ	pregnancy	Brazil	gestational age	-	Q2 (yes) vs Q1 (no)	1995 WHO
Drehmer et al. 2010	ECCAGE	2006-2007	667 healthy	25.0 ± 6.4	24.2 ± 4.7	138 (20.7)	88-item FFQ	-	Brazil	none	-	Q2 (yes) vs Q1 (no)	2009 IOM
Gaillard et al. 2013	Generation R	2001-2005	1,474 healthy	30.3 (90% CIs: 20.4, 37.9)	23.6 ± 4.4	1,713 (25.9)	293-item FFQ	prior 3 mo	The Netherlands	age, ethnicity, partiy, education, smoking status, folic acid supplement use	-	Q2 (yes) vs Q1 (no)	2009 IOM

Abbreviations: %E, percentage of daily energy; APrON, Alberta Pregnancy Outcomes and Nutrition; BMI, body mass index; CHO, carbohydrates; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; ECCAGE, Study of Food Intake and Eating Behavior in Pregnancy; EPA, eicosapentaenoic acid; FFQ, food frequency questionnaire; g/d, grams per day; GDM, gestational diabetes mellitus; IOM, Institute of Medicine; kcal/d, calories per day; kg, kilogram; mo, month; MoBa, Norwegian Mother and Child Cohort Study; NHS, Nurses Health Study; NEST, Newborn Epigenetic Study; OW, overweight; PIN, Pregnancy, Infection, and Nutrition; Q, quantile; WHO, World Health Organization; WIC, Women, Infant, Children; wk, week.

* Values are reported as mean ± SD unless otherwise noted.
† Drehmer et al. 2010 reported the years in which baseline values were measured; Tielemans et al. 2015 reported women's expected due date; and Lamyian et al. 2017 reported the study dates.
‡ Tielemans et al. 2015 reported pre-pregnancy BMI as median with interquartile range.
§ Pre-pregnancy body weight was recorded when BMI was not provided in the original study.
‖ Olafsdottir et al. 2005 reported first-trimester BMI.
¶ Smokers refer to the number of current smokers during pregnancy. Values are reported as count (%) or "some" when the values were not reported but there was information to suggest that smokers were included.
** Reflects the period in which the dietary assessment was trying to assess participant's food intake.
†† Reflects the country in which the study was conducted.
‡‡ Reflects the criteria that was used to classify whether weight gain was inadequate, adequate, or excessive.

Appendix Table 2.6. Table of characteristics of prospective cohort studies that reported on hypertensive disorders of pregnancy.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years	Pre-pregnancy BMI (kg/m^2) or body weight (kg)‡§	Active smokers‖	Dietary assessment	Dietary assessment period¶	Setting**	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	Pre-eclampsia ascertainment ††	PIH ascertainment ††
Lower energy intake														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	-	age, BMI, parity, SBP, smoking status, sucrose, PUFA	Q4 (≤2000 kcal/d) vs Q1 (>3350 kcal/d)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg compared with average measurement before 20 wks' gestation
Higher adherence to low-fat diet														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	age, BMI, parity, SBP, smoking status	age, BMI, parity, SBP, smoking status, total energy	Q3 (≤30.0 %E) vs Q1 (>37.0 %E)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg compared with average measurement before 20 wks' gestation
Higher adherence to high-protein diet														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	age, BMI, parity, SBP, smoking status	age, BMI, parity, SBP, smoking status, total energy	Q3 (>19.0 %E) vs Q1 (≤16.0 %E)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg compared with average measurement before 20 wks' gestation
Morris et al. 2011	CPEP	-	4,157 healthy	-	-	29 (9.0)	24-hour dietary recall	pregnancy	USA	total energy	age (for GH only), BMI, ethnicity, smoking status, total energy, calcium treatment assignment, clinical centre, private insurance	Q5 (>127.0 g/d) vs Q1 (<58.6 g/d)	medical records	
Higher adherence to anti-inflammatory diet														
Sen et al. 2016	Project Viva	1999-2002	1,808 healthy	32.2 ± 5.0	24.9 ± 5.2	202 (11.2)	FFQ	prepregnancy (first FFQ) + previous 3 mo (2nd FFQ)	USA	none	-	Q4 (more anti-inflammatory diet) vs Q1 (more pro-inflammatory diet)	2000 National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy	
Higher adherence to DASH-style diet														
Torjusen et al. 2014	MoBa	-	28,192 healthy	27.6 ± 4.9 (frequent) 28.6 ± 4.3 (infrequent)	23.3 ± 3.9 (frequent) 23.8 ± 4.1 (infrequent)	274 (11.0) (frequent) 1,696 (6.6) (infrequent)	255-item FFQ	first 4-5 mo of pregnancy	Norway	none	age, BMI, GWG, height, pre-pregnancy hypertension, household income, education, smoking status, total energy, organic vegetable	Q3 (higher adherence) vs Q1 (lower adherence)	medical registry	
Higher adherence to healthy eating diet														
Brantsaeter et al. 2009	MoBa	2002-2007	23,423 healthy	-	-	2,003 (8.6)	255-item FFQ	first 4-5 mo of pregnancy	Norway	processed food, potatoes and fish, cakes and sweets	age, BMI, height, pre-pregnancy hypertension, education, smoking status, physical activity, total energy, processed food, potatoes and fish, cakes and sweets, dietary supplement use	Q3 (higher adherence) vs Q1 (lower adherence)	medical registry	
Gicevic et al. 2017	NHS II	1991-2001	15,232 healthy	-	-	-	FFQ	previous 12 mo	USA	-	-	Q5 (higher adherence) vs Q1 (lower adherence)	self-reported	
Higher adherence to Mediterranean-style diet														
Timmermans et al. 2011	Generation R	-	3,187 healthy	-	-	471 (14.8)	193-item FFQ	previous 3 mo	Denmark	none	-	Q3 (higher adherence) vs Q1 (lower adherence)	2001 International Society for the Study of Hypertension in Pregnancy	
Schoenaker et al. 2015	ALSWH	2003-2012	3,582 healthy	28.0 ± 1.5 (HDP) 28.0 ± 1.4 (no HDP)	-	70 (23.1) (HDP) 639 (19.5) (non HDP)	101-item FFQ	previous 12 mo	Australia	total energy, vitamin and mineral supplement use	-	Q3 (higher adherence) vs Q1 (lower adherence)	self-reported	
Higher adherence to Nordic diet														
Hillesund et al. 2014 (Eur J Epidemiol)	MoBa	1999-2013	72,072 healthy	30.1 ± 4.6	24.0 ± 4.3	5,169 (7.8)	MoBa FFQ	first 4-5 mo of pregnancy	Norway	none	age, maternal age squared, BMI, parity, education, smoking status, diabetes status, chronic hypertension status, total energy	Q3 (higher adherence) vs Q1 (lower adherence)	medical registry	
Higher adherence to Western diet														
Timmermans et al. 2011	Generation R	-	3,187 healthy	-	-	471 (14.8)	193-item FFQ	previous 3 mo	Denmark	gestational age	-	Q3 (higher adherence) vs Q1 (lower adherence)	2001 International Soceity for the Study of Hypertension in Pregnancy	
Schoenaker et al. 2015	ALSWH	2003-2012	3,582 healthy	28.0 ± 1.5 (HDP) 28.0 ± 1.4 (no HDP)	-	70 (23.1) (HDP) 639 (19.5) (non HDP)	101-item FFQ	previous 12 mo	Australia	total energy, vitamin and mineral supplement use	-	Q4 (highest adherence) vs Q1 (lowest adherence)	self-reported	
Higher organic foods														
Torjusen et al. 2014	MoBa	-	28,192 healthy	27.6 ± 4.9 (frequent) 28.6 ± 4.3 (infrequent)	23.3 ± 3.9 (frequent) 23.8 ± 4.1 (infrequent)	274 (11.0) (frequent) 1,696 (6.6) (infrequent)	255-item FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q2 (frequent) vs Q1 (infrequent)	medical registry	
Higher processed foods														
Brantsaeter et al. 2009	MoBa	2002-2007	23,423 healthy	-	-	2,003 (8.6)	255-item FFQ	first 4-5 mo of pregnancy	Norway	healthy eating diet, potatoes and fish, cakes and sweets	age, BMI, height, pre-pregnancy hypertension, education, smoking status, physical activity, total energy, healthy eating diet, potatoes and fish, cakes and sweets, dietary supplement use	Q3 (higher adherence) vs Q1 (lower adherence)	medical registry	

Appendix Table 2.6. CONTINUED. Table of characteristics of prospective cohort studies that reported on hypertensive disorders of pregnancy.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years	Pre-pregnancy BMI (kg/m^2) or body weight (kg)‡§	Active smokers‖	Dietary assessment	Dietary assessment period¶	Setting**	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	Pre-eclampsia ascertainment ††	PIH ascertainment ††
Higher desserts and sweets														
Brantsaeter et al. 2009	MoBa	2002-2007	23,423 healthy	-	-	2,003 (8.6)	255-item FFQ	first 4-5 mo of pregnancy	Norway	healthy eating diet, potatoes and fish, processed foods	age, BMI, height, pre-pregnancy hypertension, education, smoking status, physical activity, total energy, healthy eating diet, potatoes and fish, processed foods, dietary supplement use	Q3 (higher adherence) vs Q1 (lower adherence)	medical registry	
Higher milk														
Richardson et al. 1995	CHD	1959-1966	9,793 healthy	-	-	6,792 (69.4)	interview + questionnaire	-	-	age, BMI, parity, GWG, history of pre-eclampsia	-	Q5 (≥4 glasses/d) va Q1 (<1 glasses/d)	1952 American Committee on Maternal Welfare	
Torjusen et al. 2014	MoBa	-	28,192	27.6 ± 4.9 (frequent)	23.3 ± 3.9 (frequent)	274 (11.0) (frequent)	255-item	first 4-5 mo of pregnancy	Norway	none	-	Q2 (frequent) vs	medical registry	
Higher fruits														
Klemmensen et al. 2009	DNBC	1996-2002	49,373 healthy	-	-	13,815 (24.1)	360-item FFQ	past 4 wks	Denmark	age, BMI, height, parity, marital status, socio-economic status, ownership of residence, smoking status, physical activity, vitamins C and E	-	Q5 (frequent) vs Q1 (infrequent)	2002 ACOG	
Borgen et al. 2012	MoBa	1999-2009	32,933	-	-	2,487 (7.6)	255-item	first 4-5 mo of pregnancy	Norway	age, BMI, height, education,	age, BMI, height, education,	Q4 (>330 g/d) vs	medical registry	
Torjusen et al. 2014	MoBa	-	28,192 healthy	27.6 ± 4.9 (frequent) 28.6 ± 4.3 (infrequent)	23.3 ± 3.9 (frequent) 23.8 ± 4.1 (infrequent)	274 (11.0) (frequent) 1,696 (6.6) (infrequent)	255-item FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q2 (frequent) vs Q1 (infrequent)	medical registry	
Soto et al. 2015	PROTECT	2011-2014	180	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (>1 serving/wk) vs	-	SBP >140 mmHg
Higher vegetables														
Longo-Mbenza et al. 2008	-	2002-2003	238	27.0 ± 6.4	-	none	questionnaire	past wk	Congo	none	-	Q2 (≥3 servings/d) vs	-	1988 ACOG
Torjusen et al. 2014	MoBa	-	28,192 healthy	27.6 ± 4.9 (frequent) 28.6 ± 4.3 (infrequent)	23.3 ± 3.9 (frequent) 23.8 ± 4.1 (infrequent)	274 (11.0) (frequent) 1,696 (6.6) (infrequent)	255-item FFQ	first 4-5 mo of pregnancy	Norway	none	age, BMI, GWG, height, pre-pregnancy hypertension, household income, education, smoking status, total energy, DASH-style diet	Q2 (frequent) vs Q1 (infrequent)	medical registry	
Schoenaker et al. 2015	ALSWH	2003-2012	3,582 healthy	28.0 ± 1.5 (HDP) 28.0 ± 1.4 (no HDP)	-	70 (23.1) (HDP) 639 (19.5) (non HDP)	101-item FFQ	previous 12 mo	Australia	total energy, vitamin and mineral supplement use	-	Q4 (higher adherence) vs Q1 (lower adherence)	self-reported	
Soto et al. 2015	PROTECT	2011-2014	180	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (>1 serving/wk) vs	-	SBP >140 mmHg
Higher total meats														
Torjusen et al. 2014	MoBa	-	28,192 healthy	27.6 ± 4.9 (frequent) 28.6 ± 4.3 (infrequent)	23.3 ± 3.9 (frequent) 23.8 ± 4.1 (infrequent)	274 (11.0) (frequent) 1,696 (6.6) (infrequent)	255-item FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q2 (frequent) vs Q1 (infrequent)	Medical registry	
Soto et al. 2015	PROTECT	2011-2014	180	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (>1 serving/wk) vs	-	SBP >140 mmHg
Higher seafoods														
Mohanty et al. 2016	Omega	1996-2008	3,279 healthy	32.7 ± 4.4	23.5 ± 4.8	179 (5.4)	FFQ	3 mo prior to pregnancy + 3 mo after pregnancy	USA	none	age, BMI, ethnicity, parity, marital status, education, smoking status, physical activity, alcohol, total energy, intake of red and processed meats	Q4 (>1 serving/wk) vs Q1 (<0.2 serving/mo)	2000 National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy	
Higher fish														
Soto et al. 2015	PROTECT	2011-2014	180 healthy	27.4 ± 5.4	-	-	FFQ	-	Puerto Rico	none	-	Q2 (>1 serving/wk) vs Q1 (<1 serving/mo)	-	SBP >140 mmHg
Higher eggs														
Torjusen et al. 2014	MoBa	-	28,192 healthy	27.6 ± 4.9 (frequent) 28.6 ± 4.3 (infrequent)	23.3 ± 3.9 (frequent) 23.8 ± 4.1 (infrequent)	274 (11.0) (frequent) 1,696 (6.6) (infrequent)	255-item FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q2 (frequent) vs Q1 (infrequent)	medical registry	
Higher total SSBs														
Borgen et al. 2012	MoBa	1999-2009	32,933 healthy	-	-	2,487 (7.6)	255-item FFQ	first 4-5 mo of pregnancy	Norway	age, BMI, height, education, smoking status, physical activity	age, BMI, height, education, smoking status, physical activity, total energy, dietary fibre	Q4 (>125 mL/d) vs Q1 (no intake)	medical registry	
Higher dark chocolate														
Triche et al. 2008	-	1996-2000	2,291 healthy	-	-	227 (13.5)	interview	pregnancy	USA	none	-	Q3 (>5 servings/wk) vs Q1 (<1 serving/wk)	2000 National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy or medical records	SBP ≥140 mmHg or ≥90 mmHg or medical records
Saftlas et al. 2010	Yale Health in Pregnancy	1988-1991	2,508 healthy	-	-	367 (14.6)	interview	pregnancy	USA	none	-	Q2 (during 1st and 3rd trimester) vs Q1 (infrequent)	ACOG	
Higher honey														
Borgen et al. 2012	MoBa	1999-2009	32,933 healthy	-	-	2,487 (7.6)	255-item FFQ	first 4-5 mo of pregnancy	Norway	age, BMI, height, education, smoking status, physical activity	age, BMI, height, education, smoking status, physical activity, total energy, dietary fibre	Q2 (0.01 to 50.0 g/d) vs Q1 (no intake)	medical registry	

Appendix Table 2.6. CONTINUED. Table of characteristics of prospective cohort studies that reported on hypertensive disorders of pregnancy.*

Study	Cohort study	Years when participants were recruited†	Participant	Age, years	Pre-pregnancy BMI (kg/m^2) or body weight (kg)†§	Active smokers‖	Dietary assessment	Dietary assessment period¶	Setting**	Covariates in least-adjusted model	Covariates in most-adjusted model	Quantile comparison	Pre-eclampsia ascertainment ††	PIH ascertainment ††
Higher added sugars														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	age, BMI, parity, SBP, smoking status	age, BMI, parity, SBP, smoking status, total energy, PUFA	Q4 (>25.0 %E) vs Q1 (≤8.5 %E)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg compared with average measurement before 20 wks' gestation
Borgen et al. 2012	MoBa	1999-2009	32,933	-	-	2,487 (7.6)	255-item	first 4-5 mo of pregnancy	Norway	age, BMI, height, education,	age, BMI, height, education,	Q4 (>77 g/d) vs	medical registry	
Higher dietary fibre														
Qiu et al. 2008	Omega	1996-2002	1,538	32.2 ± 3.9	23.1 ± 3.9	92 (6.0)	121-item WHI	previous 3 mo	USA	total energy	age, BMI, ethnicity, parity,	Q4 (25.0 g/d) vs	1996 ACOG	
Higher insoluble fibre														
Qiu et al. 2008	Omega	1996-2002	1,538 healthy	32.2 ± 3.9	23.1 ± 3.9	92 (6.0)	121-item WHI FFQ	previous 3 mo	USA	total energy	age, BMI, ethnicity, parity, total energy, vitamin C	Q4 (16.48 g/d) vs Q1 (5.74 g/d)	1996 ACOG	
Higher soluble fibre														
Qiu et al. 2008	Omega	1996-2002	1,538 healthy	32.2 ± 3.9	23.1 ± 3.9	92 (6.0)	121-item WHI FFQ	previous 3 mo	USA	total energy	age, BMI, ethnicity, parity, total energy, vitamin C	Q4 (8.41 g/d) vs Q1 (3.18 g/d)	1996 ACOG	
Higher saturated fat														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	age, BMI, parity, SBP, smoking status	age, BMI, parity, SBP, smoking status, total energy	Q3 (>15.0 %E) vs Q1 (≤12.0 %E)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg compared with average measurement before 20 wks' gestation
Higher PUFA														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	age, BMI, parity, SBP, smoking status	age, BMI, parity, SBP, smoking status, total energy, sucrose	Q3 (>7.5 %E) vs Q1 (≤5.2 %E)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg compared with average measurement before 20 wks' gestation
Morris et al. 2011	CPEP	-	4,157 healthy	-	-	29 (9.0)	24-hour dietary recall	pregnancy	USA	total energy	age (for GH only), BMI, ethnicity, smoking status, total energy, calcium treatment assignment, clinical centre, private insurance	Q5 (>25.9 g/d) vs Q1 (<8.6 g/d)	medical records	
Higher MUFA														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	age, BMI, parity, SBP, smoking status	age, BMI, parity, SBP, smoking status, total energy	Q4 (>13.0 %E) vs Q1 (≤10.5 %E)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg
Lower trans fat														
Chavarro et al. 2011	DNBC	1996-2002	63,226	-	-	some	360-item	past 4 wks	Denmark	age, total energy	age, BMI, height, parity, year	Q5 (<1.48 g/d) vs	medical registry	
Higher n-3 to n-6 ratio														
Haugen et al. 2009	MoBa	2002-2007	23,423 healthy	-	-	2,003 (8.6)	255-item FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q3 (>9.0) vs Q1 (<3.0)	Norwegian Society for Gynecology	-
Higher n-3														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	age, BMI, parity, SBP, smoking status	age, BMI, parity, SBP, smoking status, total energy	Q3 (>1.6 %E) vs Q1 (≤0.9 %E)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg compared with average measurement before 20 wks' gestation
Haugen et al. 2009	MoBa	2002-2007	23,423 healthy	-	-	2,003 (8.6)	255-item FFQ	first 4-5 mo of pregnancy	Norway	none	-	Q3 (>9.0) vs Q1 (<3.0)	Norwegian Society for Gynecology	-
Freeman et al. 2014	National Pregnancy Registry for Atypical Antipsychotics	2011-2013	233 healthy, high-risk for psychiatric illnesses	32.2 ± 4.7	-	53 (22.8)	interview	pregnancy	USA	none	-	Q2 (user) vs Q1 (non-user)	maternal report + medical records	
Higher fish oil/DHA and EPA														
Olafsdottir et al. 2006	-	1999-2001	488 healthy	-	-	18 (4.5)	FFQ	previous 3 mo	Iceland	BMI x GWG, GWG, SBP, DBP, parity, smoking status	-	Q2 (user) vs Q1 (non-user)	2000 National High Blood Pressure Education Program Working Group on High Blood Pressure in	
Mohanty et al. 2016	Omega	1996-2008	3,279 healthy	32.7 ± 4.4	23.5 ± 4.8	179 (5.4)	FFQ	3 mo prior to pregnancy + 3 mo after pregnancy	USA	none	age, BMI, ethnicity, parity, marital status, education, smoking status, physical activity, alcohol, total energy, red and processed meats	Q4 (12.64 g/mo) vs Q1 (1.02 g/mo)	2000 National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy	
Lower n-6														
Clausen et al. 2001	-	1994-1996	3,133 healthy	29.8 ± 4.5	22.9 ± 3.7	693 (22.0)	180-item FFQ	pregnancy	Norway	age, BMI, parity, SBP, smoking status	age, BMI, parity, SBP, smoking status, total energy	Q3 (>5.8 %E) vs Q1 (≤3.8 %E)	proteinuria + PIH	≥140/90 mmHg or as an increase in DBP ≥15 mmHg compared with average measurement before 20 wks' gestation
Lower alcohol														
McCarthy et al. 2013	SCOPE	2004-2011	5,690 healthy	-	-	607 (10.8)	interview	prior and during pregnancy	Australia, Ireland, New Zealand, United Kingdom	study centres	-	Q3 (0 mL/wk) vs Q1 (≥80 mL/wk)	2000 ANZJOG	-
Egeland et al. 2016	CONOR	1994-2012	8,321 healthy	27.9 ± 4.5	23.9 ± 3.8	3,582 (27.1)	survey	previous 12 mo	Norway	age, parity, pre-pregnancy diabetes, hypertension, or pre-eclampsia status, region of survey, education, marital status, smoking status, time between study enrollment and delivery	-	Q3 (less than monthly) vs Q1 (weekly serving)	proteinuria + PIH	≥140/90 mmHg after 20 wks' gestation

Abbreviations: %E, percent of t energy; ACOG, American College of Obstetrics and Gynecology; ALSWH, Australian Longitudinal Study on Women's Health; ANZJOG, Australian and New Zealand Journal of Obstetrics and Gynaecology; BMI, body mass index; CHD, Child Health and Development Study; CONOR, Cohort Norway; CPEP, Calcium for Preeclampsia Prevention; DASH, Dietary Approach to Stop Hypertension; DBP, diastolic blood pressure; DHA, docosahexaenoic acid; DNBC, Danish National Birth Cohort; EPA, eicosapentaenoic acid; FFQ, food frequency questionnaire; g/d, grams per day; GWG, gestational weight gain; HDP, hypertensive disorders of pregnancy; kcal/d, calories per day; mo, month; MoBa, Norwegian Mother and Child Cohort Study; MUFA, monounsaturated fatty acids; n-3, omega-3; n-6, omega-6; NHS, Nurses' Health Study; PIH, pregnancy-induced hypertension; PROTECT, Puerto Rico Test-site for Exploring Contamination Threats; PUFA, polyunsaturated fatty acids; Q, quantile; SBP, systolic blood pressure; SCOPE, Screening for Pregnancy Endpoints; SSB, sugar-sweetened beverage; WHI, Women's Health Initiative; wks, weeks.

* Values are expressed as mean ± SD unless otherwise noted.

† Clausen et al. 2001 reported the years in which FFQs were filled; Richardson et al. 1995, Chavarro et al. 2001, Sen et al. 2006, and Mohanty et al. 2016 reported study dates; Egeland et al. 2016 and Gicevic et al. 2017 reported years in which data was collected.

‡ Pre-pregnancy body weight was recorded when BMI was not provided in the original study.

§ Clausen et al. 2001 reported BMI at the first prenatal visit.

‖ Smokers refer to the number of current smokers during pregnancy. Values are reported as count (%) or "some" when the values were not reported but there was information to suggest that smokers were included.

¶ Reflects the period in which the dietary assessment was trying to assess participant's food intake.

** Reflects the country in which the study was conducted.

†† Reflects the criteria that was used to diagnose PE and/or PIH.

Appendix Table 2.7. Table of characteristics of randomized controlled trials that reported on gestational diabetes mellitus *

Trial	Trial name	Years in which the trial was active†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§	Active smokers‖	Setting¶	Food provided**	Comparator description CHO:FAT:PRO	Intervention description CHO:FAT:PRO	Follow-up duration, wks ††	Gestational wk at which the intervention started	GDM ascertainment‡‡
ENERGY NEUTRAL TRIALS													
Low-CHO & high-fat diet													
Hernandez et al. 2016	-	-	12 GDM	28 ± 4.9 (low-CHO/high-fat) 30 ± 2.5 (ctrl)	-	-	USA	yes	CHOICE diet 60:15:25	low CHO/high-fat 40:45:15	~8	31.7 ± 2.4 31.2 ± 1.0	Carpenter and Coustan
Low-fat diet													
Assaf et al. 2017	-	2015-2016	874 healthy	32.7 ± 5.3 (low-fat) 33.2 ± 5.0 (ctrl)	23.3 ± 4.0 (low fat) 22.9 ± 3.6 (ctrl)	40 (8.0) (low-fat) 43 (8.6) (ctrl)	Spain	partial	EVOO (40mL/d) + pistachios (40g/d) + basic Mediterranean diet + GWG advice	low fat + basic Mediterranean diet + GWG advice	~28	12.1 ± 0.6 (low-fat) 12.0 ± 0.3 (ctrl)	IADPSG
High-protein diet													
Simmons et al. 2017	DALI	2012-2015	185 OW/Ob	32.5 ± 5.5 (high-PRO) 31.8 ± 5.6 (ctrl)	33.9 ± 4.4 (high PRO) 33.4 ± 3.5 (ctrl)	20 (18) (high PRO) 18 (17) (ctrl)	UK, Ireland, Netherlands, Austria, Poland, Italy, Spain, Denmark, Belgium	no	GWG (limit to <5kg)	healthy eating + GWG (increase PRO; reduce CHO + fat)	~21	15.3 ± 2.5 (high-PRO) 15.2 ± 2.4 (ctrl)	IADPSG + 2013 WHO
Diabetes management diet													
Reece et al. 1995	-	-	50 GDM, T1DM	-	-	-	USA	yes	ADA diet + high-fiber (80g/d) 60:-:20	ADA diet 50:-:30	~12	first trimester (T1DM) 24-29 (GDM)	-
Healthy eating diet													
Moses et al. 2014	PREGGIO	-	576 healthy	29.9 ± 5.0 (healthy eating) 29.9 ± 5.16 (ctrl)	67.5 ± 16.7 kg (healthy eating) 66.7 ± 13.8 kg (ctrl)	-	Australia	no	low GI	healthy eating	~24	16.2 ± 1.67 (healthy eating) 16.5 ± 1.72 (ctrl)	1991 ADIPS + IADPSG
Low glycemic index or load													
Grant et al. 2011	-	2006-2007	38 IGT, GDM	34 ± 0.5 (low GI) 34 ± 5.3 (ctrl)	27 ± 4.9 (low GI) 26 ± 4.8 (ctrl)	-	Canada	partial	intermediate- and high-GI	low GI	7	29 ± 3.43 (low GI) 29 ± 2.40 (ctrl)	2008 CDA
Louie et al. 2011	-	2008-2010	92 GDM	34.0 ± 4.1 (low GI) 32.4 ± 4.5 (ctrl)	23.9 ± 4.4 (low GI) 24.1 ± 5.7 (ctrl)	no	Australia	partial	high-fiber/moderate GI 40-45:15-25:25-30	low GI (≤50) 40-45:15-25:25-30	~9	29.0 ± 4.0 (low GI) 29.7 ± 3.5 (ctrl)	modified ADIPS
Perichart-Perera et al. 2012	-	2004-2008	107 GDM, T2DM	32.3 ± 4.8 (low GI) 31.8 ± 5.3 (ctrl)	30.5 ± 5.2 (low GI) 32.0 ± 6.3 (ctrl)	-	Mexico	no	moderate and high GI + caloric restriction <45:20-25:<40	low GI + caloric restriction <45:20-25:<40	~19	22.50 ± 4.9 (low GI) 20.70 ± 6.7 (ctrl)	2004 ADA
Valentini et al. 2012	-	2008	20 GDM	28.9 ± 3.3 (low GI) 30.2 ± 4.7 (ctrl)	25.7 ± 3.6 (low GI) 24.1 ± 4.7 (ctrl)	-	Italy	no	ADA diet 53:18:28	ethnic meal plan 55:17:28	~14	-	2004 ADA
Walsh et al. 2012	ROLO	2007-2011	759 previously delivered macrosomic infant	32.0 ± 4.2 (low GI) 32.0 ± 4.2 (ctrl)	26.8 ± 5.1 (low GI) 26.8 ± 4.8 (ctrl)	29 (3.7)	Ireland	no	routine care	low GI	~27	13.0 ± 2.3 (low GI) 12.9 ± 2.2 (ctrl)	Carpenter and Coustan
Moses et al. 2014	PREGGIO	-	576 healthy	29.9 ± 5.2 (low GI) 29.9 ± 5.0 (ctrl)	66.7 ± 13.8 kg (low GI) 67.5 ± 16.7 kg (ctrl)	-	Australia	no	healthy eating	low GI	~24	16.5 ± 1.72 (low GI) 16.2 ± 1.67 (ctrl)	1991 ADIPS + IADPSG
Ma et al. 2015	-	2008-2009	83 GDM	30.1 ± 3.8 (low GI) 30.0 ± 3.5 (ctrl)	21.9 ± 3.1 (low GI) 21.1 ± 2.7 (ctrl)	-	China	no	starch 45-50:20-24:25-30	low GL 45-50:20-24:25-30	~12	27.5 ± 1.1 (low GI) 27.9 ± 1.1 (ctrl)	Chinese Medical Association + 1979 and 2004 ADA
Markovic et al 2016	GI Baby 3	2011-2012	139 increased risk for GDM	35.7 ± 4.7 (low GI) 34.9 ± 4.1 (ctrl)	25.2 ± 5.2 (low GI) 25.2 ± 5.2 (ctrl)	-	Australia	partial	high-fiber/moderate GI 40-45:15-25:25-30	low GI (≤50) 40-45:15-25:25-30	~22	17.5 ± 2.0 (low GI) 17.7 ± 1.7 (ctrl)	modified 1998 ADIPS
High complex CHO													
Hernandez et al. 2016	-	-	12 GDM	30 ± 2.5 (CHOICE) 28 ± 4.9 (ctrl)	-	-	USA	yes	low-CHO/high-fat 40:15:45	CHOICE diet 60:15:25	~8	31.2 ± 1.0 (CHOICE) 31.7 ± 2.4 (ctrl)	Carpenter and Coustan
High unsaturated-fat-to-low-saturated fat ratio													
Laitinen et al. 2009	-	2002-2005	130 healthy	30.1 ± 5.2 (fat quality) 30.2 ± 5.0 (ctrl)	24.3 ± 4.4 (fat quality) 23.7 ± 3.5 (ctrl)	-	Finland	partial	routine care	amount and type of fat 55-60:10-15:30	~26	13.9 ± 1.6	IADPSG
Luoto et al. 2012	-	2002-2005	117 healthy	30.1 ± 5.1 (fat quality) 29.9 ± 5.0 (ctrl)	24.3 ± 4.2 (fat quality) 24.3 ± 3.6 (ctrl)	-	Finland	partial	routine care	amount and type of fat 55-60:10-15:30	~26	13.9 ± 1.7	IADPSG
High unsaturated fat													
Wang et al. 2015	-	2011-2013	84 GDM	30.3 ± 4.2 (sunflower oil) 29.7 ± 4.6 (ctrl)	21.4 ± 3.0 (sunflower oil) 22.2 ± 3.6 (ctrl)	no	China	partial	routine care 55-60:15-20:25-30	sunflower oil 50-54:15-20:31-35	~12	27.4 ± 1.52 (sunflower oil) 27.3 ± 1.96 (ctrl)	IADPSG
Assaf et al. 2017	-	2015-2016	874 healthy	33.2 ± 5.0 (high-fat) 32.7 ± 5.3 (ctrl)	22.9 ± 3.6 (high-fat) 23.3 ± 4.0 (ctrl)	43 (8.6) (high-fat) 40 (8.0) (ctrl)	Spain	partial	low-fat + basic Mediterranean diet + GWG advice	EVOO (40mL/d) + pistachios (40g/d) + basic Mediterranean diet + GWG advice	~28	12.0 ± 0.3 (high fat) 12.1 ± 0.6 (ctrl)	IADPSG
High MUFA													
Lauszus et al. 2001	-	-	25 GDM	31 ± 3.6 (MUFA) 29 ± 3.7 (ctrl)	-	-	Denmark	partial	high-CHO	high MUFA (sunflower oil; almonds + hazelnuts)	5	33	75 g OGTT, where 2+ glucose measures above 3 SDs of the mean

Appendix Table 2.7. CONTINUED. Table of characteristics of randomized controlled trials that reported on gestational diabetes mellitus *

Trial	Trial name	Years in which the trial was active†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§	Active smokers‖	Setting¶	Food provided**	Comparator description CHO:FAT:PRO	Intervention description CHO:FAT:PRO	Follow-up duration, wks ††	Gestational wk at which the intervention started	GDM ascertainment‡‡
High n-3													
Tehrani et al. 2016	-	-	140 Vitamin D deficient	-	normal	-	Iran	partial	vitamin D (50,000 IU per 2 wks)	n-3	10	14-16	2013 ACOG
ENERGY CONSCIOUS TRIALS													
Lower energy intake													
Garner et al. 1997	-	-	299 GDM	30.7 ± 4.6 (low energy) 30.7 ± 4.8 (ctrl)	71.2 ± 19.8 kg (low energy) 68.9 ± 16.9 kg (ctrl)	some	Canada	no	Canada's Food Guide	35 kcal/kg ideal body weight/day	~12	24-32	investigator initiated
Bonomo et al. 2005	-	1997-2002	300 IGT	31.1 ± 4.7 (low energy) 30.7 ± 5.1 (ctrl)	-	no	Italy	no	routine care	24–30 kcal/kg/day 50–55:25–30:20–25	~14	-	1-hr OGTT ≥7.8 mmol/l + Carpenter and Coustan
Wolff et al. 2008	-	-	50 Ob	28 ± 4 (low energy) 30 ± 5 (ctrl)	97.0 ± 9 kg (low energy) 95.6 ± 12 kg (ctrl)	no	Denmark	no	no dietary advice	Danish guidelines + low energy 50-55:15-20:<30	~20	16 ± 3 (low energy) 15 ± 2 (ctrl)	-
Zhang et al. 2015	-	2011	256 healthy	27.8 ± 3.6 (nutrition education) 27.7 ± 3.7 (ctrl)	-	-	China	no	routine care	nutrition education + low energy (emphasis on healthy diet, nutrition imbalance, and daily nutrient intake)	~28	-	-
Low-CHO diet													
Thornton et al. 2009	-	1998-2005	232 Ob	26.8 (low-CHO) 27.3 (ctrl)	92.8 ± 23.6 kg (low-CHO) 97.3 ± 23.1 kg (ctrl)	-	USA	no	routine care	low-CHO + low energy (24kcal/d) 40:30:30	~19	-	-
Healthy eating diet													
Pecci et al. 2017	-	2009-2015	272 OW/Ob	-	-	10 (5.6) (healthy eating) 8 (8.7) (ctrl)	USA	no	healthy eating	healthy eating + low energy 45:25:30	>24	<16	-

Abbreviations: ACOG, American College of Obstetrics and Gynecology; ADA, American Diabetes Association; ADIPS, Australasian Diabetes in Pregnancy Society; CDA, Canadian Diabetes Association' CHO, carbohydrate; CHOICE, choosing healthy options in carbohydrate energy; ctrl, control; d, day; DALI, vitamin D and lifestyle intervention for GDM prevention; EVOO, extra-virgin olive oil; GDM, gestational diabetes mellitus; GI, glycemic index; GL, glycemic load; GWG, gestational weight gain; IADPSG, International Association for Diabetes and Pregnancy Study Group; IGT, impaired glucose tolerance; kcal, energy; kg, kilogram; MUFA, monounsaturated fatty acids; n-3, omega-3; Ob, obese; OW, overweight; PREGGIO, Pregnancy and Glycemic Index Outcomes study; PRO, protein; OGTT, oral glucose tolerance test; ROLO, RCT Of LOw glycaemic index diet vs usual diet to prevent macrosomia; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; UK, United Kingdom; WHO, World Health Organization.

* Values are expressed as mean ± SD unless otherwise noted.

†Bonomo et al. 2005, Laitinen et al. 2009, Grant et al. 2011, Louie et al. 2011, Luoto et al. 2012, Ma et al. 2015, and Markovic 2016 reported the years in which participants were recruited.

‡ Thornton et al. 2009 reported age in median.

§ Pre-pregnancy body weight was recorded when BMI was not provided in the original study.

‖ Reflects the inclusion/exclusion of active smokers during pregnancy in the cohort study. Values are reported as count (%), "some" when the values were not reported but there was information to suggest that smokers were included, or"no" when none of the included participants were smokers.

¶ Reflects the country in which the study was conducted.

** Reflects the amount of food that was given to participants during the study period. Partial reflects some foods were given; yes reflects all foods were given; and no reflects no food were given (i.e. dietary advice).

†† Reflects the number of weeks participants were followed up. A "~" before a value indicates that the duration was calculated.

‡‡ Reflects the criteria that was used to confirm participants' GDM status.

Appendix Table 2.8. Table of characteristics of randomized controlled trials that reported on gestational weight gain.*

Trial	Trial Name	Years in which the trial was active†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖¶	Active smokers**	Setting††	Food provided‡‡	Comparator description CHO:PRO:FAT	Intervention description CHO:PRO:FAT	Follow-up duration, wks§§	Gestational wk at which intervention started ‖ ‖	Weight gain classification¶¶
ENERGY NEUTRAL TRIALS													
Low-CHO and high-fat diet													
Ney et al. 1982	-	-	20 T1DM, T2DM	26.6 ± 4.4 (T1DM) 32.2 ± 6.6 (T2DM)	-	-	USA	partial	high-fiber/low-fat (60-70g/d) 65:20:15	low-CHO/high-fat 40:20:40	16 ± 6.0 (low-CHO/high-fat) 16 ± 7.6 (ctrl)	10-30	-
Moreno-Castilla et al. 2013	-	2008-2011	150 GDM	33.5 ± 3.7 (low CHO/high-fat) 32.1 ± 4.4 (ctrl)	25.4 ± 5.7 (low-CHO/high-fat) 26.6 ± 5.5 (ctrl)	some	Spain	no	rountine care 55:20:25	low-CHO/high-fat 40:20:40	~6	30.4 ± 3.0 (low-CHO/low-fat) 30.1 ± 3.5 (ctrl)	-
Hernandez et al. 2016	-	-	12 GDM	28 ± 4.9 (low-CHO/high-fat) 30 ± 2.5 (ctrl)	-	-	USA	yes	CHOICE (complex CHO) 60:15:25	low-CHO/high-fat 40:15:45	~8	31.7 ± 2.4 (low-CHO/high-fat) 31.2 ± 1.0 (ctrl)	-
Low-CHO diet													
Trout et al. 2016	-	-	68 GDM	30.09 ± 6.15 (low-CHO) 29.63 ± 5.19 (ctrl)	33.84 ± 8.84 (low-CHO) 31.80 ± 8.68 (ctrl)	no	USA	no	routine care 50-55:-:-	low-CHO 35-40:-:-	~10	29.17 ± 2.78 (low-CHO) 30.50 ± 2.85 (ctrl)	-
Low-fat diet													
Assaf et al. 2017	-	2015	874 healthy	32.7 ± 5.3 (low-fat) 33.2 ± 5.0 (ctrl)	23.3 ± 4.0 (low-fat) 22.9 ± 3.6 (ctrl)	40 (8.0) (low-fat) 43 (8.6) (ctrl)	Spain	partial	EVOO (40mL/d) + pistachios (40g/d) + basic Mediterranean diet + GWG advice	Low fat + basic Mediterranean diet + GWG advice	~28	12.1 ± 0.6 (low-fat) 12.0 ± 0.3 (ctrl)	-
High-protein diet													
Simmons et al. 2017	DALI	2012-2015	185 OW/Ob	32.5 ± 5.5 (high PRO) 31.8 ± 5.6 (ctrl)	33.9 ± 4.4 (high PRO) 33.4 ± 3.5 (ctrl)	20 (18) (high PRO) 18 (17) (ctrl)	UK, Ireland, Netherlands, Austria, Poland, Italy, Spain, Denmark, Belgium	no	GWG (limit to <5kg)	healthy eating + GWG (increase PRO; reduce CHO + fat)	~21	15.3 ± 2.5 (high PRO) 15.2 ± 2.4 (ctrl)	2009 IOM
DASH-style diet													
Asemi et al. 2014	-	2013	52 GDM	31.9 ± 6.1 (DASH) 30.7 ± 6.3 (ctrl)	26.9 ± 3.4 (DASH) 28.8 ± 4.8 (ctrl)	-	Iran	no	routine care 45-55:15-20:25-30	rich in fruits, vegetables, whole grains and low-fat dairy products, and low in saturated fats, cholesterol, refined grains and sweets. Daily intake of sodium was 2400mg per day 45-55:15-20:25-30	4	-	-
Yao et al. 2015	-	-	33 GDM	30.7 ± 5.6 (DASH) 28.3 ± 5.1 (ctrl)	30.9 ± 4.3 (DASH) 29.6 ± 5.3 (ctrl)	-	China	no	rountine care 45-55:15-20:25-30	rich in fruits, vegetables, whole grains and low-fat dairy products, and low in saturated fats, cholesterol, refined grains and sweets. Daily intake of sodium was 2400mg per day 45-55:15-20:25-30	4	26.9 ± 1.4 (DASH) 25.7 ± 1.3 (ctrl)	-
Diabetes management diet													
Reece et al. 1995	-	-	50 GDM, T1DM	-	-	-	USA	yes	high-fiber (80g/d) 60:-:20	ADA diet 50:-:30	~12	first trimester (T1DM) 24-29 (GDM)	-
Landon et al. 2009	-	-	931 GDM	29.2 ± 5.7 (ADA diet) 28.9 ± 5.6 (ctrl)	-	some	USA	no	routine care	ADA diet	~10	28.8 ± 1.6 (ADA diet) 28.9 ± 1.5 (ctrl)	-
Healthy eating diet													
Moses et al. 2014	PREGGIO	-	631 healthy	29.9 ± 5.0 (healthy eating) 29.9 ± 5.16 (ctrl)	67.5 ± 16.7 kg (healthy eating) 66.7 ± 13.8 kg (ctrl)	-	Australia	no	low GI	healthy eating	~24	16.2 ± 1.67 (healthy eating) 16.5 ± 1.72 (ctrl)	-
Mediterranean-style diet													
Khoury et al. 2005	CARRDIP	1999-2001	259 healthy	29.6 ± 3.7 (Mediterranean) 29.8 ± 3.4 (ctrl)	19-32	no	Norway	no	routine care 50-52:16-17:32	rich in olive and rapeseed oil, nuts, nut butters, no fat or low fat dairy, fish, and avocado to replace meat, butter, cream, and dairy, fruits and vegetables, legumes, cholesterol (150 mg/d), while limit fatty meats	~21	19 ± 1.1 (Mediterranean diet) 19 ± 1.1 (ctrl)	-
Di Carlo et al. 2014	-	2010-2011	120 healthy	31.3 ± 4.7 (Mediterranean) 28.2 ± 5.3 (ctrl)	26.5 ± 6.3 (Mediterranean) 25.0 ± 4.2 (ctrl)	some	Italy	no	healthy eating	rich in olive oil, fruits and vegetables, pasta or rice, white meat or fish intakes, while limit potatoes, tomato sauce, dairy products, cheese, eggs, and processed meat	~31	8 (6, 13) (Mediterranean diet) 9 (5, 13) (ctrl)	-
High dairy products													
Chan et al. 2006	-	-	48 healthy	16.6 ± 0.6 (dairy products) 16.6 ± 0.6 (ctrl)	-	no	USA	no	orange juice (4 servings/d) + calcium supplements	dairy products (4 servings/d) (milk, yogurt, cheese)	~21	18	-
High dark chocolate													
Di Renzo et al. 2012	-	2008	90 healthy	29.9 ± 4.9 (chocolate) 29.4 ± 5.1 (ctrl)	-	no	Italy	partial	routine care	dark chocolate (70% cocoa; 161 kcal/d)	~25	12.1 (chocolate) 12.0 (ctrl)	-
Low glycemic index or load													
Rhodes et al. 2010	-	-	46 Ob	33.7 ± 3.9 (low GL) 33.2 ± 3.7 (ctrl)	-	no	USA	partial	routine care 55:20:25	low GL 45:20:35	~16	19.8 ± 5.0 (low GL) 19.6 ± 4.3 (ctrl)	-
Louie et al. 2011	-	2008-2009	92 GDM	34.0 ± 4.1 (low GI) 32.4 ± 4.5 (ctrl)	23.9 ± 4.4 (low GI) 24.1 ± 5.7 (ctrl)	no	Australia	partial	routine care 40-45:15-25:25-30	low GI (≤50) 40-45:15-25:25-30	~9	29.0 ± 4.0 (low GI) 29.7 ± 3.5 (ctrl)	2009 IOM
Perichart-Perera et al. 2012	-	2004-2008	107 GDM, T2DM	32.3 ± 4.8 (low GI) 31.8 ± 5.3 (ctrl)	30.5 ± 5.2 (low GI) 32.0 ± 6.3 (ctrl)	-	Mexico	no	moderate and high GI + caloric restriction <45:20-25:<40	low GI + caloric restriction <45:20-25:<40	~19	22.50 ± 4.9 (low GI) 20.70 ± 6.7 (ctrl)	2009 IOM
Valentini et al. 2012	-	2008	20 GDM	28.9 ± 3.3 (low GI) 30.2 ± 4.7 (ctrl)	25.7 ± 3.6 (low GI) 24.1 ± 4.7 (ctrl)	-	Italy	no	ADA diet 53:18:28	ethnic meal plan 55:17:28	~14	-	-
Walsh et al. 2012	ROLO	2007-2011	759 previously delivered macrosomic infant	32.0 ± 4.2 (low GI) 32.0 ± 4.2 (ctrl)	26.8 ± 5.1 (low GI) 26.8 ± 4.8 (ctrl)	29 (3.7)	Ireland	no	routine care	low GI	~27	13.0 ± 2.3 (low GI) 12.9 ± 2.2 (ctrl)	-
McGowan et al. 2013	ROLO	2007-2011	520 previously delivered macrosomic infant	32.0 ± 3.8 (low GI) 31.7 ± 4.2 (ctrl)	26.4 ± 4.4 (low GI) 26.3 ± 4.2 (ctrl)	26 (5.0)	Ireland	no	routine care	low GI	~28	-	2009 IOM
Moses et al. 2014	PREGGIO	-	631 healthy	29.9 ± 5.2 (low GI) 29.9 ± 5.0 (ctrl)	66.7 ± 13.8 kg (low GI) 67.5 ± 16.7 kg (ctrl)	-	Australia	no	healthy eating	low GI	~24	16.5 ± 1.72 (low GI) 16.2 ± 1.67 (ctrl)	-
Ma et al. 2015	-	2008-2009	83 GDM	30.1 ± 3.8 (low GL) 30.0 ± 3.5 (ctrl)	21.90 ± 3.14 (low GL) 21.15 ± 2.75 (ctrl)	-	China	no	starch 45-50:20-24:25-30	low GL 45-50:20-24:25-30	12-14	27.5 ± 1.1 (low GL) 27.9 ± 1.1 (ctrl)	-
Markovic et al. 2016	GI Baby 3	2011-2012	139 increased risk for GDM	35.7 ± 4.7 (low GI) 34.9 ± 4.1 (ctrl)	25.2 ± 5.2 (low GI) 25.2 ± 5.2 (ctrl)	-	Australia	partial	routine care 40-45:15-25:25-30	low GI (≤50) 40-45:15-25:25-30	~22	17.5 ± 2.0 (low GI) 17.7 ± 1.7 (fiber)	-

Appendix Table 2.8. CONTINUED. Table of characteristics of randomized controlled trials that reported on gestational weight gain.*

Trial	Trial Name	Years in which the trial was active†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖¶	Active smokers**	Setting††	Food provided‡‡	Comparator description CHO:PRO:FAT	Intervention description CHO:PRO:FAT	Follow-up duration, wks§§	Gestational wk at which intervention started ‖ ‖	Weight gain classification¶¶
ENERGY NEUTRAL TRIALS													
High dietary fiber													
Ney et al. 1982	-	-	20 T1DM, T2DM	26.6 ± 4.4 (T1DM) 32.2 ± 6.6 (T2DM)	-	-	USA	partial	low CHO/high fat (20 g/d fiber) 40:20:40	high-fiber/low-fat (60-70g/d) 65:20:15	16 ± 7.6 (high-fibre) 16 ± 6.0 (ctrl)	10-30	-
Reece et al. 1995	-	-	50 GDM, T1DM	-	-	-	USA	partial	ADA diet (20g/d fiber) 50:-:30	high fiber (80g/d) 60:-:20	~12	first trimester (T1DM) 24-29 (GDM)	-
High unsaturated-to saturated-fat ratio													
Ilmonen et al. 2011	-	2002-2005	156 healthy	30.1 ± 5.2 (fat quality) 30.2 ± 5.0 (ctrl)	24.3 ± 4.4 (fat quality) 23.7 ± 3.5 (ctrl)	-	Finland	partial	routine care	amount and type of fat 55-60:10-15:30	~26	first trimester	-
High unsaturated fat													
Wang et al. 2015	-	2011-2013	84 GDM	30.3 ± 4.2 (sunflower oil) 29.7 ± 4.6 (ctrl)	21.4 ± 3.0 (sunflower oil) 22.2 ± 3.6 (ctrl)	no	China	partial	routine care 55-60:15-20:25-30	sunflower oil 50-54:15-20:31-35	~12	27.4 ± 1.52 (high-fat) 27.3 ± 1.96 (ctrl)	-
Assaf et al. 2017	-	2015	874 healthy	33.2 ± 5.0 (high-fat) 32.7 ± 5.3 (ctrl)	22.9 ± 3.6 (high-fat) 23.3 ± 4.0 (ctrl)	43 (8.6) (high-fat) 40 (8.0) (ctrl)	Spain	partial	Low-fat + basic Mediterranean diet + GWG advice	EVOO (40mL/d) + pistachios (40g/d) + basic Mediterranean diet + GWG advice	~28	12.0 ± 0.3 (high fat) 12.1 ± 0.6 (ctrl)	-
High n-3													
Ostadrahimi et al. 2017	-	-	150 healthy	25.9 ± 4.8 (fish oil) 26.9 ± 4.5 (ctrl)	60.4 ± 9.3 kg (fish oil) 60.4 ± 10.4 kg (ctrl)	no	Iran	partial	liquid paraffin (1000 mg/d)	n-3	20	20	-
High DHA and EPA													
Shoji et al. 2006	-	2001-2002	46 healthy	29.97 ± 5.28 (DHA + EPA) 30.42 ± 4.51 (ctrl)	25.62 ± 3.84 (DHA + EPA) 25.32 ± 3.12 (ctrl)	no	Spain	partial	Blemil Plus (vitamin and mineral milk-based mix)	Blemil Plus + 500mg DHA + 150mg EPA	~20	19.80 ± 0.82 (DHA & EPA) 19.73 ± 0.77 (ctrl)	-
Ranjkesh et al. 2011	-	2007-2008	100 high risk for PE	26 ± 8 (DHA + EPA) 25 ± 9 (placebo)	23 ± 3 (DHA + EPA) 23 ± 3 (ctrl)	-	Iran	partial	starch	DHA + EPA (1000 mg)	~24	14 ± 1 (DHA + EPA) 15 ± 1 (ctrl)	-
Jamilian et al. 2016	-	2014	54 GDM	30.0 ± 5.5	28.4 ± 4.5	no	Iran	partial	placebo	DHA + EPA (1000 mg/d)	6	25.7 ± 1.3 (DHA + EPA) 25.5 ± 1.2 (ctrl)	-
ENERGY CONSCIOUS TRIALS													
Lower energy intake													
Garner et al. 1997	-	-	299 GDM	30.7 ± 4.8 (low energy) 30.7 ± 4.6 (ctrl)	68.9 ± 16.9 kg (low energy) 71.2 ± 19.8 kg (ctrl)	some	Canada	no	Canada's Food Guide	35 kcal/kg/d	~12	24-32	-
Rae et al. 2000	-	1992-1995	124 OW/Ob, GDM	30.2 (low energy) 30.6 (ctrl)	-	-	Australia	no	diabetes diet	1590-1776 kcal/d	≥3	-	-
Bonomo et al. 2005	-	1997-2002	300 IGT	31.1 ± 4.7 (low energy) 30.7 ± 5.1 (ctrl)	-	no	Italy	no	routine care	24–30 kcal/kg/day 50–55:25–30:20–25	~14	-	2009 IOM
Wolff et al. 2008	-	-	50 Ob	28 ± 4 (low energy) 30 ± 5 (ctrl)	97.0 ± 9 kg (low energy) 95.6 ± 12 kg (ctrl)	no	Denmark	no	routine care	Danish guidelines + low energy 50-55:15-20:<30	~20	16 ± 3 (low energy) 15 ± 2 (ctrl)	-
Deveer et al. 2013	-	-	100 IGT	29.5 ± 5.8 (low energy) 31.2 ± 5.6 (ctrl)	-	-	Turkey	no	routine care	1800-2500 kcal/d 45:20:35	~13	24-28	-
Low-CHO diet													
Thornton et al. 2009	-	1998-2005	232 Ob	26.8 (low CHO) 27.3 (ctrl)	92.8 ± 23.6 kg (low CHO) 97.3 ± 23.1 kg (ctrl)	-	USA	no	routine care	low CHO + low energy (24 kcal/kg) 40:30:30	~19	~20	-
Healthy eating diet													
Briley et al. 2002	-	-	20 healthy	-	24.7 ± 3.4 (healthy eating) 23.2 ± 4.1 (ctrl)	-	USA	no	routine care	healthy eating + low energy	≥12	≤24	-
Vitolo et al. 2011	-	2007-2008	307 healthy	-	-	-	Brazil	no	routine care	increased fruits and vegetables, and restrict the intakes of soft drinks and sweets, industrialized foods rich in fat and also the oil of the preparations + low energy	~20	17.8 ± 5.0	2009 IOM
Pecci et al. 2017	-	2009-2015	272 OW/Ob	-	-	10 (5.6) (healthy eating) 8 (8.7) (ctrl)	USA	no	healthy eating	healthy eating + low energy 45:25:30	>24	<16	2010 IOM

Abbreviations: ADA, American Diabetes Association; CARRDIP, Cardiovascular Risk Reduction Diet in Pregnancy; CHO, carbohydrate; CHOICE, choosing healthy options in carbohydrate energy; ctrl, control arm; DALI, vitamin D and lifestyle intervention for GDM prevention; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; EVOO, extra-virgin olive oil; GDM, gestational diabetes mellitus; GI, glycemic index; GL, glycemic load; GWG, gestational weight gain; IGT, impaired glucose tolerance; IOM, Institute of Medicine; n-3, omega-3; Ob, obese; OW, overweight; PE, pre-eclampsia; PREGGIO, Pregnancy and Glycemic Index Outcomes study; ROLO, RCT Of LOw glycaemic index

diet vs usual diet to prevent macrosomia; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; HTN, hypertension.

* Values are expressed as mean ± SD unless otherwise noted.
† Asemi et al. 2014, Jamilian et al. 2016, Perichart-Perera et al. 2012, Rae et al. 2000, Ranjkesh et al. 2011, and Thornton et al. 2009 who reported the years of study conduct.
‡ Thornton et al. 2009 reported age in median.
§ Pre-pregnancy body weight was recorded when BMI was not provided in the original study.
‖ Khoury et al. 2005 reported BMI in range.
¶ Shoji et al. 2006 reported BMI that was recorded in the second trimester.
** Reflects the inclusion/exclusion of active smokers during pregnancy in the cohort study. Values are reported as count (%), "some" when the values were not reported but there was information to suggest that smokers were included, or"no" when none of the included participants were smokers.
†† Reflects the country in which the study was conducted.
‡‡ Reflects the amount of food that was given to participants during the study period. Partial reflects some foods were given; yes reflects all foods were given; and no reflects no food were given (i.e. dietary advice).
§§ Reflects the number of weeks participants were followed up. A "~" before a value indicates that the duration was calculated.
‖ ‖ Ney et al. 1982, Reece et al. 1995, Garner et al. 1997, and Deveer et al. 2013 reported gestational week in a range; Di Carlo et al. 2014 reported gestational age in median and range; Ostadrahimi et al. 2017 reported the absolute start week.
¶¶ Reflects the criteria that was used to classify whether weight gain was inadequate, adequate, or excessive.
†† Jamilian et al. reported pre-pregnancy BMI for the entire group.

Appendix Table 2.9. Table of characteristics of randomized controlled trials that reported on hypertensive disorders of pregnancy.*

Trial	Trial name	Years in which the trial was active†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Setting**	Food provided††	Comparator description CHO:FAT:PRO	Intervention description CHO:FAT:PRO	Follow-up duration, wks ‡‡§§	Gestational wk at which the intervention started ‖‖	Pre-eclampsia ascertainment††	PIH ascertainment††
ENERGY NEUTRAL TRIALS														
Low-CHO and high-fat diet														
Moreno-Castilla et al. 2013	-	2008-2011	150 GDM	33.5 ± 3.7 (low-CHO/high-fat) 32.1 ± 4.4 (ctrl)	25.4 ± 5.7 (low-CHO/high-fat) 26.6 ± 5.5 (ctrl)	some	Spain	no	routine care 55:20:25	low-CHO and high-fat 40:20:40	9	30.4 ± 3.0 (low-CHO/high-fat) 30.1 ± 3.5 (ctrl)	-	-
High-CHO diet														
Lauszus et al. 2001	-	-	25 GDM	31 ± 3.61 (MUFA) 29 ± 3.74 (ctrl)	-	-	Denmark	partial	high MUFA (sunflower oil; almonds + hazelnuts)	high-CHO	5	33	-	-
Low-fat diet														
Rhodes et al. 2010	-	2007-2009	46 Ob	33.2 ± 3.7 (low-fat) 33.7 ± 3.92 (ctrl)	19.6 ± 4.3 (low-fat) 19.8 ± 5.0 (ctrl)	no	USA	partial	low GL 45:35:20	low fat, high GL 55:20:25	~16	19.6 ± 4.3 (low-fat) 19.8 ± 5.0 (ctrl)	-	
Assaf et al. 2017	-	2015-2016	874 healthy	32.7 ± 5.3 (low-fat) 33.2 ± 5.0 (ctrl)	23.3 ± 4.0 (low-fat) 22.9 ± 3.6 (ctrl)	40 (8.0) (low-fat) 43 (8.6) (ctrl)	Spain	partial	EVOO (40mL/d) + pistachios (40g/d) + basic Mediterranean diet + GWG advice	low fat + basic Mediterranean diet + GWG advice	~28	12.1 ± 0.6 (low-fat) 12.0 ± 0.3 (ctrl)	proteinuria + PIH	SBP 140mmHg/DBP 90mmHg after 20 gestational wk
DASH-style diet														
Asemi et al. 2013 (BJN)	-	2011	34 GDM	30.7 ± 6.7 (DASH) 29.4 ± 6.2 (ctrl)	26.7 ± 3.0 (DASH) 29.6 ± 5.9 (ctrl)	no	Iran	no	routine care 45–55:15–20:25–30	fruits, vegetables, whole grains, low-fat dairy products, and was low in saturated fats, cholesterol, refined grains and sweets. Daily intake of sodium was 2400mg/d 45–55:15–20:25–30	4	~26 (24, 28)	-	
Asemi et al. 2013 (Nutrition)	-	2011	32 GDM	27.7 ± 5.4 kg (DASH) 29.7 ± 5.6 kg (ctrl)	27.9 ± 4.4 (DASH) 27.5 ± 3.5 (ctrl)	no	Iran	no	routine care 40-55:10-20:25-30	rich in fruits, vegetables, whole grains, low-fat dairy products, and was low in saturated fats, cholesterol, refined grains, and sweets. Daily intake of sodium was 2000mg/d 40-55:10-20:25-30	4	~26 (24, 28)	-	
Asemi et al. 2014	-	2013	54 GDM	31.9 ± 6.1 (DASH) 30.7 ± 6.3 (ctrl)	26.9 ± 3.4 (DASH) 28.8 ± 4.8 (ctrl)	-	Iran	no	routine care 45-55:15-20:25-30	rich in fruits, vegetables, whole grains and low-fat dairy products, and low in saturated fats, cholesterol, refined grains and sweets. Daily intake of sodium was 2000mg/d 45-55:15-20:25-30	4	25.8 ± 1.4 (DASH) 25.9 ± 1.4 (ctrl)	-	
Yao et al. 2015	-	2014	35 GDM	30.7 ± 5.6 (DASH) 28.3 ± 5.1 (ctrl)	30.9 ± 4.3 (DASH) 29.6 ± 5.3 (ctrl)	-	China	no	routine care 45-55:15-20:25-30	fruits, vegetables, whole grains and low-fat dairy products, and low in saturated fats, cholesterol, refined grains and sweets. Daily intake of sodium was 2400mg/d	4	26.9 ± 1.4 (DASH) 25.7 ± 1.3 (ctrl)	-	
Diabetes management diet														
Landon et al. 2009	-	-	931 GDM	29.2 ± 5.7 (ADA diet) 28.9 ± 5.6 (ctrl)	-	some	USA	no	routine care	ADA diet	~10	28.8 ± 1.6 (ADA diet) 28.9 ± 1.5 (ctrl)	proteinuria + PIH	SBP ≥140 mmHg or DBP ≥90 mmHg on 2+ occassions and one elevated BP value subsequently treated with medication
Mediterranean-style diet														
Khoury et al. 2005	CARRDIP	1999-2001	259 healthy	29.8 ± 3.4 (ctrl) 29.6 ± 3.7 (Med diet)	19-32	no	Norway	no	routine care 50-52:16-17:32	fish, vegetable oils, especially olive oil and rapeseed oil, nuts, nut butters, margarine based on olive- or rapeseed oil, and avocado to replace meat, butter, cream, and diary, fruits and vegetables, legumes, cholesterol (150 mg/d)	~21	19 ± 1.1 (Mediterranean diet) 19 ± 1.1 (ctrl)	proteinuria + PIH	<140/90 mmHg after 20 wks of gestation
Higher dairy foods														
Chan et al. 2013	-	-	49 healthy	16.6 ± 0.6 (dairy product) 16.6 ± 0.6 (juice)	-	no	USA	no	orange juice	dairy products (4 servings of milk, yogurt, or cheese)	~21	18.0 ± 0.8 (dairy) 18.0 ± 0.7 (juice)		
Higher dark chocolate														
di Renzo et al. 2012	-	2008	90 healthy	29.93 ± 4.91 (chocolate) 29.43 ± 5.07 (ctrl)	-	no	Italy	partial	ad libitum + folic acid supplements (400 mcg/d)	dark chocolate (161 kcal/d) + folic acid supplement (400 mcg/d)	25	11-13	2000 Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy and 2002 ACOG Practice Bulletin	
Lower glycemic index or load														
Valentini et al. 2012	-	2008	20 GDM	28.9 ± 3.3 (low GI) 30.2 ± 4.7 (ctrl)	25.7 ± 3.6 (low GI) 24.1 ± 4.7 (ctrl)	-	Italy	no	ADA 53:18:28	low GI 55:17:28	-	21.3 ± 6.8 (low GI) 27.1 ± 5.9 (ctrl)	-	
Ma et al. 2015	-	2008-2009	83 GDM	30.1 ± 3.8 (low GL) 30.0 ± 3.5 (ctrl)	21.90 ± 3.14 (low GL) 21.15 ± 2.75 (ctrl)	-	China	no	starch 45-50:20-24:25-30	low GL 45-50:20-24:25-30	12-14	27.5 ± 1.1 (low GL) 27.9 ± 1.1 (ctrl)	-	
Rhodes et al. 2010	-	2007-2009	46 Ob	33.7 ± 3.92 (low GL) 33.2 ± 3.7 (ctrl)	19.8 ± 5.0 (low GL) 19.6 ± 4.3 (ctrl)	no	USA	partial	low-fat, high-GL 55:20:25	low GL 45:35:20	~16	19.8 ± 5.0 (low GL) 19.6 ± 4.3 (ctrl)	-	

Appendix Table 2.9. CONTINUED. Table of characteristics of randomized controlled trials that reported on hypertensive disorders of pregnancy.*

Trial	Trial name	Years in which the trial was active†	Participant	Age, years‡	Pre-pregnancy BMI (kg/m^2) or body weight (kg)§‖	Active smokers¶	Setting**	Food provided††	Comparator description CHO:FAT:PRO	Intervention description CHO:FAT:PRO	Follow-up duration, wks ‡‡§§	Gestational wk at which the intervention started ‖‖	Pre-eclampsia ascertainment††	PIH ascertainment††
ENERGY NEUTRAL TRIALS														
Higher unsaturated fat														
Assaf et al. 2017	-	2015-2016	874 healthy	33.2 ± 5.0 (high-fat) 32.7 ± 5.3 (ctrl)	22.9 ± 3.6 (high-fat) 23.3 ± 4.0 (ctrl)	43 (8.6) (high-fat) 40 (8.0) (ctrl)	Spain	partial	low-fat + basic Mediterranean diet + GWG advice	EVOO (40mL/d) + pistachios (40g/d) + basic Mediterranean diet + GWG advice	~28	12.0 ± 0.3 (high-fat) 12.1 ± 0.6 (ctrl)	proteinuria + PIH	SBP 140mmHg/DBP 90mmHg after 20 gestational wk
Higher MUFA														
Lauszus et al. 2001	-	-	25 GDM	31 ± 3.61 (MUFA) 29 ± 3.74 (ctrl)	-	-	Denmark	partial	high-CHO	high MUFA (sunflower oil; almonds + hazelnuts)	5	33	-	-
Higher n-3														
Jamilian et al. 2016	-	2014	54 GDM	30.0 ± 5.5	28.4 ± 4.5	no	Iran	partial	placebo (400µg/d of folic acid + 60 mg/d Fe)	n-3 (1000 mg/d) (400µg/d of folic acid + 60 mg/d Fe)	6	25.7 ± 1.3 (n-3) 25.5 ± 1.2 (ctrl)	-	-
Higher DHA and EPA														
Bulstra-Ramakers et al. 1994	-	1987-1990	63 history of IUGR	-	-	-	The Netherlands	partial	placebo (coconut oil)	DHA + EPA (DHA: -; EPA: 3g/d)	~27	~27	-	DBP increase ≥25 mmHg during pregnancy, with a final DBP> 90 mmHg
Onwude et al. 1995	-	1990-1992	232 high risk for HDP or IUGR	26.8 (18, 39) (fish oil) 26.1 (16, 40) (ctrl)		-	UK	partial	air capsules	DHA + EPA (DHA: 1.08 g/d; EPA: 1.62 g/d)	~14	24.0 (18, 32) (fish oil) 24.4 (18, 32) (ctrl)	proteinuria + DBP >90 mm Hg on 2 occassions at least 4hr apart	DBP >90 mm Hg on 2 occassions at least 4hr apart
Salvig et al. 1996 (olive oil)	-	1989-1990	533 healthy	29.4 ± 4.4 (fish oil) 29.7 ± 4.3 (ctrl)	61.5 ± 9.1 kg (fish oil) 60.7 ± 9.4 kg (ctrl)	some	Denmark	partial	olive oil (4 capsules x 1g/d)	fish oil (4 capsules x 1g/d)	~10	30	proteinuria + PIH	>SBP 140/DBP 90 mmHg
Olsen et al. 2000 (Recurrence PIH)	Earl-PIH	-	350 previous history of PIH	30.3 ± 7.01 (fish oil) 28.9 ± 5.32 (ctrl)	-	some	Denmark, Scotland, Sweden, England, Italy, The Netherlands, Norway, Belgium, Russia	partial	olive oil (4 capsules/d)	fish oil (4 capsules/d)	~21	18.5 ± 3.06 (fish oil) 18.9 ± 3.80 (ctrl)	proteinuria + PIH	>DBP 90 mmHg
Olsen et al. 2000 (Twins)	Twins	-	553 pregnant with twins	30.2 ± 6.18 (fish oil) 30.7 ± 6.35 (ctrl)	-	yes	Denmark, Scotland, Sweden, England, Italy, The Netherlands, Norway, Belgium, Russia	partial	olive oil (4 capsules/d)	fish oil (4 capsules/d)	~21	20.2 ± 3.01 (fish oil) 20.2 ± 3.04 (ctrl)	proteinuria + PIH	>DBP 90 mmHg
Barden et al. 2006	-	-	83 suffered from allergy	31.0 ± 3.79 (fish oil) 32.4 ± 3.28 (ctrl)	23.7 ± 3.79 (fish oil) 24.1 ± 3.93 (ctrl)	no	Australia	partial	olive oil (4 capsules x 1g/d)	fish oil (4 capsules x 1g/d)	>16	<20	-	-
Ranjkesh et al. 2011	-	2007-2008	100 high risk for PE	26 ± 8 (DHA + EPA) 25 ± 9 (ctrl)	23 ± 3 (DHA + EPA) 23 ± 3 (ctrl)	-	Iran	partial	starch	DHA + EPA (1000 mg)	~24	14 ± 1 (DHA + EPA) 15 ± 1 (ctrl)	-	-
ENERGY CONSCIOUS TRIALS														
Lower energy														
Rae et al. 2000	-	1992-1995	124 OW/Ob, GDM	30.2 (low energy) 30.6 (ctrl)	-	-	Australia	no	diabetes diet	low energy (1590-1776 kcal/d)	-	-	-	
Wolff et al. 2008	-	-	50 Ob	28 ± 4 (low energy) 30 ± 5 (ctrl)	97.0 ± 9 kg (low energy) 95.6 ± 12 kg (ctrl)	no	Denmark	no	no dietary advice	Danish guidelines + low energy 50-55:15-20:<30	~25	15 ± 2 (low energy) 16 ± 3 (ctrl)	-	
Deveer et al. 2013	-	-	100 IGT	29.46 ± 5.82 (low energy) 31.22 ± 5.58 (ctrl)	-	-	Turkey	no	routine care	low energy (1800-2500 kcal/d) 45:20:35	~13	~26 (24, 28)	proteinuria + increased BP	-
Low-CHO diet														
Thornton et al. 2009	-	1998-2005	232 Ob	26.8 (low-CHO) 27.3 (ctrl)	92.78 ± 23.55 kg (low-CHO) 97.27 ± 23.05 kg (ctrl)	-	USA	no	routine care	low-CHO + low energy (24 kcal/kg) 40:30:30	~20	12-28	-	-
Healthy eating diet														
Zhang et al. 2015	-	2011	256 healthy	27.84 ± 3.60 (healthy eating) 27.70 ± 3.73 (ctrl)	-	-	China	no	routine care	nutrition education + low energy (emphasis on healthy diet, nutrition imbalance, and daily nutrient intake)	28	<12	-	
Pecci et al. 2017	-	2009-2015	272 OW/Ob	-	-	10 (5.6) (healthy eating) 8 (8.7) (ctrl)	USA	no	healthy eating	healthy eating + low energy 45:25:30	>24	<16	-	

Abbreviations: ACOG, American College of Obstetrics and Gynecology; ADA, American Diabetes Association; BP, blood pressure; CHO, carbohydrate; CARRDIP, Cardiovascular Risk Reduction Diet in Pregnancy; d, day; DASH, Dietary Approach to Stop Hypertension; DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; EVOO, extra-virgin

olive oil; Fe, iron; GDM, gestational diabetes mellitus; GI, glycemic index; GL, glycemic load; GWG, gestational weight gain; HDP, hypertensive disorder of pregnancy; IGT, impaired glucose tolerance; IUGR, intrauterine growth restriction; MUFA, monounsaturated fatty acids; n-3, omega-3; Ob, obese; OW, overweight; PE, pre-eclampsia; PIH, pregnancy induced hypertension; SBP, systolic blood pressure.

* Values are expressed as mean ± SD unless otherwise noted.

† Bulstra-Ramakers et al. 1994, Onwude et al. 1995, Rhodes et al. 2010, Khoury et al. 2005, di Renzo et al. 2012, Moreno-Castilla et al. 2012, Valentini et al. 2012, Ma et al. 2015, and Zhang et al. 2015 reported the years in which participants were recruited.

‡ Thornton et al. 2009 reported age in median.

§ Pre-pregnancy body weight was recorded when BMI was not provided in the original study.

‖ Khoury et al. 2005 reported BMI in range.

¶ Reflects the inclusion/exclusion of active smokers during pregnancy in the cohort study. Values are reported as count (%), "some" when the values were not reported but there was information to suggest that smokers were included, or"no" when none of the included participants were smokers.

** Reflects the country in which the study was conducted.

†† Reflects the amount of food that was given to participants during the study period. Partial reflects some foods were given; yes reflects all foods were given; and no reflects no food were given (i.e. dietary advice).

‡‡ Reflects the number of weeks participants were followed up. A "~" before a value indicates that the duration was calculated.

§§ Ma et al. 2015 reported the absolute weeks that participants were followed.

‖‖ Salvig et al. 1996, Lauszus et al. 2005, Thornton et al. 2009, and Di Renzo et al. 2012 reported the absolute gestational week; Asemi et al. 2013 (BJN) and (Nutrition) reported ranges.

†† Reflects the criteria that was used to diagnose PE and/or PIH.

Appendix Table 2.10. Table of characteristics of randomized controlled trials that reported on blood lipids.*

Trial	Trial name	Years in which the trial was active	Participant	Age, years	Pre-pregnancy BMI (kg/m^2) or body weight (kg)†	Active smokers‡	Setting§	Food provided‖	Comparator description CHO:FAT:PRO	Intervention description CHO:FAT:PRO	Follow-up duration, wks ¶	Gestational wk at which the intervention started
ENERGY NEUTRAL TRIALS												
Low-CHO and high-fat diet												
Hernandez et al. 2016	-	-	12 GDM	28 ± 4.9 (low-CHO/high-fat) 30 ± 2.5 (ctrl)	-	-	USA	yes	CHOICE (complex CHO) 60:15:25	low-CHO/high-fat 40:15:45	~8	31.7 ± 2.4 (low-CHO/high-fat) 31.2 ± 1.0 (ctrl)
Mediterranean-style diet												
Khoury et al. 2005	CARRDIP	1999-2001	259 healthy	29.6 ± 3.7 (Mediterranean) 29.8 ± 3.4 (ctrl)	19-32	no	Norway	no	routine care 50-52:16-17:32	rich in olive and rapeseed oil, nuts, nut butters, no fat or low fat dairy, fish, and avocado to replace meat, butter, cream, and dairy, fruits and vegetables, legumes, cholesterol (150 mg/d), while limit fatty meats	~21	19 ± 1.1 (Mediterranean diet) 19 ± 1.1 (ctrl)
Low glycemic index or load												
Ma et al. 2015	-	2008-2009	83 GDM	30.1 ± 3.8 (low GL) 30.0 ± 3.5 (ctrl)	21.9 ± 3.1 (low GL) 21.1 ± 2.7 (ctrl)	-	China	no	starch 45-50:20-24:25-30	low-GL 45-50:20-24:25-30	12-14	27.5 ± 1.1 (low GL) 27.9 ± 1.1 (ctrl)
Markovic et al 2016	GI Baby 3	2011-2012	139 increased risk for GDM	35.7 ± 4.7 (low GI) 34.9 ± 4.1 (ctrl)	25.2 ± 5.2 (low GI) 25.2 ± 5.2 (ctrl)	-	Australia	partial	routine care 40-45:15-25:25-30	low-GI (≤50) 40-45:15-25:25-30	~22	17.5 ± 2.0 (low GI) 17.7 ± 1.7 (fiber)
High complex CHO												
Hernandez et al. 2016	-	-	12 GDM	30 ± 2.5 (complex CHO) 28 ± 4.9 (ctrl)	-	-	USA	yes	low-CHO/high-fat 40:15:45	CHOICE (complex CHO) 60:15:25	~8	31.2 ± 1.0 (complex CHO) 31.7 ± 2.4 (ctrl)
High unsaturated-to-saturated fat ratio												
Hoppu et al. 2014	-	-	156 healthy	30.1 ± 5.2 (fat quality) 30.2 ± 5.0 (ctrl)	24.3 ± 4.4 (fat quality) 23.7 ± 3.5 (ctrl)	-	Finland	partial	routine care	amount and type of fat 55-60:10-15:30	~26	13.9 ± 1.6
High unsaturated fat												
Wang et al. 2015	-	2011-2013	84 GDM	30.3 ± 4.2 (sunflower oil) 29.7 ± 4.6 (ctrl)	21.4 ± 3.0 (sunflower oil) 22.2 ± 3.6 (ctrl)	no	China	partial	routine care 55-60:15-20:25-30	sunflower oil 50-54:15-20:31-35	~12	27.4 ± 1.52 (high-fat) 27.3 ± 1.96 (ctrl)
High MUFA												
Lauszus et al. 2001	-	-	25 GDM	31 ± 3.6 (MUFA) 29 ± 3.7 (ctrl)	-	-	Denmark	partial	high-CHO	high MUFA (sunflower oil; almonds + hazelnuts)	5	33
High DHA and EPA												
Barden et al. 2006	-	-	83 suffered allergies	31.0 ± 3.8 (fish oil) 32.4 ± 3.3 (crtl)	23.7 ± 3.8 (fish oil) 24.1 ± 3.9 (ctrl)	no	Australia	partial	olive oil (4 capsules x 1g/d)	fish oil (4 capsules x 1g/d)	>16	<20

Abbreviations: CARRDIP, Cardiovascular Risk Reduction Diet in Pregnancy; CHO, carbohydrate; CHOICE, choosing healthy options in carbohydrate energy; d, day; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GI, glycemic index; GL, glycemic load; GDM, gestational diabetes mellitus; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

* Values are expressed as mean ± SD unless otherwise noted.

† Khoury et al. 2005 reported BMI in range.

‡ Reflects the inclusion/exclusion of active smokers during pregnancy in the cohort study. "no" reflects that none of the included participants were smokers.

§ Reflects the country in which the study was conducted.

‖ Reflects the amount of food that was given to participants during the study period. Partial reflects some foods were given; yes reflects all foods were given; and no reflects no food were given (i.e. dietary advice).

¶ Reflects the number of weeks participants were followed up. A "~" before a value indicates that the duration was calculated.

Appendix Table 2.11. GRADE evidence profile of the most-adjusted associations of diet, foods, and nutrients and gestational diabetes mellitus in cohort studies.

Dietary factor	*n* studies (*n* participants)	RR (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Other considerations	Overall quality of evidence
Gestational Diabetes Mellitus										
Red meat	2 (18,592)	2.13 (1.68, 2.70)	0%	not serious	not serious	not serious	not serious	could not assess[1]	strong association dose-response	⊕⊕⊕⊕ **HIGH**
Fried food	1 (15,027)	1.78 (1.27, 2.49)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	dose-response	⊕⊕⊕◯ **MODERATE**
PUFA-to-SFA ratio	1 (13,475)	0.98 (0.77, 1.24)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	dose-response	⊕⊕⊕◯ **MODERATE**
Low-fat diet	2 (13,800)	0.71 (0.53, 0.95)	0%	not serious	not serious	serious[3]	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
DASH-style diet	1 (15,245)	0.66 (0.53, 0.82)	-	serious[4]	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Healthy eating diet	1 (14,437)	0.75 (0.59, 0.95)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Mediterranean-style diet	3 (19,275)	0.66 (0.55, 0.79)	45%	serious[4]	not serious[5]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Prudent diet	1 (13,110)	0.73 (0.58, 0.93)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Western diet	2 (16,963)	1.50 (1.15, 1.95)	0%	not serious	not serious	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Total dairy foods	1 (15,294)	0.95 (0.90, 1.01)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Total meats	1 (3,298)	1.68 (1.07, 2.64)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Processed meat	2 (18,592)	1.51 (1.19, 1.91)	49%	not serious	not serious[6]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Unprocessed meat	1 (15,294)	1.60 (1.22, 2.11)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Fish	2 (18,705)	0.96 (0.79, 1.15)	0%	not serious	not serious	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Nuts and peanuts	1 (15,294)	0.73 (0.57, 0.95)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Glycemic load	1 (13,110)	0.62 (0.39, 0.97)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Whole grains	1 (3,414)	0.61 (0.39, 0.96)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Cereal fibre	1 (13,110)	0.76 (0.59, 0.98)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Fruit fibre	1 (13,110)	0.67 (0.51, 0.88)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**

Appendix Table 2.11. CONTINUED. GRADE evidence profile of the most-adjusted associations of diet, foods, and nutrients and gestational diabetes mellitus in cohort studies.

Dietary factor	*n* studies (*n* participants)	RR (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Other considerations	Overall quality of evidence
Gestational Diabetes Mellitus										
MUFA	1 (13,475)	1.55 (1.03, 2.34)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Trans fat	1 (13,475)	0.99 (0.90, 1.09)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Dietary cholesterol	2 (16,633)	0.63 (0.49, 0.80)	58%	not serious	not serious[7]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Animal protein	1 (15,294)	1.49 (1.03, 2.16)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Vegetable protein	1 (15,294)	0.69 (0.50, 0.96)	-	not serious	could not assess[2]	not serious	not serious	could not assess[1]	none	⊕⊕◯◯ **LOW**
Low-CHO diet	2 (13,435)	1.29 (0.86, 1.93)	68%	not serious	serious[8]	serious[3]	serious[9]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
High-protein diet	2 (15,619)	0.92 (0.80, 1.05)	0%	not serious	not serious	serious[3]	not serious	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Processed food	2 (4,074)	1.88 (1.29, 2.74)	0%	serious[4]	not serious	not serious	not serious	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Vegetables	2 (4,021)	1.00 (0.99, 1.01)	0%	not serious	not serious	serious[11]	not serious	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Low-fat dairy foods	1 (3,414)	0.57 (0.32, 1.03)	-	not serious	could not assess[2]	not serious	serious[12]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Seafoods	2 (3,447)	0.83 (0.69, 1.00)	0%	not serious	not serious	serious[11]	serious[12]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Poultry	2 (18,592)	1.01 (0.81, 1.26)	0%	not serious	not serious	not serious	serious[9]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Eggs	3 (18,620)	0.98 (0.91, 1.06)	63%	not serious	serious[13]	serious[11]	not serious	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Legumes	1 (15,294)	1.06 (0.84, 1.34)	-	not serious	could not assess[2]	not serious	serious[9]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Nuts and seeds	1 (168)	0.94 (0.76, 1.17)	-	not serious	could not assess[2]	serious[11]	serious[14]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Total SSBs	1 (168)	0.99 (0.97, 1.01)	-	not serious	could not assess[2]	serious[11]	serious[14]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Vegetable oil	1 (168)	0.80 (0.59, 1.10)	-	not serious	could not assess[2]	serious[11]	serious[12, 14]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Energy	1 (1,135)	0.36 (0.21, 0.62)	-	not serious	could not assess[2]	serious[15]	serious[14]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**
Glycemic index	1 (13,110)	0.77 (0.59, 1.00)	-	not serious	could not assess[2]	not serious	serious[12]	could not assess[1]	none	⊕◯◯◯ **VERY LOW**

Appendix Table 2.11. CONTINUED. GRADE evidence profile of the most-adjusted associations of diet, foods, and nutrients and gestational diabetes mellitus in cohort studies.

Dietary factor	*n* studies (*n* participants)	RR (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Other considerations	Overall quality of evidence
Gestational Diabetes Mellitus										
Dietary fibre	2 (13,435)	0.72 (0.56, 0.93)	41%	not serious	serious[16]	serious[3]	not serious	could not assess[1]	none	⊕◯◯◯ VERY LOW
Vegetable fibre	1 (13,110)	0.87 (0.67, 1.13)	-	not serious	could not assess[2]	not serious	serious[12]	could not assess[1]	none	⊕◯◯◯ VERY LOW
Saturated fat	1 (13,475)	1.13 (0.79, 1.60)	-	not serious	could not assess[2]	not serious	serious[9]	could not assess[1]	none	⊕◯◯◯ VERY LOW
PUFA	1 (13,475)	1.01 (0.77, 1.33)	-	not serious	could not assess[2]	not serious	serious[9]	could not assess[1]	none	⊕◯◯◯ VERY LOW
n-3	1 (13,475)	1.03 (0.78, 1.36)	-	not serious	could not assess[2]	not serious	serious[9]	could not assess[1]	none	⊕◯◯◯ VERY LOW
Fish oil/DHA & EPA	1 (3,279)	1.16 (0.74, 1.82)	-	not serious	could not assess[2]	not serious	serious[9, 12]	could not assess[1]	none	⊕◯◯◯ VERY LOW
n-6	1 (13,475)	1.22 (0.89, 1.67)	-	not serious	could not assess[2]	not serious	serious[9]	could not assess[1]	none	⊕◯◯◯ VERY LOW

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MUFA, monounsaturated fatty acids; *n*, number; n-3, omega-3; n-6, omega-6; PUFA, polyunsaturated fatty acids; RR, relative risk; SFA, saturated fatty acids; SSBs, sugar-sweetened beverages.

[1] As <10 trials were included, publication bias could not be assessed.

[2] As there was only one included study, inconsistency could not be assessed.

[3] One of the included studies used a 3-day food record to capture dietary intake and has >10% weight on the pooled effect estimate. As the effect of diet on health outcome is likely due to long term exposure, using a 4-day food record may capture only short-term intake; thus biasing the pooled effect estimate and therefore, the dietary relationship was downgraded.

[4] Most or all of the included study or the study with the most weight on the pooled effect estimate (>60%) did not adjust for potential confounding factors of GDM including ethnicity, and pre-gestational diabetes.

[5] I^2 = 45%, which suggests substantial heterogeneity between study effect estimates. However, all included studies lie on the

same side of the line of no effect and there is substantial overlap between the studies.

[6] I^2=49% which suggests moderate heterogeneity between study effect estimates. However, all included studies lie on the same side of the line of no effect and there is substantial overlap between the studies.

[7] I^2= 58% which suggests moderate heterogeneity between study effect estimates. However, all included studies lie on the same side of the line of no effect and there is substantial overlap between the studies.

[8] I^2= 68% which suggests substantial heterogeneity between study effect estimates. Furthermore, a visual inspection of the forest plot shows that one study showed null association and the other showed harm.

[9] The pooled effect estimate crossed RR= 1.0 and MID of RR= 1.25.

[10] I^2= 73% which suggests substantial heterogeneity between study effect estimates. However, all included studies lie on the same side of the line of no effect and there is substantial overlap between the studies.

[11] One of the included studies, which also has the greatest weight (>60%) weight on the pooled effect estimate, used a 4-day food record to ascertain the dietary factor. As the effect of diet on health outcome is likely due to long term exposure, using a 4-day food record may capture only short-term intake; thus biasing the pooled effect estimate.

[12] The pooled effect estimate crossed RR= 1.0 and MID of RR= 0.75.

[13] I^2= 63% which suggests substantial heterogeneity between study effect estimates. Furthermore, a visual inspection of the forest plot shows that two studies showed null association and the other showed harm.

[14] Optimal information size (OIS) was not met.

[15] The included study used 3 24-hour dietary recalls to ascertain the dietary factor. As the effect of diet on health outcome is likely due to long term exposure, using 24-hour dietary recalls may capture only short-term intake; thus biasing the pooled effect estimate.

[16] I^2= 41% which suggests moderate heterogeneity between study effect estimates. Furthermore, a visual inspection of the forest plot shows that one study showed null association and the other showed protection.

Appendix Table 2.12. GRADE evidence profile of the effects of diets, foods, and nutrients on gestational diabetes mellitus and glycemic outcomes in RCTs (energy neutral comparisons).

Dietary factor	*n* of trials (*n* participants)	RR or MD or RD (95% CIs)*	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Gestational Diabetes Mellitus									
Low-fat diet	1 (874)	1.37 (1.05, 1.79)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[3]	⊕⊕⊕◯ **MODERATE**
Unsaturated fat	1 (874)	0.73 (0.56, 0.95)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[3]	⊕⊕⊕◯ **MODERATE**
High-protein diet	1 (185)	1.34 (0.74, 2.41)	-	not serious	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
n-3	1 (140)	1.13 (0.39, 3.25)	-	could not assess[6]	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
Healthy eating diet	1 (631)	0.92 (0.55, 1.52)	-	not serious	could not assess[1]	very serious[7]	very serious[2, 4, 5]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Glycemic index	3 (1491)	0.87 (0.60, 1.26)	0%	not serious	not serious	very serious[8]	very serious[2, 4, 5]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Unsaturated-to-saturated fat ratio	1 (117)	1.44 (0.83, 2.49)	-	not serious	could not assess[1]	very serious[9]	very serious[2, 4]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Impaired Glucose Tolerance (abnormal 1-hour or 2-hour OGTT)									
Unsaturated-to-saturated fat ratio	1 (130)	1.03 (0.41, 2.59)	-	not serious	could not assess[1]	very serious[9]	very serious[2, 4, 5]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Fasting glucose (mmol/L)									
Low-CHO & high-fat diet	1 (12)	0.46 (0.05, 0.87)	-	not serious	could not assess[1]	serious[10]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Low-fat diet	1 (874)	-0.20 (-0.32, -0.08)	-	not serious	could not assess[1]	serious[10]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Glycemic load	1 (83)	-0.31 (-0.55, -0.07)	-	not serious	could not assess[1]	serious[10]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Complex CHO	1 (12)	-0.46 (-0.87, -0.05)	-	not serious	could not assess[1]	serious[10]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
MUFA	1 (25)	0.50 (-0.17, 1.17)	-	not serious	could not assess[1]	serious[10]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Glycemic Index	4 (241)	-0.40 (-0.50, -0.31)	86%	not serious	serious[11]	very serious[8, 10]	serious[2]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Unsaturated-to-saturated fat ratio	1 (130)	0.04 (-0.10, 0.18)	-	not serious	could not assess[1]	very serious[9, 10]	serious[2]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Unsaturated fat	2 (958)	-0.17 (-0.28, -0.05)	73%	could not assess[6]	serious[12]	serious[10]	serious[2]	could not assess[3]	⊕◯◯◯ **VERY LOW**
1-hour OGTT (mmol/L)									
High-protein diet	1 (185)	0.10 (-0.33, 0.53)	-	not serious	could not assess[1]	serious[10]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**

Appendix Table 2.12. CONTINUED. GRADE evidence profile of the effects of diets, foods, and nutrients on gestational diabetes mellitus and glycemic outcomes in RCTs (energy neutral comparisons).

Dietary factor	*n* of trials (*n* participants)	RR or MD or RD (95% CIs)*	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
2-hour OGTT (mmol/L)									
High-protein diet	1 (185)	0.21 (-0.14, 0.56)	-	not serious	could not assess[1]	serious[10]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Number of hypoglycemic events									
Diabetes management diet	1 (50)	5.00 (-3.19, 13.19)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[3]	⊕⊕⊕◯ **MODERATE**
Higher fibre intake	1 (50)	-5.00 (-13.19, 3.19)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[3]	⊕⊕⊕◯ **MODERATE**

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; MUFA, monounsaturated fatty acids; *n*, number; n-3, omega-3; OGTT, oral glucose tolerance test.

*Relative risk (RR) was reported in gestational diabetes mellitus and impaired glucose tolerance. Mean difference (MD) was reported in fasting glucose, and 1-hour and 2-hour OGTT. Risk difference (RD) was reported in number of hypoglycemic events.

[1] As there was only one included study, inconsistency could not be assessed.
[2] Optimal information size (OIS) was not met.
[3] As <10 trials were included, publication bias could not be assessed.
[4] The pooled effect estimate crossed RR= 1.0 and MID of RR= 1.25.
[5] The pooled effect estimate crossed RR= 1.0 and MID of RR= 0.75.
[6] Could not be assessed because most of the domains in the Cochrane Risk of Bias Tool was rated as "unclear risk of bias."
[7] The included trial failed to achieve the intended dietary contrast. The median GI difference between the healthy eating diet and its comparator (low GI) was 3 units. This difference between diets may be too small to detect any clinically important effect on outcome.
[8] All or most of the included trials failed to achieve the intended dietary contrast. The median GI difference between the low

GI diet and its comparator was ~5 units. This difference between diets may be too small to detect any clinically important effect on outcome.

[9] All included trials failed to achieved their intended dietary contrast. The intake of polyunsaturated (PUFA), monounsaturated (MUFA), and saturated (SFA) were similar between the intervention and comparator arms. The difference between diets may be too small to detect any clinically important effect on outcome.

[10] Fasting glucose is a surrogate marker of gestational dysglycemia.

[11] I^2= 86%, which suggests considerable heterogeneity between study effect estimates. Furthermore, 3 of the trials with the least weight on the pooled effect estimate showed FG null effects, while the study with the most weight on the pooled effect estimate (67.0%) showed FG reducing effects.

[12] I^2= 73% which suggests substantial heterogeneity between study effect estimates. Furthermore, one trial showed FG null effects while the other showed FG reducing effects.

Appendix 2.13. GRADE evidence profile of the effects of diets, foods, and nutrients on

gestational diabetes mellitus and glycemic outcomes in RCTs (energy conscious comparisons).

Dietary factor	*n* of trials (*n* participants)	RR or MD (95% CIs)*	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Gestational Diabetes Mellitus									
Low-CHO diet	1 (232)	0.58 (0.29, 1.16)	-	could not assess[1]	could not assess[2]	not serious	serious[3, 4]	could not assess[5]	⊕⊕⊕◯ **MODERATE**
Energy	2 (309)	0.61 (0.39, 0.97)	0%	could not assess[1]	not serious	not serious	serious[3]	could not assess[5]	⊕⊕⊕◯ **MODERATE**
Healthy eating diet	1 (272)	1.20 (0.33, 4.28)	-	could not assess[1]	could not assess[2]	not serious	serious[3, 4, 6]	could not assess[5]	⊕⊕⊕◯ **MODERATE**
Fasting glucose (mmol/L)									
Energy	3 (647)	-0.50 (-0.58, -0.42)	96%	very serious[7]	serious[8]	serious[9]	serious[3]	could not assess[5]	⊕◯◯◯ **VERY LOW**
2-hour OGTT (mmol/L)									
Energy	1 (50)	0.30 (-0.41, 1.01)	-	could not assess[1]	could not assess[2]	serious[9]	serious[2]	could not assess[5]	⊕⊕◯◯ **LOW**

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; FG, fasting glucose; *n*, number; OGTT, oral glucose tolerance test.

*Relative risk (RR) was reported in gestational diabetes mellitus and impaired glucose tolerance. Mean difference (MD) was reported in fasting glucose, and 2-hour OGTT.

[1] Could not be assessed because most of the domains in the Cochrane Risk of Bias Tool was rated as "unclear risk of bias."

[2] As there was only one included study, inconsistency could not be assessed.

[3] Optimal information size (OIS) was not met.

[4] The effect estimate crossed RR= 1.0 and MID of RR=0.75.

[5] The effect estimate crossed RR= 1.0 and MID of RR=1.25.

[6] As <10 trials were included, publication bias could not be assessed.

[7] Two of the 3 included trials were rated as high risk of bias in the incomplete domain of the Cochrane's Risk of Bias Tool. In these two trials, a higher proportion of women dropped out of the active intervention arm, and in one of these 2 trials, drop-outs were replaced with new recruits.

[8] I^2= 96% which suggests considerable heterogeneity between study effect estimates. Furthermore, two trials showed FG

reducing effects while one showed FG increasing effect.

[9] Fasting glucose or OGTT results are surrogate markers of gestational dysglycemia.

Appendix Table 2.14. GRADE evidence profile of the most-adjusted associations of diets, foods, and nutrients and gestational weight gain in cohort studies.

Dietary factor	*n* studies (*n* participants)	MD (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Other considerations	Overall quality of evidence
Gestational weight gain (kg)										
Glycemic load	1 (1,186)	-0.82 (-1.92, 0.28)	-	not serious	could not assess[1]	serious[2]	serious[3]	could not assess[4]	none	⨁◯◯◯ **VERY LOW**

Abbreviations: CIs, confidence interval; MD, mean difference; *n*, number.

[1] This criteria could not be assessed because only one study was included.
[2] Gestational weight gain is a surrogate marker for appropriate weight gain.
[3] Optimal information size (OIS) was not met.
[4] As <10 trials were included, publication bias could not be assessed.

Appendix Table 2.15. GRADE evidence profile of the effects of diets, foods, and nutrients on weight gain in RCTs (energy neutral comparisons).

Dietary factor	*n* of trials (*n* participants)	RR or MD (95% CIs)*	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Inadequate gestational weight gain									
Glycemic index	3 (736)	1.27 (1.00, 1.62)	0%	not serious	not serious	very serious[1]	serious[2,3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Adequate gestational weight gain									
Mediterranean-style diet	1 (120)	2.40 (1.77, 3.25)	-	not serious	could not assess[5]	not serious	serious[3]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
n-3	1 (150)	1.58 (0.80, 3.15)	-	not serious	could not assess[5]	not serious	serious[2, 3]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
High protein diet	1 (185)	1.11 (0.52, 2.33)	-	not serious	could not assess[5]	not serious	very serious[2, 3, 6]	could not assess[4]	⊕⊕◯◯ **LOW**
Glycemic index	3 (736)	1.12 (0.93, 1.35)	0%	not serious	not serious	very serious[1]	serious[2, 3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Unsaturated-to-saturated fat ratio	1 (156)	1.23 (0.81, 1.89)	-	not serious	could not assess[5]	very serious[7]	serious[2, 3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Excessive gestational weight gain									
Glycemic index	4 (833)	0.74 (0.61, 0.90)	63%	not serious	serious[8]	very serious[1]	serious[3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Unsaturated-to-saturated fat ratio	1 (156)	0.87 (0.60, 1.26)	-	not serious	could not assess[5]	very serious[7]	very serious[2, 3, 6]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Gestational weight gain (kg)									
Low CHO diet	1 (68)	0.71 (0.06, 1.36)	-	could not assess[9]	could not assess[5]	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
Low fat diet	1 (874)	-0.20 (-0.32, -0.08)	-	not serious	could not assess[5]	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
High protein diet	1 (185)	-0.28 (-1.67, 1.11)	-	not serious	could not assess[5]	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
DASH-style diet	2 (85)	-1.63 (-4.31, 1.05)	40%	could not assess[9]	not serious[11]	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
Diabetes management diet	2 (981)	-2.57 (-4.99, -0.15)	0%	not serious	not serious	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
Glycemic load	2 (121)	-0.48 (-1.95, 1.00)	0%	not serious	not serious	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
Complex CHO	1 (12)	0.60 (-3.32, 4.52)	-	not serious	could not assess[5]	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
n-3	1 (150)	0.25 (-0.97, 1.47)	-	not serious	could not assess[5]	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
Fish oil/ DHA and EPA	3 (200)	0.70 (0.16, 1.23)	0%	could not assess[9]	not serious	serious[10]	serious[3]	could not assess[4]	⊕⊕◯◯ **LOW**
Low-CHO and high-fat diet	3 (182)	-0.87 (-1.46, -0.27)	70%	could not assess[9]	very serious[12]	serious[10]	serious[3]	could not assess[4]	⊕◯◯◯ **VERY LOW**

Appendix Table 2.15. CONTINUED. GRADE evidence profile of the effects of diets, foods, and nutrients on weight gain in RCTs (energy neutral comparisons).

Dietary factor	*n* of trials (*n* participants)	RR or MD (95% CIs)*	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Gestational weight gain (kg)									
Healthy eating diet	1 (576)	0.30 (-0.50, 1.10)	-	not serious	could not assess[5]	very serious[10, 13]	serious[3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Mediterranean-style diet	2 (397)	0.34 (-0.20, 0.88)	91%	not serious	serious[14]	serious[10, 15]	serious[3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Dairy foods	1 (49)	0.20 (-5.90, 6.30)	-	not serious	could not assess[5]	serious[10, 16]	very serious[3, 17]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Chocolate	1 (90)	-1.40 (-7.50, 4.70)	-	not serious	could not assess[5]	serious[10]	very serious[3, 17]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Glycemic index	5 (1571)	0.00 (-0.49, 0.49)	50%	not serious	not serious[18]	very serious[1, 10]	serious[3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Total fibre	2 (70)	-0.32 (-7.46, 6.82)	89%	could not assess[9]	very serious[19]	serious[10]	serious[3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Unsaturated-to-saturated fat ratio	1 (156)	-0.10 (-1.70, 1.50)	-	not serious	could not assess[5]	very serious[7, 10]	serious[3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Unsaturated fat	2 (958)	0.33 (-0.27, 0.94)	75%	not serious	serious[20]	serious[10]	serious[3]	could not assess[4]	⊕◯◯◯ **VERY LOW**

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; *n*, number; n-3, omega-3.

*Relative risk (RR) was reported in inadequate gestational weight gain, adequate weight gain, and excessive weight gain. Mean difference (MD) was reported in gestational weight gain.

[1] All or most included trials failed to achieve the intended dietary contrast. The median GI difference between the low GI diet and its comparator was 5 units. This difference between diets may be too small to detect any clinically important effect on outcome.
[2] The pooled effect estimate crossed RR= 1.0 and MID of RR= 1.25.
[3] Optimal information size (OIS) was not met.
[4] As <10 trials were included, publication bias could not be assessed.
[5] As there was only one included study, inconsistency could not be assessed.
[6] The pooled effect estimate crossed RR= 1.0 and MID of RR= 0.75.

[7] All included trials failed to achieved their intended dietary contrast. The intake of polyunsaturated (PUFA), monounsaturated (MUFA), and saturated (SFA) were similar between the intervention and comparator arms. The difference between diets may be too small to detect any clinically important effect on outcome.

[8] I^2= 63% which suggests substantial heterogeneity between study effect estimates. Furthermore, two of the included trials showed risk reduction while the other two showed null association.

[9] Could not be assessed because most of the domains in the Cochrane Risk of Bias Tool was rated as "unclear risk of bias."

[10] Gestational weight gain is a surrogate marker for appropriate weight gain.

[11] I^2= 40%, which suggests moderate heterogeneity between study effect estimates. Furthermore, a visual inspection of the forest plot revealed that the included studies substantially overlapped one another and lie on the same side of the line of no effect.

[12] I^2= 70% which suggests substantial heterogeneity between study effect estimates. Furthermore, one trial showed weight gain, another showed null effect, and one trial showed weight reduction.

[13] The included study failed to achieve the intended dietary contrast. The nutrient profile (e.g. carbohydrates, fat, protein, fiber, glycemic index) was similar between the intervention and comparator arms. The difference between diets may be too small to detect any clinically important effect on outcome.

[14] I^2= 91% which suggests considerable heterogeneity between study effect estimates. Furthermore, one of the included trial showed weight gain and the other showed weight loss.

[15] The study with the most weight (97.2%) in the pooled effect estimate failed to achieve the intended dietary contrast. The nutrient profile of the key targets of the intervention (dietary cholesterol, saturated fat, polyunsaturated fat, monounsaturated fat) were similar between the intervention and comparator arms. The difference between diets may be too small to detect any clinically important effect on outcome.

[16] The investigators reported an issue with women consuming the comparator (orange juice). However, it was unclear the severity of non-compliance. As such, we have not downgraded indirectness for non-compliance.

[17] The pooled effect estimate crossed MD= 0 and MID of ±4.6kg.

[18] I^2= 50% which suggests substantial heterogeneity between study effect estimates. However, most trials showed null effects on weight.

[19] I^2= 89% which suggests considerable heterogeneity between study effect estimates. Furthermore, one of the included trials showed weight reduction while the other showed weight loss.

[20] I^2= 75% which suggests considerable heterogeneity between study effect estimates. Furthermore, the effect estimates of

one of the included trials showed weight reduction while the other showed weight loss.

Appendix Table 2.16. GRADE evidence profile of the effects of diets, foods, and nutrients on weight gain in RCTs (energy conscious comparisons)

Dietary factor	*n* of trials (*n* participants)	RR or MD (95% CIs)*	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Inadequate gestational weight gain									
Healthy eating diet	1 (307)	0.53 (0.27, 1.07)	-	could not assess[1]	could not assess[2]	not serious	serious[3, 4]	could not assess[5]	⊕⊕⊕◯ **MODERATE**
Adequate gestational weight gain									
Healthy eating diet	2 (579)	1.60 (1.28, 2.00)	88%	could not assess[1]	not serious[6]	not serious	serious[4]	could not assess[5]	⊕⊕⊕◯ **MODERATE**
Excessive gestational weight gain									
Healthy eating diet	1 (307)	0.95 (0.75, 1.21)	-	could not assess[1]	could not assess[2]	not serious	serious[3, 4]	could not assess[5]	⊕⊕⊕◯ **MODERATE**
Gestational weight gain (kg)									
Low CHO diet	1 (232)	-13.59 (-19.29, -7.89)	-	could not assess[1]	could not assess[2]	serious[8]	serious[4]	could not assess[5]	⊕⊕◯◯ **LOW**
Healthy eating diet	2 (292)	-2.54 (-5.31, 0.24)	0%	could not assess[1]	not serious	serious[8]	serious[4, 9]	could not assess[5]	⊕⊕◯◯ **LOW**
Energy	5 (1323)	-1.93 (-4.86, 1.00)	82%	could not assess[1]	serious[7]	serious[8]	serious[4, 9]	could not assess[5]	⊕◯◯◯ **VERY LOW**

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; *n*, number.

*Relative risk (RR) was reported in inadequate gestational weight gain, adequate weight gain, and excessive weight gain. Mean difference (MD) was reported in gestational weight gain.

[1] Could not be assessed because most of the domains in the Cochrane Risk of Bias Tool was rated as "unclear risk of bias."

[2] As there was only one included study, inconsistency could not be assessed.

[3] The pooled effect estimated crossed RR= 1.0 and RR= 0.75.

[4] Optimal information size (OIS) was not met.

[5] As <10 trials were included, publication bias could not be assessed.

[6] I^2= 86% which suggests considerable heterogeneity between study effect estimates. However, the effect estimates of both trials lie on the same side of the line of no effect.

[7] I^2= 82%, which suggests considerate heterogeneity between study effect estimates. Furthermore, two of the included trials showed weight reduction while the other 3 showed null effects.

[8] Gestational weight gain is a surrogate marker for appropriate weight gain.

[9] The pooled effect estimate crossed MD= 0 and MID of -4.6kg.

Appendix Table 2.17. GRADE evidence profile of the effects of diets, foods, and nutrients on hypertensive disorders of pregnancy in cohort studies.

Dietary factor	*n* studies (*n* participants)	RR (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Other consideration	Overall quality of evidence
Pre-eclampsia										
Lower energy	1 (3,133)	0.27 (0.11, 0.65)	-	not serious	could not assess[1]	not serious	not serious	could not assess[2]	dose-response	⊕⊕⊕◯ **MODERATE**
PUFA	1 (3,133)	2.61 (1.29, 5.29)	-	not serious	could not assess[1]	not serious	not serious	could not assess[2]	dose-response	⊕⊕⊕◯ **MODERATE**
Nordic diet	1 (72,072)	0.86 (0.79, 0.94)	-	not serious	could not assess[1]	not serious	nots serious	could not assess[2]	dose-response	⊕⊕⊕◯ **MODERATE**
DASH-style diet	1 (28,192)	0.74 (0.65, 0.84)	-	not serious	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕⊕◯◯ **LOW**
Healthy eating diet	1 (23,423)	0.72 (0.62, 0.84)	-	not serious	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕⊕◯◯ **LOW**
Processed foods	1 (23,423)	1.21 (1.03, 1.42)	-	not serious	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕⊕◯◯ **LOW**
Fruits	1 (32,933)	0.79 (0.67, 0.93)	-	serious[3]	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕⊕◯◯ **LOW**
Vegetables	1 (28,192)	0.79 (0.62, 0.99)	-	not serious	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕⊕◯◯ **LOW**
Desserts and sweets	1 (23,423)	0.90 (0.77, 1.05)	-	not serious	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕⊕◯◯ **LOW**
Low-fat diet	1 (3,133)	1.99 (0.75, 5.31)	-	not serious	could not assess[1]	not serious	serious[4, 5]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
High-protein diet	1 (3,133)	0.60 (0.27, 1.34)	-	not serious	could not assess[1]	not serious	serious[4, 5]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Seafoods	1 (3,279)	1.25 (0.55, 2.84)	-	serious[3]	could not assess[1]	not serious	serious[4, 5]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Total SSBs	1 (32,933)	1.27 (1.05, 1.54)	-	not serious	could not assess[1]	serious[6]	not serious	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Honey	1 (33,549)	0.90 (0.78, 1.03)	-	serious[3]	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Dietary fibre	1 (1,538)	0.28 (0.11, 0.73)	-	serious[3]	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Insoluble fibre	1 (1,538)	0.35 (0.14, 0.88)	-	serious[3]	could not assess[1]	not serious	serious[7]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Soluble fibre	1 (1,538)	0.30 (0.11, 0.83)	-	serious[3]	could not assess[1]	not serious	serious[7]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Added sugars	2 (36,126)	1.08 (0.91, 1.28)	82%	serious[8]	very serious[9]	not serious	serious[5]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
MUFA	1 (3,133)	1.11 (0.50, 2.43)	-	not serious	could not assess[1]	not serious	serious[4, 5]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**

Appendix Table 2.17. CONTINUED. GRADE evidence profile of the effects of diets, foods, and nutrients on hypertensive disorders of pregnancy in cohort studies.

Dietary factor	*n* studies (*n* participants)	RR (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Other consideration	Overall quality of evidence
Pre-eclampsia										
Trans fat	1 (63,226)	1.02 (0.87, 1.20)	-	serious[3]	could not assess[1]	not serious	not serious	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Fish oil/DHA and EPA	1 (3,279)	0.63 (0.33, 1.21)	-	serious[3]	could not assess[1]	not serious	serious[4]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
n-3	1 (3,133)	1.80 (0.89, 3.65)	-	not serious	could not assess[1]	not serious	serious[5]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
n-6	1 (3,133)	1.90 (0.98, 3.70)	-	not serious	could not assess[1]	not serious	serious[5]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Saturated fat	1 (3,133)	0.40 (0.12, 1.32)	-	not serious	could not assess[1]	not serious	serious[4, 5]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Gestational hypertension										
Seafoods	1 (3,279)	1.13 (0.79, 1.60)	-	serious[3]	could not assess[1]	not serious	serious[4]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**
Fish oil/DHA and EPA	1 (3,279)	1.14 (0.85, 1.53)	-	serious[3]	could not assess[1]	not serious	serious[4]	could not assess[2]	none	⊕◯◯◯ **VERY LOW**

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MUFA, monounsaturated fatty acids; n, number; n-3, omega-3; n-6, omega-6; SSBs, sugar-sweetened beverages.

[1] As there was only one included study, inconsistency could not be assessed.
[2] As <10 trials were included, publication bias could not be assessed.
[3] Study did not adjust for potential confounding factors of HDP, which includes pre-gestational hypertension and history of pre-eclampsia.
[4] The pooled effect estimate crossed RR= 1.0 and MID of RR= 0.75.
[5] The pooled effect estimate crossed RR= 1.0 and MID of RR= 1.25.
[6] The included study used a 4-day food record to ascertain the dietary factor. As the effect of diet on health outcome is likely due to long term exposure, using a 4-day food record may capture only short-term intake; thus biasing the pooled effect estimate.
[7] Optimal information size (OIS) was not met.
[8] The study with the most weight on the pooled effect estimate (~97%) did not adjust for potential confounding factors of HDP,

which includes pre-gestational hypertension and history of pre-eclampsia.

[9] I^2= 82% which suggests considerable heterogeneity between study effect estimates. Furthermore, one of the studies showed null association and the other showed harm.

Appendix Table 2.18. GRADE evidence profile of the effects of diets, foods, and nutrients on hypertensive disorders of pregnancy and related outcomes in RCTs (energy-balanced comparisons).

Dietary factor	*n* of trials (*n* participants)	RR or MD (95% CIs)*	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Pre-eclampsia									
Diabetes management diet	1 (931)	0.46 (0.24, 0.89)	-	not serious	could not assess[1]	not serious	serious [2]	could not assess[3]	⊕⊕⊕◯ **MODERATE**
Low-fat diet	1 (874)	1.54 (0.59, 4.02)	-	not serious	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
DASH-style diet	4 (163)	0.99 (0.34, 2.92)	0%	could not assess[6]	not serious	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
Chocolate	1 (90)	0.00* (-0.04, 0.04)	-	not serious	could not assess[1]	not serious	very serious[7]	could not assess[3]	⊕⊕◯◯ **LOW**
Glycemic load	1 (84)	1.00 (0.06, 15.47)	-	not serious	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
Unsaturated fat	1 (874)	0.65 (0.25, 1.70)	-	not serious	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
n-3	1 (54)	0.33 (0.01, 7.84)	-	not serious	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
Fish oil/ DHA and EPA	4 (1,536)	0.56 (0.16, 1.92)	75%	not serious	serious[8]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Mediterranean-style diet	1 (290)	0.92 (0.34, 2.48)	-	not serious	could not assess[1]	very serious[9]	very serious[2, 4, 5]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Gestational hypertension									
Diabetes management diet	1 (931)	0.75 (0.47, 1.20)	-	not serious	could not assess[1]	not serious	serious[2, 4]	could not assess[3]	⊕⊕⊕◯ **MODERATE**
Fish oil/ DHA and EPA	5 (1,731)	1.04 (0.85, 1.27)	0%	not serious	not serious	not serious	serious[2, 5]	could not assess[3]	⊕⊕⊕◯ **MODERATE**
Low-fat diet	1 (874)	1.42 (0.69, 2.93)	-	not serious	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
Chocolate	1 (90)	0.00* (-0.04, 0.04)	-	not serious	could not assess[1]	not serious	very serious[7]	could not assess[3]	⊕⊕◯◯ **LOW**
Glycemic index	1 (20)	0.33 (0.02, 7.32)	-	could not assess[6]	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
Glycemic load	1 (84)	0.35 (0.01, 8.34)	-	not serious	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
Unsaturated fat	1 (874)	0.70 (0.34, 1.46)	-	not serious	could not assess[1]	not serious	very serious[2, 4, 5]	could not assess[3]	⊕⊕◯◯ **LOW**
Low-CHO and high-fat diet	1 (150)	3.08 (0.64, 14.78)	-	could not assess[6]	could not assess[1]	serious[10]	very serious[2, 4, 5]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Mediterranean-style diet	1 (259)	0.98 (0.48, 2.01)	-	not serious	could not assess[1]	very serious[9]	very serious[2, 4, 5]	could not assess[3]	⊕◯◯◯ **VERY LOW**

Appendix Table 2.18. CONTINUED. GRADE evidence profile of the effects of diets, foods, and nutrients on hypertensive disorders of pregnancy and related outcomes in RCTs (energy neutral comparisons).

Dietary factor	*n* of trials (*n* participants)	RR or MD (95% CIs)*	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Systolic blood pressure (mm Hg)									
Low-fat diet	1 (874)	0.00 (-0.00, 0.00)	-	not serious	could not assess[1]	serious[11]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Dairy foods	1 (49)	-1.00 (-5.53, 3.53)	-	not serious	could not assess[1]	serious[11]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Chocolate	1 (90)	-6.70 (-11.23, -2.17)	-	not serious	could not assess[1]	serious[11]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Glycemic load	1 (38)	-2.00 (-7.37, 3.37)	-	not serious	could not assess[1]	serious[11]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Unsaturated fat	1 (874)	0.00 (-0.00, 0.00)	-	not serious	could not assess[1]	serious[11]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
MUFA	1 (27)	1.00 (-14.31, 16.31)	-	could not assess[6]	could not assess[1]	serious[11]	very serious[2, 12]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Fish oil/DHA and EPA	5 (1,498)	-2.57 (-2.68, -2.46)	97%	not serious	serious[13]	serious[11]	serious[2]	could not assess[3]	⊕◯◯◯ **VERY LOW**
Diastolic blood pressure (mm Hg)									
Low-fat diet	1 (874)	1.00 (-0.96, 2.96)	-	not serious	could not assess[1]	serious[11]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Dairy foods	1 (49)	1.00 (-2.19, 4.19)	-	not serious	could not assess[1]	serious[11]	serious[2, 14]	could not assess[3]	⊕⊕◯◯ **LOW**
Chocolate	1 (90)	-2.90 (-6.09, 0.29)	-	not serious	could not assess[1]	serious[11]	serious[2, 14]	could not assess[3]	⊕⊕◯◯ **LOW**
Glycemic load	1 (38)	-2.00 (-5.80, 1.80)	-	not serious	could not assess[1]	serious[11]	serious[2, 14]	could not assess[3]	⊕⊕◯◯ **LOW**
Unsaturated fat	1 (874)	1.00 (-0.96, 2.96)	-	not serious	could not assess[1]	serious[11]	serious[2]	could not assess[3]	⊕⊕◯◯ **LOW**
Fish oil/DHA and EPA	5 (1,498)	-4.08 (-4.65, -3.51)	90%	not serious	serious[15]	serious[11]	serious[2]	could not assess[3]	⊕◯◯◯ **VERY LOW**
MUFA	1 (27)	1.00 (-8.80, 10.80)	-	could not assess[6]	could not assess[1]	serious[11]	very serious[2, 14]	could not assess[3]	⊕◯◯◯ **VERY LOW**

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MUFA, monounsaturated fatty acids; *n*, number; n-3, omega-3; n-6, omega-6; SSBs, sugar-sweetened beverages.

*Relative risk (RR) was reported in pre-eclampsia and gestational hypertension. Mean difference (MD) was reported in systolic and diastolic blood pressure.

[1] As there was only one included study, inconsistency could not be assessed.
[2] Optimal information size (OIS) was not met.
[3] As <10 trials were included, publication bias could not be assessed.
[4] The pooled effect estimate crossed RR= 1.0 and MID of RR= 0.75.
[5] The pooled effect estimate crossed RR= 1.0 and MID of RR= 1.25.
[6] Could not be assessed because most of the domains in the Cochrane Risk of Bias Tool was rated as "unclear risk of bias."
[7] Imprecision could not be judged because zero events were reported in both intervention and control arm.
[8] I^2= 75% which suggests considerable heterogeneity between study effect estimates. Furthermore, two of the trials showed null effects and the other two showed protection.
[9] The included trials failed to achieve the intended dietary contrast. The intake of polyunsaturated (PUFA), monounsaturated (MUFA), and saturated (SFA) were similar between the intervention and comparator arms. The difference between diets may be too small to detect any clinically important effect on outcome.
[10] The included trials failed to achieve the intended dietary contrast. The intake of carbohydrate were similar between the intervention and comparator arms. The difference between diets may be too small to detect any clinically important effect on outcome.
[11] Blood pressure is a surrogate measure for hypertension.
[12] The pooled effect estimate crossed MD= 0.0 and MID of MD ±9 mmHg.
[13] I^2= 97% which suggests considerable heterogeneity between study effect estimates. Furthermore, three of the trials showed null effects and the other two showed protection.
[14] The pooled effect estimate crossed MD= 0.0 and MID of MD ±3 mmHg.
[15] I^2= 90% which suggests considerable heterogeneity between study effect estimates. Furthermore, 4 of the five trials showed null effect but the trial with the most weight on the pooled effect estimate (78.2%) showed significant DBP reduction.

Appendix Table 2.19. GRADE evidence profile of the effects of diets, foods, and nutrients on hypertensive disorders of pregnancy and related outcomes in RCTs (energy conscious comparisons).

Dietary factor	*n* of trials (*n* participants)	RR (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Pre-eclampsia									
Low-CHO diet	1 (232)	0.64 (0.26, 1.58)	-	could not assess[1]	could not assess[2]	not serious	very serious[3, 4, 5]	could not assess[6]	⊕⊕◯◯ **LOW**
Healthy eating diet	2 (528)	0.52 (0.22, 1.23)	74%	could not assess[1]	serious[7]	not serious	serious[3, 4]	could not assess[6]	⊕⊕◯◯ **LOW**
Energy	3 (274)	1.03 (0.55, 1.92)	0%	could not assess[1]	not serious	very serious[8]	very serious[3, 4, 5]	could not assess[6]	⊕◯◯◯ **VERY LOW**
Gestational hypertension									
Low-CHO diet	1 (232)	0.21 (0.06, 0.75)	-	could not assess[1]	could not assess[2]	not serious	serious[3, 4]	could not assess[6]	⊕⊕⊕◯ **MODERATE**
Energy	1 (50)	0.29 (0.04, 2.44)	-	could not assess[1]	could not assess[2]	not serious	very serious[3, 4, 5]	could not assess[6]	⊕⊕◯◯ **LOW**
Healthy eating diet	1 (272)	0.80 (0.12, 5.48)	-	could not assess[1]	could not assess[2]	not serious	very serious[3, 4, 5]	could not assess[6]	⊕⊕◯◯ **LOW**

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; *n*, number.

[1] Could not be assessed because most of the domains in the Cochrane Risk of Bias Tool was rated as "unclear risk of bias."
[2] As there was only one included study, inconsistency could not be assessed.
[3] Optimal information size (OIS) was not met.
[4] The pooled effect estimate crossed RR= 1.0 and MID of RR= 0.75.
[5] The pooled effect estimate crossed RR= 1.0 and MID of RR= 1.25.
[6] As <10 trials were included, publication bias could not be assessed.
[7] I^2= 74% which suggests substantial heterogeneity between study effect estimates. Furthermore, one of the trials showed risk reduction and the other showed null association.
[8] The trial with the most weight on the pooled effect estimate (88%) failed to achieve the intended dietary contrast. The energy intake between intervention and comparator arms were similar; therefore the dietary contrast may be too small to detect a clinically important effect on outcome.

Appendix Table 2.20. Summary MDs and 95% CIs for the association between each dietary factor and blood lipids.

Dietary factors	No. of Studies (*n* participants)	MD (95% CIs)	Quality of Evidence
LDL-C (mmol/L)			
Low glycemic load	1 (83)	0.02 (0.00, 0.04)	⊕⊕⊕◯ MODERATE
High MUFA	1 (25)	-1.00 (-2.05, 0.05)	⊕⊕⊕◯ MODERATE
High fish oil/DHA & EPA	1 (83)	0.36 (-0.27, 0.99)	⊕⊕⊕◯ MODERATE
Low-CHO and high-fat diet	1 (12)	0.39 (-0.55, 1.33)	⊕⊕◯◯ LOW
Low glycemic index	1 (122)	0.10 (-0.08, 0.28)	⊕⊕◯◯ LOW
High complex CHO	1 (12)	-0.39 (-1.33, 0.55)	⊕⊕◯◯ LOW
Mediterranean-style diet	1 (259)	-0.10 (-0.18, -0.02)	⊕◯◯◯ VERY LOW
High unsaturated-to-saturated fat ratio	1 (156)	-0.08 (-0.38, 0.22)	⊕◯◯◯ VERY LOW
non-HDL-C (mmol/L)			
High unsaturated fat	1 (84)	-0.44 (-0.54, -0.34)	⊕⊕⊕⊕ HIGH
High MUFA	1 (25)	-1.10 (-1.42, -0.78)	⊕⊕⊕⊕ HIGH
Low-CHO and high-fat diet	1 (12)	-0.03 (-0.71, 0.65)	⊕⊕⊕◯ MODERATE
High glycemic load	1 (83)	-0.03 (-0.46, 0.40)	⊕⊕⊕◯ MODERATE
High complex CHO	1 (12)	0.03 (-0.65, 0.71)	⊕⊕⊕◯ MODERATE
High fish oil/DHA & EPA	1 (83)	-0.29 (-0.57, -0.01)	⊕⊕⊕◯ MODERATE
High glycemic index	1 (122)	0.10 (0.04, 0.16)	⊕⊕◯◯ LOW
Mediterranean-style diet	1 (259)	-0.08 (-0.30, 0.14)	⊕◯◯◯ VERY LOW
High unsaturated-to-saturated fat ratio	1 (156)	-0.17 (-2.57, 2.23)	⊕◯◯◯ VERY LOW
Triglycerides (mmol/L)			
Low-CHO & high-fat diet	1 (12)	-0.50 (-1.67, 0.67)	⊕⊕⊕◯ MODERATE
High glycemic load	1 (83)	-0.15 (-0.27, -0.03)	⊕⊕⊕◯ MODERATE
High complex CHO	1 (12)	0.30 (-0.29, 0.89)	⊕⊕⊕◯ MODERATE
High unsaturated fat	1 (84)	-0.50 (-0.89, -0.11)	⊕⊕⊕◯ MODERATE
High MUFA	1 (25)	-0.30 (-1.17, 0.57)	⊕⊕⊕◯ MODERATE
High glycemic index	1 (122)	0.00 (-0.24, 0.24)	⊕⊕◯◯ LOW

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MUFA, monounsaturated fatty acids; *n*, number; n-3, omega-3; n-6, omega-6; SSBs, sugar-sweetened beverages.

Appendix Table 2.21. GRADE evidence profile of the effects of diets, foods, and nutrients on blood lipid outcomes in RCTs (energy neutral comparisons).

Dietary factor	*n* of trials (*n* participants)	MD (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
LDL-C (mmol/L)									
Glycemic load	1 (83)	0.02 (0.00, 0.04)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
MUFA	1 (25)	-1.00 (-2.05, 0.05)	-	could not assess[7]	could not assess[1]	not serious	serious[2, 3]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Fish oil/ DHA and EPA	1 (83)	0.36 (-0.27, 0.99)	-	could not assess[7]	could not assess[1]	not serious	serious[2, 3]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Low-CHO and high-fat diet	1 (12)	0.39 (-0.55, 1.33)	-	not serious	could not assess[1]	not serious	very serious[2, 3]	could not assess[4]	⊕⊕◯◯ **LOW**
Glycemic index	1 (122)	0.10 (-0.08, 0.28)	-	not serious	could not assess[1]	serious[5]	serious[2, 3]	could not assess[4]	⊕⊕◯◯ **LOW**
Complex CHO	1 (12)	-0.39 (-1.33, 0.55)	-	not serious	could not assess[1]	not serious	very serious[2,3]	could not assess[4]	⊕⊕◯◯ **LOW**
Mediterranean-style diet	1 (259)	-0.10 (-0.18, -0.02)	-	not serious	could not assess[1]	very serious[6]	serious[2]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Unsaturated-to-saturated fat ratio	1 (156)	-0.08 (-0.38, 0.22)	-	not serious	could not assess[1]	very serious[6]	serious[2, 3]	could not assess[4]	⊕◯◯◯ **VERY LOW**
non-HDL-C (mmol/L)									
Unsaturated fat	1 (84)	-0.44 (-0.54, -0.34)	-	could not assess[7]	could not assess[1]	not serious	not serious	could not assess[4]	⊕⊕⊕⊕ **HIGH**
MUFA	1 (25)	-1.10 (-1.42, -0.78)	-	could not assess[7]	could not assess[1]	not serious	not serious	could not assess[4]	⊕⊕⊕⊕ **HIGH**
Low-CHO and high-fat diet	1 (12)	-0.03 (-0.71, 0.65)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Glycemic load	1 (83)	-0.03 (-0.46, 0.40)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Complex CHO	1 (12)	0.03 (-0.65, 0.71)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Fish oil/ DHA and EPA	1 (83)	-0.29 (-0.57, -0.01)	-	could not assess[7]	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Glycemic index	1 (122)	0.10 (0.04, 0.16)	-	not serious	could not assess[1]	serious[5]	serious[2]	could not assess[4]	⊕⊕◯◯ **LOW**
Mediterranean-style diet	1 (259)	-0.08 (-0.30, 0.14)	-	not serious	could not assess[1]	very serious[6]	serious[2]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Unsaturated-to-saturated fat ratio	1 (156)	-0.17 (-2.57, 2.23)	-	not serious	could not assess[1]	very serious[6]	very serious[2, 8]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Triglycerides (mmol/L)									
Low-CHO and high-fat diet	1 (12)	-0.50 (-1.67, 0.67)	-	not serious	could not assess[1]	not serious	serious[2, 9]	could not assess[4]	⊕⊕⊕◯ **MODERATE**

Appendix Table 2.21. CONTINUED. GRADE evidence profile of the effects of diets, foods, and nutrients on blood lipid outcomes in RCTs (energy neutral comparisons).

Dietary factor	*n* of trials (*n* participants)	MD (95% CIs)	I^2	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence
Triglycerides (mmol/L)									
Glycemic load	1 (83)	-0.15 (-0.27, -0.03)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Complex CHO	1 (12)	0.30 (-0.29, 0.89)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Unsaturated fat	1 (84)	-0.50 (-0.89, -0.11)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
MUFA	1 (25)	-0.30 (-1.17, 0.57)	-	could not assess[6]	could not assess[1]	not serious	serious[2, 9]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Glycemic index	1 (122)	0.00 (-0.24, 0.24)	-	not serious	could not assess[1]	serious[5]	serious[2]	could not assess[4]	⊕⊕◯◯ **LOW**
Mediterranean-style diet	1 (259)	-0.10 (-0.49, 0.29)	-	not serious	could not assess[1]	very serious[6]	serious[2]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Apo-B (g/L)									
Low-CHO and high-fat diet	1 (12)	0.03 (-0.16, 0.22)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Complex CHO	1 (12)	-0.03 (-0.22, 0.16)	-	not serious	could not assess[1]	not serious	serious[2]	could not assess[4]	⊕⊕⊕◯ **MODERATE**
Mediterranean-style diet	1 (259)	-0.02 (-0.04, -0.00)	-	not serious	could not assess[1]	very serious[6]	serious[2]	could not assess[4]	⊕◯◯◯ **VERY LOW**
Unsaturated-to-saturated fat ratio	1 (156)	-0.04 (-0.14, 0.06)	-	not serious	could not assess[1]	very serious[6]	serious[2]	could not assess[4]	⊕◯◯◯ **VERY LOW**

Abbreviations: CHO, carbohydrates; CIs, confidence intervals; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; MD, mean difference; MUFA, monounsaturated fatty acids; *n*, number; n-3, omega-3; n-6, omega-6; SSBs, sugar-sweetened beverages.

[1] As there was only one included study, inconsistency could not be assessed.
[2] Optimal information size (OIS) was not met.
[3] The pooled effect estimate crossed MD= 0.0 and MID of MD= ±0.28 mmol/L.

[4] As <10 trials were included, publication bias could not be assessed.

[5] The included trials failed to achieve the intended dietary contrast. The difference in glycemic index between the intervention and comparator arms was 7 units. The difference between diets may be too small to detect any clinically important effect on outcome.

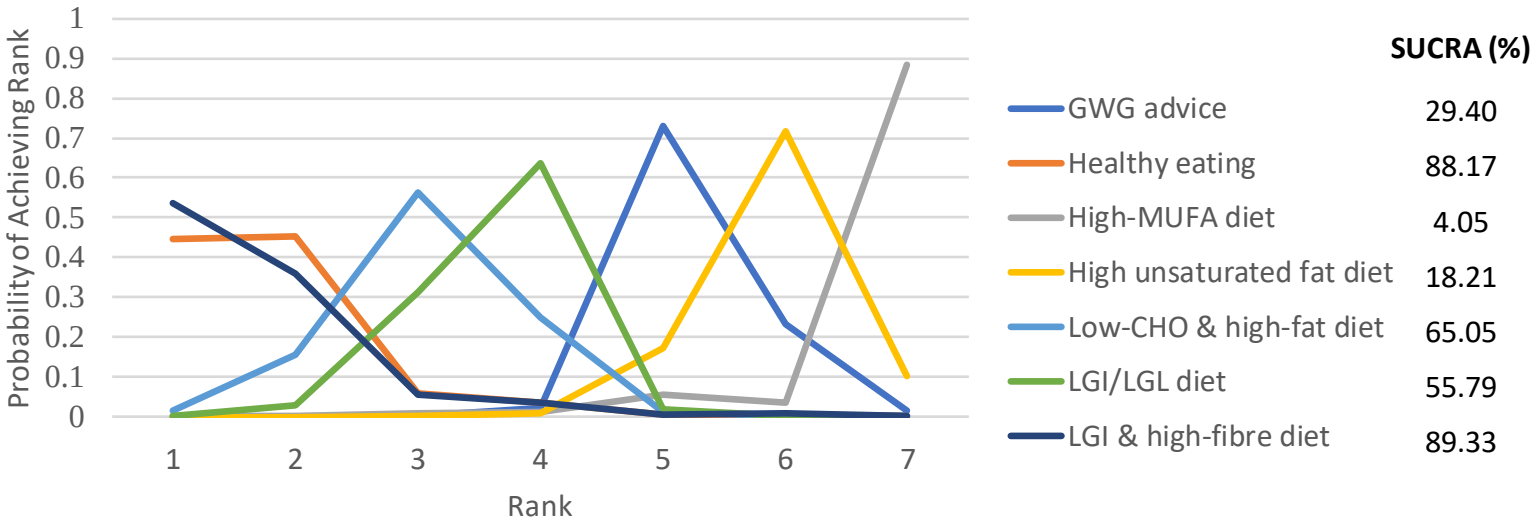
[6] The included trials failed to achieve the intended dietary contrast. The intake of polyunsaturated (PUFA), monounsaturated (MUFA), and saturated (SFA) were similar between the intervention and comparator arms. The difference between diets may be too small to detect any clinically important effect on outcome.

[7] Risk of bias could not be assessed because most of the domains in the Cochrane Risk of Bias Tool was rated as "unclear risk of bias."

[8] The pooled effect estimate crossed MD= 0.0 and MID of MD= ±0.76 mmol/L.

[9] The pooled effect estimate crossed MD= 0.0 and MID of MD= ±0.90 mmol/L.

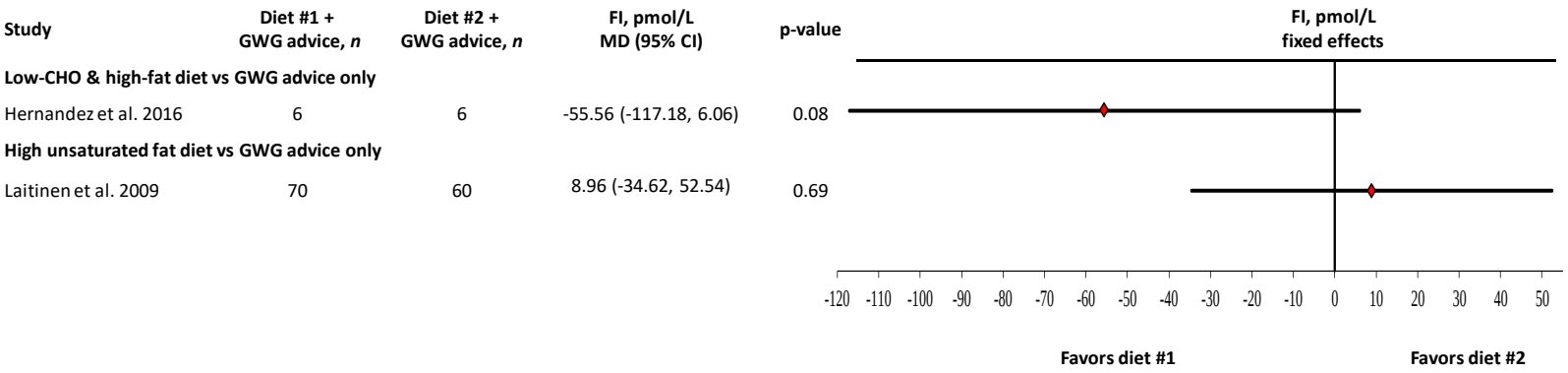
Appendix Figure 3.1. Rank of each diet that were given in addition to GWG advice as being the most effective in reducing fasting glucose.



Abbreviations: CHO, carbohydrate; GWG, gestational weight gain; LGI, low glycemic index; LGL, low glycemic load; MUFA, monounsaturated fatty acids; SUCRA, surface under the cumulative ranking.

The rankogram displays the probability of each diet achieving a particular rank and the SUCRA value reflects the probability of a given diet as being the most effective in reducing fasting glucose among all the diets being compared. The closer SUCRA is to 100, the more certain we are that it is the best overall and the closer it is to zero, the more certain we are that it is worst.

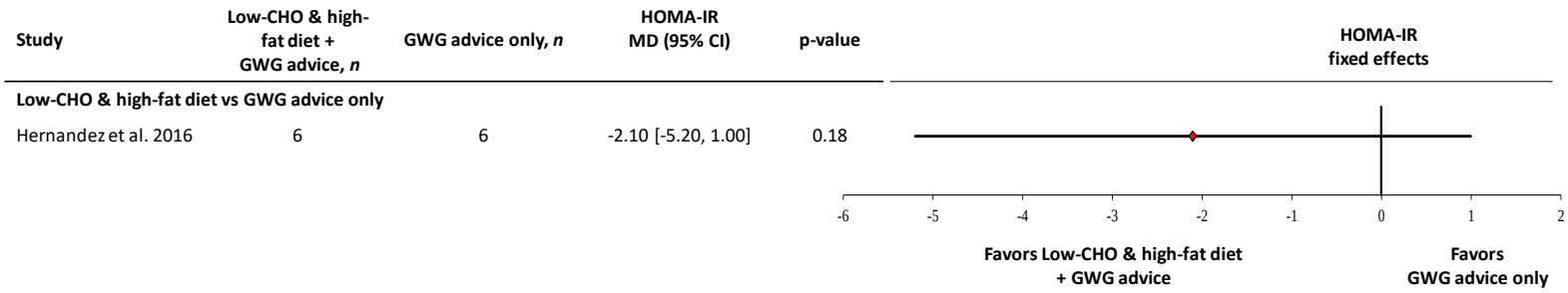
Appendix Figure 3.2. Pair-wise meta-analyses of diets and Hb_{A1c} in trials where GWG advice was provided in both dietary arms.*



Abbreviations: CHO, carbohydrate; CI, confidence interval; GWG, gestational weight gain; HbA1c, hemoglobin A1c; LGI, low glycemic index; MD, mean differences; MUFA, monounsaturated fatty acids; n, sample size.

* Diet # 1 reflects the diet that is first mentioned before “vs” and diet #2 reflects the diet that comes after “vs”.

Appendix Figure 3.3. Pair-wise meta-analyses of diets and fasting insulin in trials where GWG advice was provided in both dietary arms.*

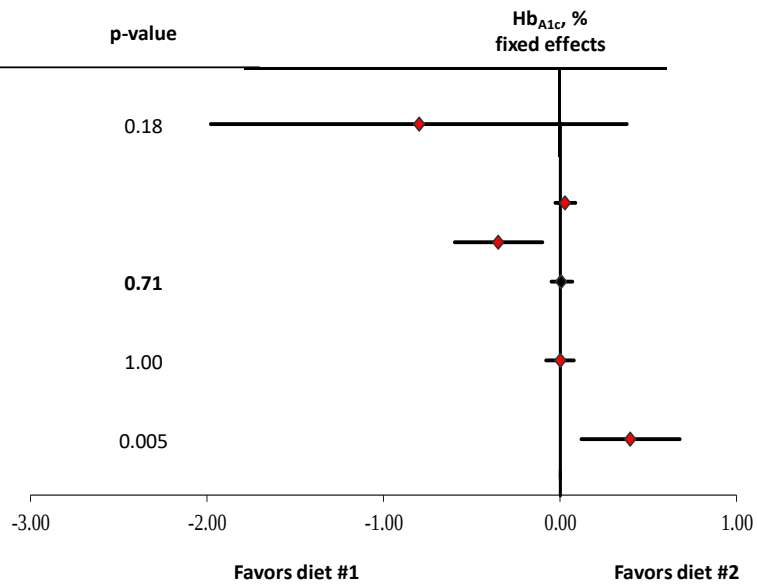


Abbreviations: CHO, carbohydrate; CI, confidence interval; FI, fasting insulin; GWG, gestational weight gain; MD, mean differences; n, sample size.

*Diet # 1 reflects the diet that is first mentioned before “vs” and diet #2 reflects the diet that comes after “vs”.

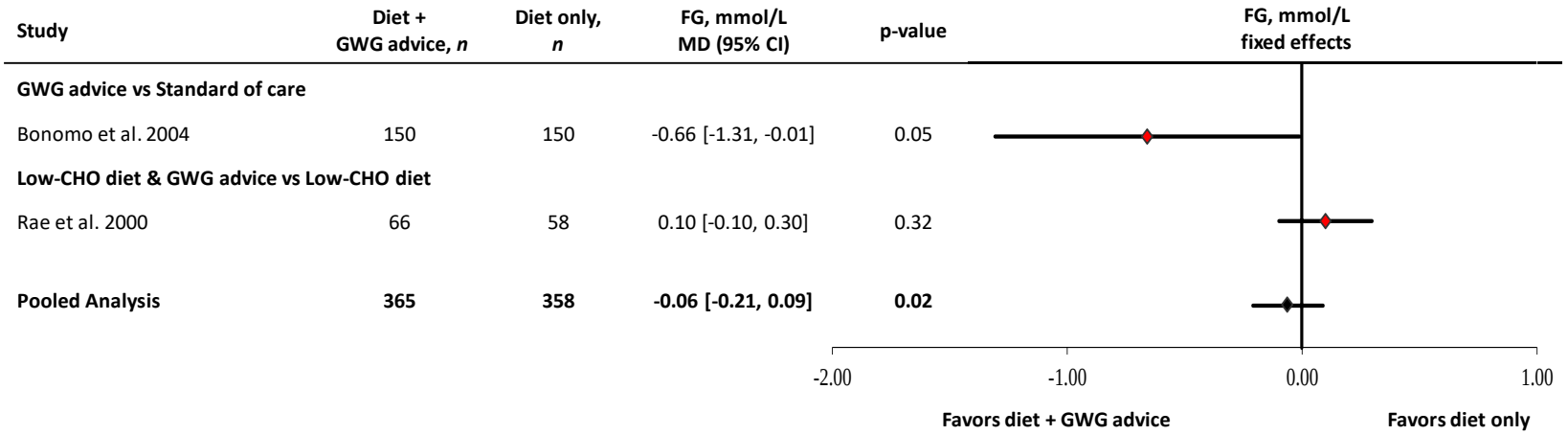
Appendix Figure 3.4. Pair-wise meta-analyses of diets and HOMA-IR in trials where GWG advice was provided in both dietary arms.

Study	Diet #1 + GWG advice, *n*	Diet #2 + GWG advice, *n*	Hb_{A1c}, % MD (95% CI)	p-value
High-fibre & low-fat diet vs low-CHO & high-fat diet				
Ney et al. 1982	11	9	-0.80 [-1.98, 0.38]	0.18
LGI diet vs GWG advice only				
Ma et al. 2011	42	41	0.03 [-0.03, 0.09]	
Valentini et al. 2012	10	10	-0.35 [-0.60, -0.10]	
Pooled Analysis	**52**	**51**	**0.01 [-0.05, 0.07]**	**0.71**
High unsaturated fat diet vs GWG advice only				
Laitinen et al. 2009	70	60	0.00 [-0.08, 0.08]	1.00
High-MUFA diet vs GWG advice only				
Lauszus et al. 2001	12	12	0.40 [0.12, 0.68]	0.005



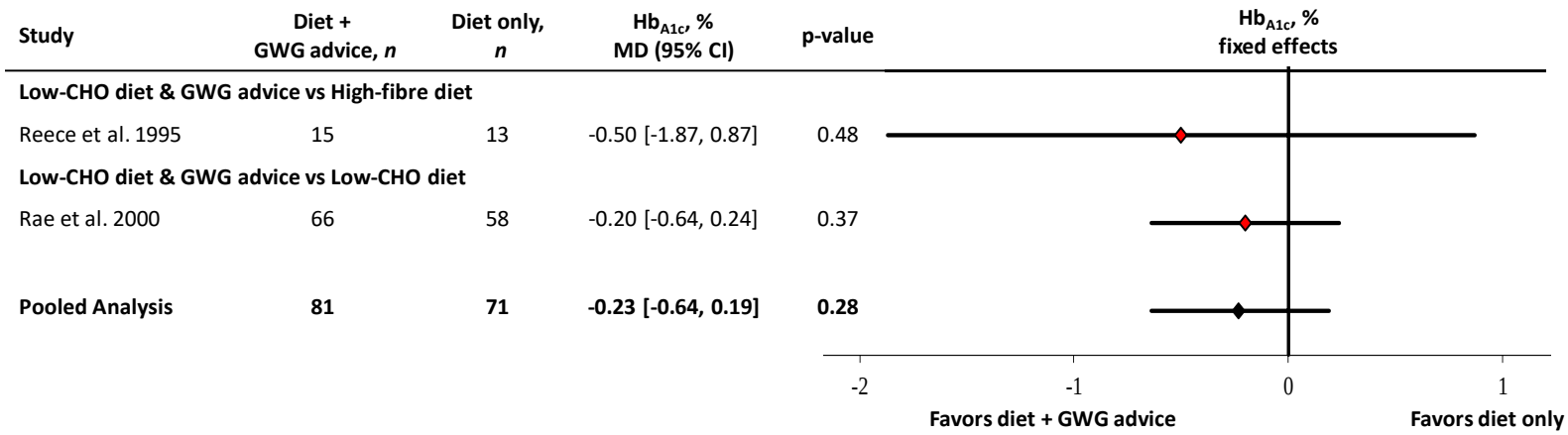
Abbreviations: CHO, carbohydrate; CI, confidence interval; GWG, gestational weight gain; HOMA-IR, homeostatic model assessment for insulin resistance; MD, mean differences; *n*, sample size.

Appendix Figure 3.5. Pair-wise meta-analysis of diets and fasting glucose in trials where GWG advice was provided in one of the dietary arms.



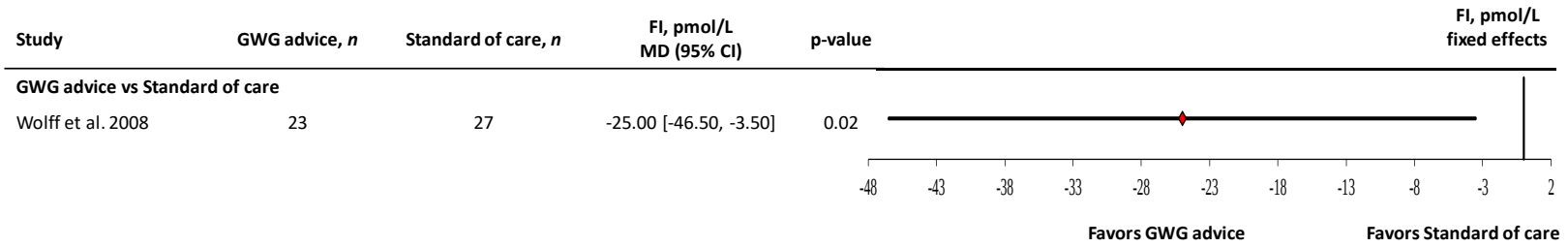
Abbreviations: CHO, carbohydrate; CI, confidence interval; FG, fasting glucose; GWG, gestational weight gain; MD, mean differences; n, sample size.

Appendix Figure 3.6. Pair-wise meta-analysis of diets and Hb_{A1c} in trials where GWG advice was provided in one of the dietary arms.



Abbreviations: CHO, carbohydrate; CI, confidence interval; GWG, gestational weight gain; Hb_{A1c}, hemoglobin A1c; MD, mean differences; *n*, sample size.

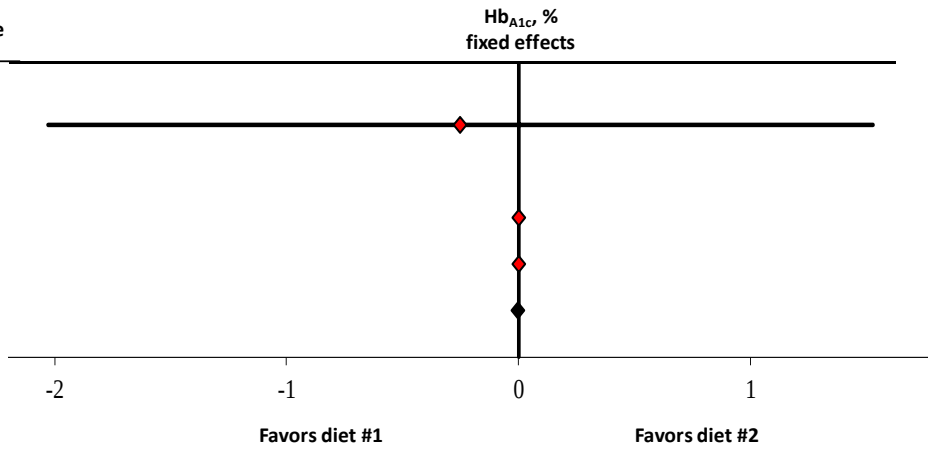
Appendix Figure 3.7. Pair-wise meta-analysis of diets and fasting insulin in trials where GWG advice was provided in one of the dietary arms.



Abbreviations: CHO, carbohydrate; CI, confidence interval; FI, fasting insulin; GWG, gestational weight gain; MD, mean differences; n, sample size.

Appendix Figure 3.8. Pair-wise meta-analysis of diets and Hb_{A1c} in trials with no GWG advice provided.*

Study	Diet #1, *n*	Diet #2, *n*	Hb_{A1c}, % MD (95% CI)	p-value
DASH-style diet vs Standard of care				
Asemi et al. 2013	17	17	-0.25 [-2.03, 1.53]	0.78
LGI diet vs High-fibre diet				
Louie et al. 2011	43	41	0.00 [-0.00, 0.00]	
Markovic et al. 2016	63	58	0.00 [-0.00, 0.00]	
Pooled Analysis	**106**	**99**	**0.00 [-0.00, 0.00]**	**1.00**

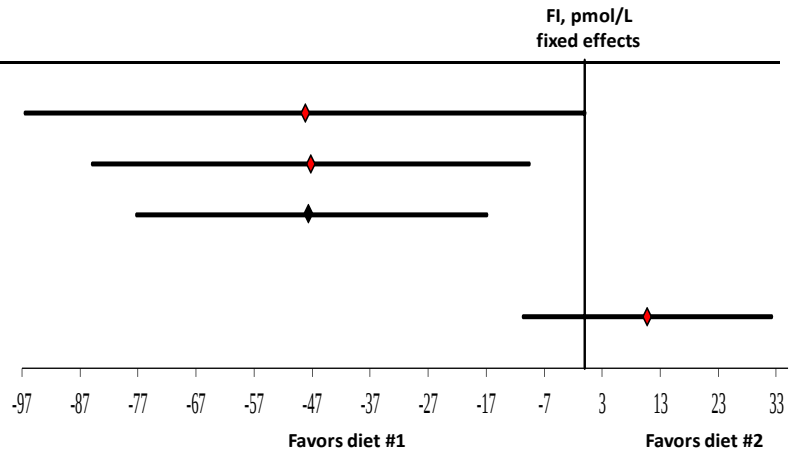


Abbreviations: CI, confidence interval; DASH, Dietary Approach to Stop Hypertension; HbA1c, hemoglobin A1c; LGI, low glycemic index; MD, mean differences; n, sample size.

*Diet # 1 reflects the diet that is first mentioned before “vs” and diet #2 reflects the diet that comes after “vs”.

Appendix Figure 3.9. Pair-wise meta-analysis of diets and fasting insulin in trials with no GWG advice provided.*

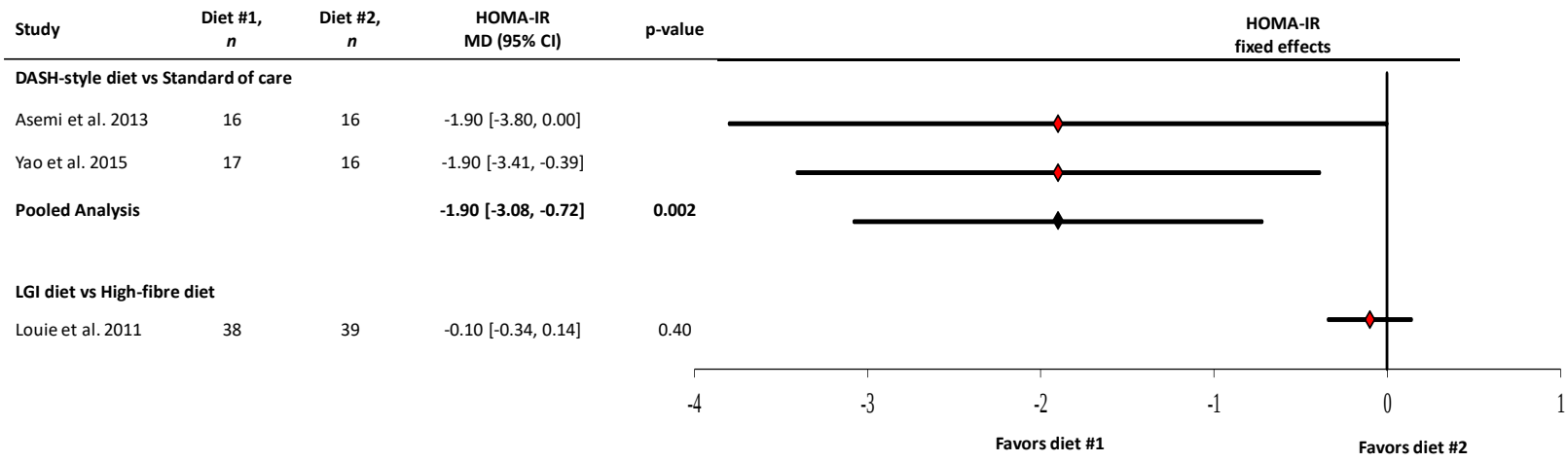
Study	Diet #1, *n*	Diet #2, *n*	FI, pmol/L MD (95% CI)	p-value
DASH-style diet vs Standard of care				
Asemi et al. 2013	16	16	-48.20 [-96.53, 0.13]	
Yao et al. 2015	17	16	-47.23 [-84.96, -9.50]	
Pooled Analysis			**-47.60 [-77.34, -17.86]**	**0.002**
LGI diet vs High-fibre diet				
Louie et al. 2011	40	30	10.80 [-10.66, 32.26]	0.32



Abbreviations: CI, confidence interval; DASH, Dietary Approach to Stop Hypertension; FI, fasting insulin; LGI, low glycemic index; MD, mean differences; n, sample size.

*Diet # 1 reflects the diet that is first mentioned before “vs” and diet #2 reflects the diet that comes after “vs”.

Appendix Figure 3.10. Pair-wise meta-analysis of diets and HOMA-IR in trials with no GWG advice provided.*



Abbreviations: CI, confidence interval; DASH, Dietary Approach to Stop Hypertension; FI, fasting insulin; LGI, low glycemic index; MD, mean differences; *n*, sample size.

*Diet # 1 reflects the diet that is first mentioned before "vs" and diet #2 reflects the diet that comes after "vs".

Appendix Table 3.1. Search strategy used to identify eligible studies.*

DATABASE	SEARCH DATE	SEARCH STRATEGY
Medline	1946 to April week 4 2015	1. pregnant women/ OR pregnan*.tw. OR prenatal care/ OR prenatal.tw. OR maternal.tw. OR expectant mother*.tw. 2. exp diet/ OR exp dietary supplements/ OR exp diet therapy/ OR diet*.tw. OR exp food/ OR exp food habits/ OR exp food quality/ OR food*.tw. OR nutri*.tw. OR nutritional status/ 3. 1 AND 2 4. exp maternal nutritional physiological phenomena/ 5. 3 OR 4 6. exp diabetes, gestational/ OR gestational diabetes.tw. OR glucose tolerance test/ OR glucose tolerance*.tw. OR OGTT OR glycaem*.tw. OR glycem*.tw. 7. 5 AND 6

*Search was conducted in November 2014 and updated in April 2015, February 2016, and April 2017.

Appendix Table 3.2. Table of study characteristics.*†

						Baseline measurements§						
Study	**Participants**	**Age (yrs)**	**Pre-pregnancy BMI (kg/m^2) or body weight (kg)‡**	**Active Smokersδ**	**Ethnicity**	**Gestational Age (wks)¶**	**FG (mmol/L)**	**Hb_{A1c} (%)**	**FI (pmol/L)**	**HOMA-IR**	**Setting**	**Duration of Intervention (wks)**
GWG advice provided in both dietary arms												
Ney et al. 1982												
Low-CHO & high-fat diet	20 T1DM, T2DM	T1DM: 26.6 (4.4) T2DM: 32.2 (6.6)	-	-	African White-Caucasian Hispanic	10-30	-	10.2 (1.8)	-	-	USA	16
High-fiber & low-fat diet			-				-	11.0 (1.7)	-	-		16
Lauszus et al. 2001												
GWG advice only	27	29 (3.7)	-	-	White-Caucasian	34	4.8 (0.7)	5.3 (0.4)	186.1 (30.6)	-	Denmark	7
High-MUFA diet	GDM	31 (3.6)	-				5.2 (1.1)	5.6 (0.7)	184.0 (36.8)	-		7
Laitinen et al. 2009												
GWG advice only	135	30.2 (5.0)	-	-	White-Caucasian	13.9 (1.6)	4.7 (0.3)	5.1 (0.3)	5.2 (3.5)	1.1 (0.9)	Finland	~20
High unsaturated fat diet	Healthy	30.1 (5.2)	-				4.4 (0.4)	5.0 (0.2)	5.1 (4.4)	1.1 (0.8)		~20
Grant et al. 2011												
Healthy eating	38 GDM, IGT	34.0 (5.3)	26.0 (4.8)	-	Carribean White-Caucasian East Asian Hispanic	29.0 (2.4)	5.0 (1.0)	5.4 (0.5)	65 (42.2)	-	Canada	8
LGI diet		34.0 (0.5)	27.0 (4.9)		Southeast Asian Mixed	29.0 (3.4)	4.5 (1.0)	5.3 (0.5)	61 (32.1)	-		8
Ma et al. 2011												
GWG advice only	83	30.0 (3.5)	21.2 (2.8)	-	East Asian	24-30	4.8 (0.6)	-	-	-	China	8
Low GL diet	GDM, IGT	30.1 (3.8)	21.9 (3.1)				5.0 (0.8)	-	-	-		8
Perichart-Perera et al. 2012												
Low-CHO & high-fat diet	107 GDM or pre-gestational T2DM	31.8 (5.3)	32.0 (6.3)	-	-	20.70 (6.7)	5.7 (11.9)	-	-	-	Mexico	~18
Low GI diet		32.3 (4.8)	30.5 (5.2)		-	22.50 (4.9)	5.2 (6.0)	-	-	-		~18
Valentini et al. 2012												
GWG advice only	20 GDM	30.2 (4.7)	24.1 (4.7)	-	African Asian White-Caucasian Southeast Asian	24-28	4.7	5.4	-	-	Italy	~12
Low GI diet		28.9 (3.3)	25.7 (3.6)				5.3	5.3	-	-		~12
Afaghi et al. 2013												
Low GI/low GL diet	31	20-40	-	-	Middle Eastern	24-28	5.9 (1.1)	-	-	-	Iran	~14
Low GI/low GL & high-fibre diet	GDM		-				5.5 (0.9)	-	-	-		~14
Wang et al. 2015												
GWG advice only	84	29.7 (4.6)	22.2 (3.6)	-	Southeast Asian	27.3 (2.0)	4.82 (0.5)	-	-	-	China	~12
High unsaturated fat diet	GDM	30.3 (4.2)	21.4 (3.0)			27.4 (1.5)	4.73 (1.0)	-	-	-		~13
Hernandez et al. 2016 **												
GWG advice only	12	28 (4.9)	-	-	-	31.2 (0.5)	4.51 (0.5)	-	180.6 (56.1)	5.2 (2.0)	USA	~8
Low-CHO & high-fat diet	GDM	30 (2.4)	-			31.7 (2.4)	4.4 (0.3)	-	132.0 (56.1)	3.7 (1.7)		~9
GWG advice provided in one of the dietary arms												
Reece et al. 1995												
High-fibre diet	28 GDM	-	-	-	-	24-29	-	-	-	-	USA	~12
Low-CHO & GWG advice			-				-	-	-	-		~12
Rae et al. 2000												
Low-CHO	124	30.6	38.0 (0.7)	-	-	8-35	-	-	-	-	Australia	~11
Low-CHO & GWG advice only	OW/Ob, GDM	30.2	37.9 (0.7)				-	-	-	-		~11
Bonomo et al. 2004												
Routine care	300	30.7 (5.1)	-	-	White-Caucasian	-	4.8 (0.5)	-	-	-	Italy	≥4
GWG advice only	IGT	31.1 (4.7)	-				4.7 (0.4)	-	-	-		≥4
Wolff et al. 2008												
Routine care	50	30.0 (5.0)	95.6 (12.0)	-	White-Caucasian	16.0 (3.0)	3.8 (0.4)	-	68.0 (35.0)	-	Denmark	~25
GWG advice only	Ob, Non-diabetic	28.0 (4.0)	97.0 (9.0)			15.0 (2.0)	3.9 (0.5)	-	64.0 (27.0)	-		~25
Walsh et al. 2012												
Routine care	759	32.0 (4.2)	-	-	-	12.9 (2.2)	4.5 (0.4)	-	-	-	Ireland	~15
Low GI diet	previous delivered	32.0 (4.2)	-	-		13.0 (2.3)	4.5 (0.4)	-	-	-		~15

Appendix Table 3.2. CONTINUED. Table of study characteristics.*†

						Baseline measurements§						
Study	**Participants**	**Age (yrs)**	**Pre-pregnancy BMI (kg/m^2) or body weight (kg)‡**	**Active Smokersδ**	**Ethnicity**	**Gestational Age (wks)¶**	**FG (mmol/L)**	**Hb_{A1c} (%)**	**FI (pmol/L)**	**HOMA-IR**	**Setting**	**Duration of Intervention (wks)**
GWG advice not provided in both dietary arms												
Cypryk et al. 2007												
Routine care	30	28.7 ± 3.7	-	-	White-Caucasian	29.2 ± 5.4	-	4.24 ± 0.44	-	-	Poland	2
Low-fat diet	GDM		-				-	4.51 ± 0.55	-	-		2
Louie et al. 2011												
High-fibre diet	92 GDM	32.4 (4.5)	24.1 (5.7)	0 (0.0)	Asian	29.7 (3.5)	4.6 (0.7)	5.4 (0.6)	70.5 (34.4)	1.3 (0.6)	Australia	~6
Low-CHO & Low GI diet		34.0 (4.1)	23.9 (4.4)	0 (0.0)	White-Caucasian Others	29.0 (4.0)	4.7 (0.5)	5.4 (0.7)	73.1 (62.4)	1.3 (1.3)		~9
Asemi et al. 2013- BJN												
Routine care	34	29.4 (6.2)	80.0 (15.8)	0 (0.0)	Middle Eastern	-	5.1 (0.8)	4.4 (0.8)	-	-	Iran	4
DASH-style diet	GDM	30.7 (6.7)	73.4 (9.3)	0 (0.0)			5.2 (0.9)	4.4 (0.7)	-	-		4
Asemi et al. 2013- Nutrition												
Routine care	32	29.7 (5.6)	75.6 (8.3)	0 (0.0)	Middle Eastern	-	4.9 (0.6)	-	43.8 (23.1)	1.4 (0.2)	Iran	4
DASH-style diet	GDM	27.7 (5.4)	75.0 (11.2)	0 (0.0)			5.1 (0.6)	-	69.3 (44.4)	2.3 (0.4)		4
Yao et al. 2015												
Routine care	33	28.3 (5.1)	71.5 (7.8)	-	Southeast Asian	25.6 (1.3)	5.40 (0.68)	-	-	-	China	4
DASH-style diet	GDM	30.7 (5.6)	70.7 (6.1)			26.9 (1.4)	5.38 (0.78)	-	-	-		4
Markovic et al. 2016												
High-Fiber Diet	121 High-risk for GDM	34.9 (4.1)	25.2 (5.2)	-	Asian White-Caucasian Others	17.7 (1.7)	-	4.9 (0.3)	-	-	Australia	~22
Low-CHO & Low GI diet		35.7 (4.7)	25.2 (5.2)			17.5 (2.0)	-	4.9 (0.3)	-	-		~22

Abbreviations: "-," not reported; "~," calculated; BMI, body mass index; CHO, carbohydrate; DASH, Dietary Approach to Stop Hypertension; FG, fasting glucose; FI, fasting insulin; GDM, gestational diabetes mellitus; GI, glycemic index; GL, glycemic load; GWG, gestational weight gain; Hb_{A1c}, hemoglobin A1c; HOMA-IR, homeostatic model assessment-insulin resistance; IGT, Impaired Glucose Tolerance; MUFA, monounsaturated fatty acids; Ob, Obese; OW, overweight; T1DM, type 1 Diabetes; T2DM, type 2 diabetes.

* All data expressed as mean ± SD unless otherwise noted.

† Dietary definitions: DASH-style intake, diets rich in fruits, vegetables, whole grains, low-fat dairy products but low in saturated fats, cholesterol, refined grains, sweets, and sodium; GWG advice only, advice given to help women achieve optimal GWG; healthy eating, advice followed general healthy eating guidelines (e.g. Canada's Food Guide); high-fat, >30% of energy came from fat; high-fibre, >30 g/d of dietary fibre; high unsaturated fat, increased in unsaturated fat intake compared to no intervention; low-CHO, <45% energy came from CHO; low-fat, <20% of energy from fat; routine care, no dietary advice given

or macronutrient intake was 45-56% energy from CHO: 10-35% energy from protein: 20-35% energy from fat.

‡ Pre-pregnancy body weight was recorded when BMI was not provided in the original study.

δ The number of active smokers during pregnancy. Counts were reported with the percentage of the total participants as smokers reported in brackets.

¶ The gestational week at which the participants started the dietary intervention.

§ Baseline characteristics were based on the number of randomised participants for Grant et al n=43, Laitenin et al n= 171, Rae et al n= 124, and Valentini et al n= 781.

**All foods were provided.

Appendix Table 3.3. Quality of the evidence in the direct dietary comparisons in the fasting glucose analysis.

Dietary Comparison	No of trials (*n* participants)	FG, mmol/L MeD (95% CrIs)	Risk of Bias	Consistency	Directness	Precision	Publication Bias	Quality of Evidence
GWG advice provided in both dietary arms								
LGI/LGL diet vs Low-CHO & High-fat diet	1 (107)	-0.10 (-0.43, 0.22)	0	0[b]	-2[e]	-1[f]	0[h]	⊕○○○ **VERY LOW**
LGI/LGL diet vs High-fibre & LGI/LGL diet	1 (31)	0.55 (-0.13, 1.24)	-1[a]	0[b]	0	-1[f,g]	0[h]	⊕⊕○○ **LOW**
LGI/LGL diet vs Healthy eating	1 (38)	0.50 (-0.08, 1.08)	0	0[b]	0	-1[f,g]	0[h]	⊕⊕⊕○ **MODERATE**
LGI/LGL diet vs GWG advice only	2 (103)	-0.18 (-0.41, 0.04)	0	0[c]	-2[e]	-1[f]	0[h]	⊕○○○ **VERY LOW**
Low-CHO & High-fat diet vs GWG advice only	1 (12)	-0.60 (-1.00, -0.21)	0	0[b]	0	-1[f,g]	0[h]	⊕⊕⊕○ **MODERATE**
High unsaturated fat diet vs GWG advice only	2 (219)	0.06 (-0.07, 0.19)	0	0[d]	-1[e]	-1[f]	0[h]	⊕⊕○○ **LOW**
High-MUFA diet vs GWG advice only	1 (27)	0.50 (-0.22, 1.20)	0	0[b]	0	-1[f,g]	0[h]	⊕⊕⊕○ **MODERATE**
GWG advice provided in one of the dietary arms								
GWG advice vs Standard of care	1 (300)	-0.66 (-1.31, -0.01)	-1[a]	0[b]	0	-1[f,g]	0[h]	⊕⊕○○ **LOW**
Low-CHO diet & GWG advice vs Low-CHO diet	1 (124)	0.10 (-0.10, 0.30)	0	0[b]	0	-1[f]	0[h]	⊕⊕⊕○ **MODERATE**
GWG advice not provided in any of the dietary arms								
DASH-style diet vs Standard of dare	3 (99)	-0.47 (-0.73, -0.21)	0	0	0	-1[f,g]	0[h]	⊕⊕⊕○ **MODERATE**
Low-fat diet vs Standard of care	1 (30)	0.27 (-0.002, 0.55)	0	0[b]	0	-1[f,g]	0[h]	⊕⊕⊕○ **MODERATE**
LGI diet vs High-fibre diet	1 (92)	-0.10 (-0.38, 0.18)	0	0[b]	-2[e]	-1[f]	0[h]	⊕○○○ **VERY LOW**

Abbreviations: CHO, carbohydrate; CrI, credible intervals; DASH, Dietary Approach to Stop Hypertension; FG, fasting glucose; GWG, gestational weight gain; LGI, low glycemic index; LGL, low glycemic load; MeD, median difference; MUFA,

monounsaturated fatty acids; *n*, sample size.

[a]Dietary comparison was downgraded because the attrition rate of the included trial was considered to have high risk of bias.
[b]Inconsistency could not be assessed because only one trial was included.
[c]Although there was evidence of moderate inter-study heterogeneity (I^2= 44.6%), this was not a cause of concern because the credible intervals of the two included trials substantially overlapped one another and their point estimate laid on the same side of the line of no effect.
[d]No evidence of inter-study heterogeneity (I^2= 0%).
[e]The included trial(s) failed to achieve its dietary goals and therefore, the contrast of the dietary interventions may be too small to affect FG.
[f]Optimal information size (OIS) was not met.
[g]The effect estimate crosses the minimally important difference (MID) of ±0.5 mmol/L.
[h]Publication bias could not be assessed because there were <10 included trials.

Appendix Table 3.4. Quality of the evidence in the indirect dietary comparisons in the fasting glucose analysis.

Dietary Comparison	FG, mmol/L MeD (95% CrIs)	Quality of First-Order Link	Similarity	Overall Quality of Evidence
GWG advice provided in both dietary arms				
High unsaturated fat diet vs LGI/LGL diet	0.33 (0.08, 0.57)	Very Low	0[a]	⊕◯◯◯ **VERY LOW**
High unsaturated fat diet vs High-MUFA diet	-0.44 (-1.15, 0.29)	Low	-1[b]	⊕◯◯◯ **VERY LOW**
High unsaturated fat diet vs High-fibre & LGI/LGL diet	0.88 (0.16, 1.60)	-[c]	-	⊕◯◯◯ **VERY LOW**
High unsaturated fat diet vs Low-CHO & high-fat diet	0.41 (0.10, 0.71)	Low	-1[a]	⊕◯◯◯ **VERY LOW**
High unsaturated fat diet vs Healthy eating	0.83 (0.20, 1.46)	-[c]	-	⊕◯◯◯ **VERY LOW**
LGI/LGL diet vs High-MUFA diet	-0.77 (-1.49, -0.02)	Very Low	-1[d]	⊕◯◯◯ **VERY LOW**
LGI/LGL diet vs Low-CHO & high-fat diet	0.42 (-0.03, 0.86)	Very Low	-1[e]	⊕◯◯◯ **VERY LOW**
LGI/LGL diet vs GWG advice only	-0.71 (-1.20, -0.20)	Very Low	-1[e]	⊕◯◯◯ **VERY LOW**
High-MUFA diet vs High-fibre & LGI/LGL diet	1.32 (0.32, 2.33)	-[c]	-	⊕◯◯◯ **VERY LOW**
High-MUFA diet vs Low-CHO & high-fat diet	0.85 (0.08, 1.60)	Moderate	0	⊕⊕⊕◯ **MODERATE**
High-MUFA diet vs Healthy eating	1.27 (0.33, 2.20)	-[c]	-	⊕◯◯◯ **VERY LOW**
High-fibre & LGI/LGL diet vs Low-CHO & high-fat diet	-0.47 (-1.20, 0.25)	Very Low	0	⊕◯◯◯ **VERY LOW**
High-fibre & LGI/LGL diet vs Healthy eating	-0.05 (-0.95, 0.85)	Low	0	⊕⊕◯◯ **LOW**
High-fibre & LGI/LGL diet vs GWG advice only	-0.82 (-1.53, -0.11)	Very Low	-1[f]	⊕◯◯◯ **VERY LOW**
Low-CHO & high-fat diet vs Healthy eating	0.42 (-0.21, 1.06)	Very Low	0	⊕◯◯◯ **VERY LOW**
Low-CHO & high-fat diet vs GWG advice only	-0.08 (-0.48, 0.32)	Very Low	-1[g]	⊕◯◯◯ **VERY LOW**
Healthy eating vs GWG advice only	-0.77 (-1.38, -0.16)	Very Low	0	⊕◯◯◯ **VERY LOW**
GWG advice not provided in any of the dietary arms				
DASH-style diet vs Low-fat diet	-0.74 (-1.12, -0.36)	Moderate	0	⊕⊕⊕◯ **MODERATE**

Abbreviations: CHO, carbohydrate; CrI, credible intervals; DASH, Dietary Approach to Stop Hypertension; FG, fasting glucose; GWG, gestational weight gain; LGI, low glycemic index; LGL, low glycemic load; MeD, median difference; MUFA, monounsaturated fatty acids.

[a]There were important differences in GDM status and at the trimester in which the dietary interventions began between the two first order links.

[b]There were important differences in GDM status, ethnicity, and at the trimester in which the dietary interventions began between the two first order links.

[c]Quality of comparisons was assumed as very low because the link order is ≥2.

[d]There were important differences in ethnicity and at the trimester in which the dietary interventions began between the two first order links.

[e]There were important differences at the trimester in which the dietary interventions began between the two first order links.

[f]There were important differences in ethnicity between the two first order links.

[g]There were important differences in pre-pregnancy BMI and at the trimester in which the dietary interventions began between the two first order links.

Appendix Table 3.5. Quality of evidence in the mixed dietary comparisons in the fasting glucose analysis.

	Direct Comparisons		Indirect Comparisons		Overall Network	
Dietary Comparison	**FG, mmol/L MeD (95% CrIs)**	**Quality of Evidence**	**FG, mmol/L MeD (95% CrIs)**	**Quality of Evidence**	**FG, mmol/L MeD (95% CrIs)**	**Quality of Evidence**
GWG advice provided in both dietary arms						
Low-CHO & high-fat diet vs GWG advice only	-0.60 (-1.00, -0.21)	⊕⊕⊕◯ **MODERATE**	-0.08 (-0.48, 0.32)	⊕◯◯◯ **VERY LOW**	-0.35 (-0.63, -0.07)	⊕⊕⊕◯ **MODERATE**
LGI/LGL diet vs GWG advice only	-0.18 (-0.41, 0.04)	⊕◯◯◯ **VERY LOW**	-0.71 (-1.20, -0.20)	⊕◯◯◯ **VERY LOW**	-0.27 (-0.47, -0.06)	⊕◯◯◯ **VERY LOW**
LGI/LGL diet vs Low-CHO & high-fat diet	-0.10 (-0.43, 0.22)	⊕◯◯◯ **VERY LOW**	0.42 (-0.03, 0.86)	⊕◯◯◯ **VERY LOW**	0.08 (-0.18, 0.34)	⊕◯◯◯ **VERY LOW**

Abbreviations: CHO, carbohydrate; CrI, credible intervals; FG, fasting glucose; GWG, gestational weight gain; LGI, low glycemic index; LGL, low glycemic load; MeD, median difference.

Appendix Table 3.6. Quality of the evidence in the direct dietary comparisons in the Hb_{A1c} analysis.

Dietary Comparison	No of trials (*n* participants)	Hb_{A1c} (%) MD (95% CIs)	Risk of Bias	Consistency	Directness	Precision	Publication Bias	Quality of Evidence
GWG advice provided in both dietary arms								
High-fibre & low-fat diet vs Low-CHO & high-fat diet	1 (20)	-0.80 (-1.98, 0.38)	0	0[a]	0	-2[d,e]	0[f]	⊕⊕◯◯ **LOW**
LGI/LGL diet vs GWG advice only	2 (103)	0.01 (-0.05, 0.07)	0	-1[b]	-2[c]	-1[e]	0[f]	⊕◯◯◯ **VERY LOW**
High unsaturated fat diet vs GWG advice only	1 (135)	0.00 (-0.08, 0.08)	0	0[a]	-2[c]	-1[e]	0[f]	⊕◯◯◯ **VERY LOW**
High-MUFA diet vs GWG advice only	1 (27)	0.40 (0.12, 0.68)	0	0[a]	0	-1[d,e]	0[f]	⊕⊕⊕◯ **MODERATE**
GWG advice provided in one of the dietary arms								
Low-CHO diet & GWG advice vs High-fibre diet	1 (28)	-0.50 (-1.87, 0.87)	0	0[a]	0	-2[d,e]	0[f]	⊕⊕◯◯ **LOW**
Low-CHO diet & GWG advice vs Low-CHO diet	1 (124)	-0.20 (-0.64, 0.24)	0	0[a]	-2[c]	-1[d,e]	0[f]	⊕◯◯◯ **VERY LOW**
GWG advice not provided in any of the dietary arms								
DASH-style diet vs Standard of care	1 (34)	-0.25 (-2.03, 1.53)	0	0[a]	0	-2[d,e]	0[f]	⊕⊕◯◯ **LOW**
LGI diet vs High-fibre diet	2 (213)	0.00 (-0.00, 0.00)	0	0[g]	-2[c]	-1[e]	0[f]	⊕◯◯◯ **VERY LOW**

Abbreviations: CHO, carbohydrate; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; GWG, gestational weight gain; Hb_{A1c}, hemoglobin A1c; LGI, low glycemic index; LGL, low glycemic load; MD, mean difference; MUFA, monounsaturated fatty acids; *n*, sample size.

[a]Inconsistency could not be assessed because only one trial was included.

[b]There was evidence of high inter-study heterogeneity (I^2= 88%). Further the two included trials showed different effects, one showed protection and the other showed null.

[c]The included trial(s) failed to achieve its dietary goals and therefore, the contrast of the dietary interventions may be too small to affect Hb_{A1c}.
[d]The effect estimate crosses the minimally important difference (MID) of ±0.3%.
[e]Optimal information size (OIS) was not met.
[f]Publication bias could not be assessed because there were <10 included trials.
[g]No evidence of inter-study heterogeneity (I^2= 0%).

Appendix Table 3.7. Quality of the evidence in the direct dietary comparisons in the fasting insulin analysis.

Dietary Comparison	No of trials (*n* participants)	FI, pmol/L MD (95% CIs)	Risk of Bias	Consistency	Directness	Precision	Publication Bias	Quality of Evidence
GWG advice provided in both dietary arms								
Low-CHO & high-fat diet vs GWG advice only	1 (12)	-55.56 (-117.18, 6.06)	0	0[b]	0	-2[e,f]	0[g]	⊕⊕○○ **LOW**
High-MUFA diet vs GWG advice only	1 (27)	8.96 (-34.62, 52.54)	0	0[b]	0	-2[e,f]	0[g]	⊕⊕○○ **LOW**
GWG advice provided in one of the dietary arms								
GWG advice only vs Standard of care	1 (50)	-25.00 (-46.50, -3.50)	0[a]	0[b]	0	-1[f]	0[g]	⊕⊕⊕○ **MODERATE**
GWG advice not provided in any of the dietary arms								
DASH-style diet vs Standard of care	2 (65)	-47.60 (-77.34, -17.86)	0	0[c]	0	-1[f]	0[g]	⊕⊕⊕○ **MODERATE**
LGI diet vs High-fibre diet	1 (92)	10.80 (-10.66, 32.26)	0	0[b]	-2[d]	-2[e,f]	0[g]	⊕○○○ **VERY LOW**

Abbreviations: CHO, carbohydrate; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; FI, fasting insulin; GWG, gestational weight gain; LGI, low glycemic index; MD, mean difference; MUFA, monounsaturated fatty acids; *n*, sample size.

[a]Dietary comparison was downgraded because the attrition rate of the included trial was considered to have high risk of bias.
[b]Inconsistency could not be assessed because only one trial was included.
[c]No evidence of inter-study heterogeneity (I^2= 0%).
[d]The included trial(s) failed to achieve its dietary goals and therefore, the contrast of the dietary interventions may be too small to affect FI.
[e]The effect estimate crosses the minimally important difference (MID) of ±0.5 pmol/L.
[f]Optimal information size (OIS) was not met.
[g]Publication bias could not be assessed because there were <10 included trials.

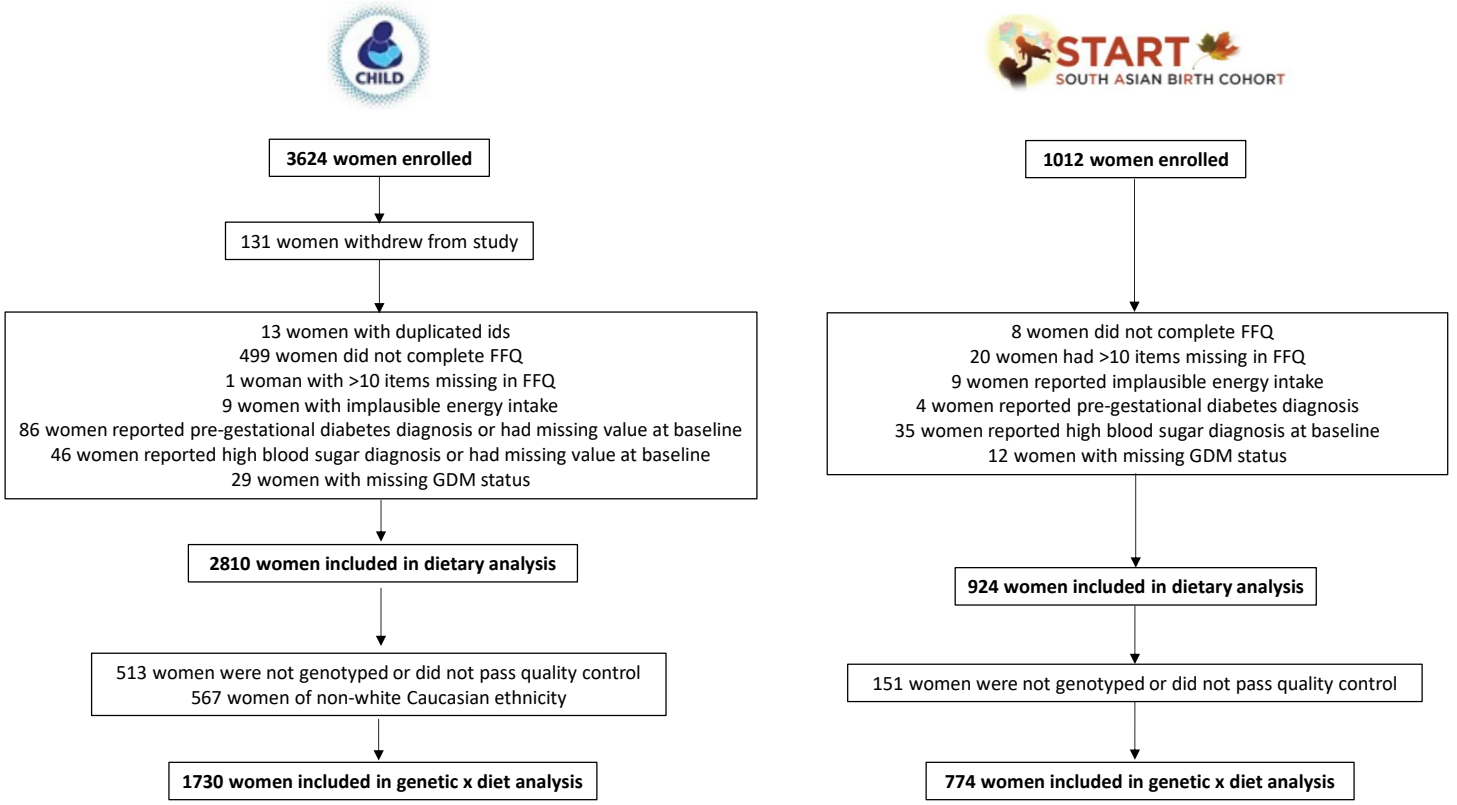
Appendix Table 3.8. Quality of the evidence in the direct dietary comparisons in the HOMA-IR analysis.

Dietary Comparison	No of trials (*n* participants)	HOMA-IR MD (95% CIs)	Risk of Bias	Consistency	Directness	Precision	Publication Bias	Quality of Evidence
GWG advice provided in both dietary arms								
Low-CHO & high-fat diet vs GWG advice only	1 (12)	-2.10 (-5.20, 1.00)	0	0[a]	0	-2[b,c]	0[d]	⊕⊕◯◯ **LOW**
GWG advice not provided in any of the dietary arms								
DASH-style diet vs Standard of care	2 (65)	-1.90 (-3.08, -0.72)	0	0[e]	0	-1[b,c]	0[d]	⊕⊕⊕◯ **MODERATE**
LGI diet vs High-fibre diet	1 (92)	-0.10 (-0.34, 0.14)	0	0[a]	-2[f]	-1[c]	0[d]	⊕◯◯◯ **VERY LOW**

Abbreviations: CHO, carbohydrate; CIs, confidence intervals; DASH, Dietary Approach to Stop Hypertension; GWG, gestational weight gain; HOMA-IR, homeostatic model assessment for insulin resistance; LGI, low glycemic index; MD, mean difference; *n*, sample size.

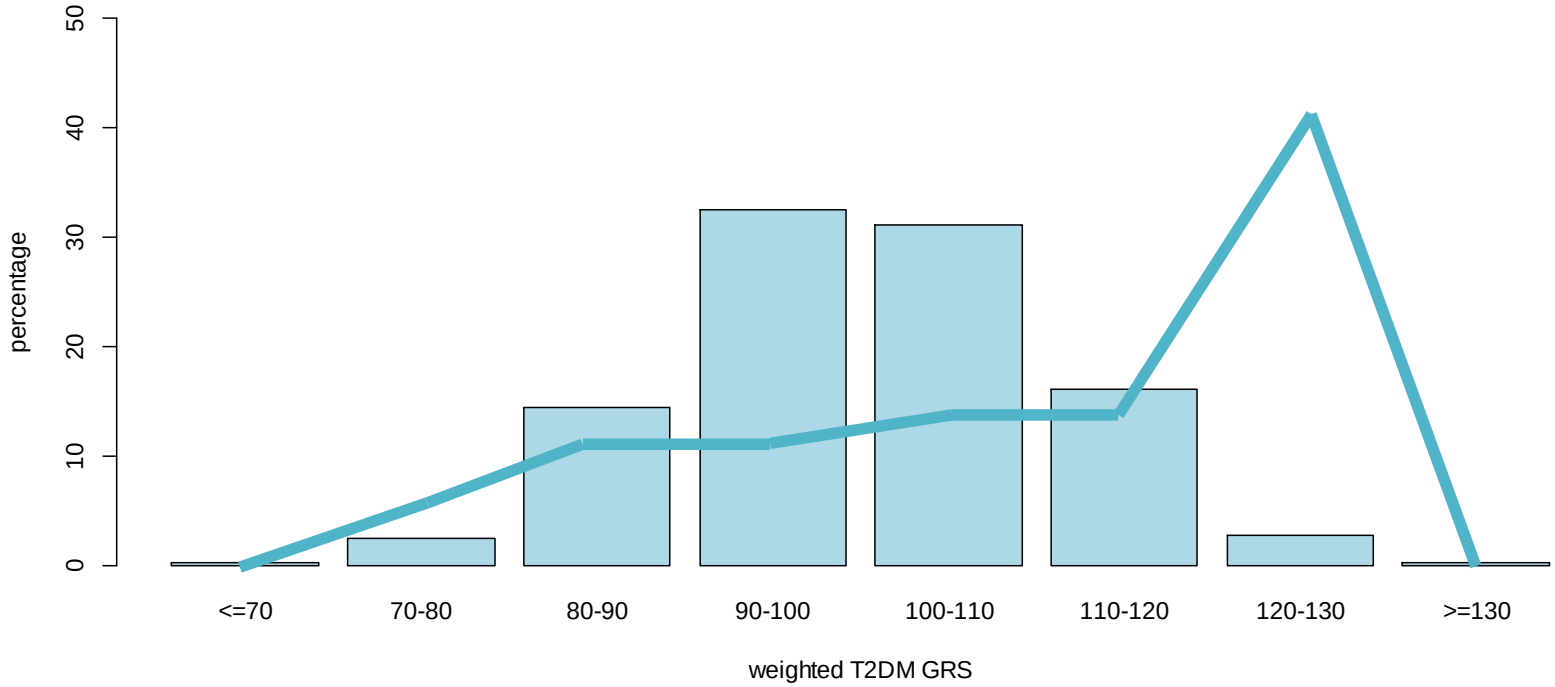
[a]Inconsistency could not be assessed because only one trial was included.
[b]The effect estimate crosses the minimally important difference (MID) of ±1 unit.
[c]Optimal information size (OIS) was not met.
[d]Publication bias could not be assessed because there were <10 included trials.
[e]No evidence of inter-study heterogeneity (I^2= 0%).
[f]The included trial failed to achieve its dietary goals and therefore, the contrast of the dietary interventions may be too small to affect HOMA-IR.

Appendix Figure 4.1. Flow diagram of participants in CHILD and START.



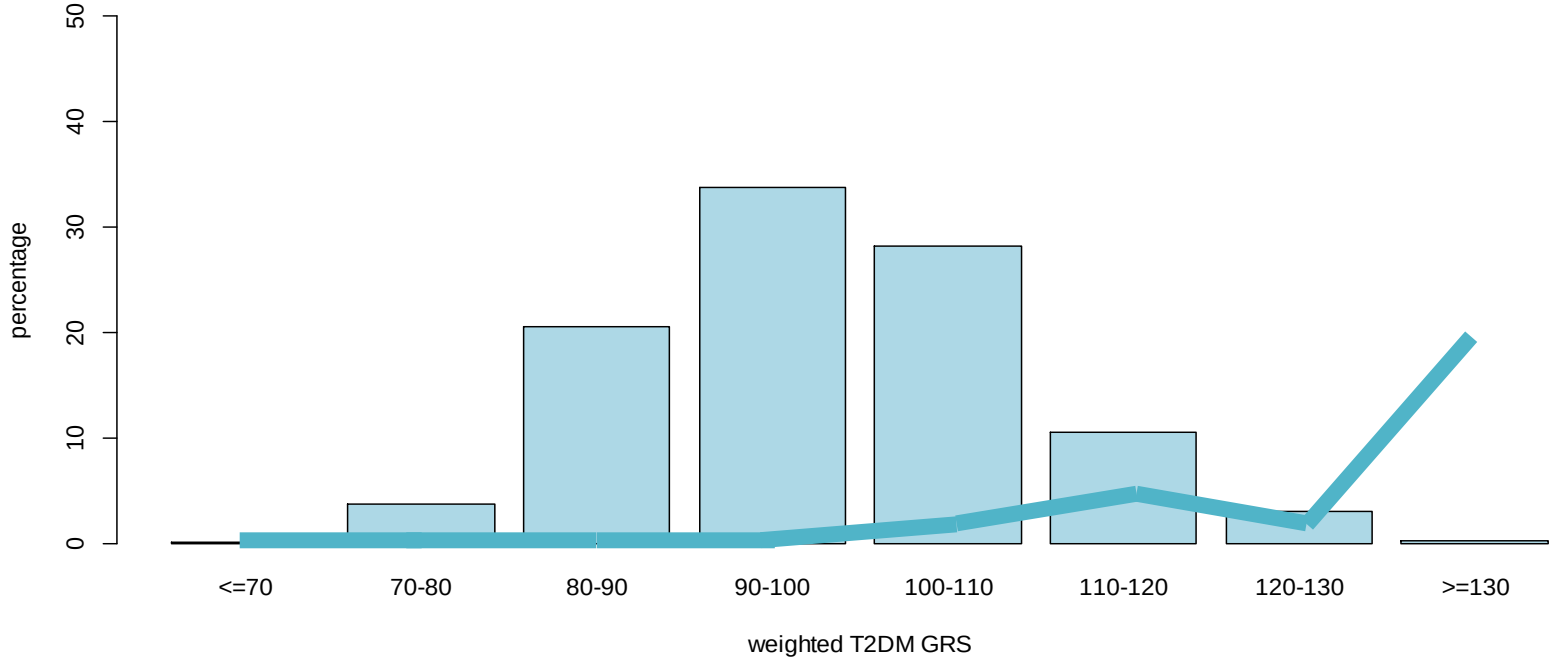
Abbreviations: FFQ, food frequency questionnaire; GDM, gestational diabetes mellitus.

Appendix Figure 4.2. Genetic risk score and GDM cases in the START study.



N, total	2	19	112	252	241	125	21	2
GDM cases	0	1	14	31	34	18	9	0
% GDM cases	0	5.26	12.50	12.30	14.11	14.40	42.86	0

Appendix Figure 4.3. Genetic risk score and GDM cases in the CHILD study.



N, total	1	63	356	583	488	181	53	5
GDM cases	0	0	5	11	14	12	1	1
% GDM cases	0	0	1.40	1.89	2.87	6.63	1.89	20.00

Appendix Table 4.1. Characteristics of 102 SNPs associated with T2DM that were used to build GDM-GRS.

SNP name	Chromosome	Associated gene*	Risk Allele	Beta	CHILD-EAF	START-EAF
rs10193447	2	MIR4432HG	T	0.071	0.62	0.83
rs6757251	2	THADA	C	0.130	0.89	0.86
rs6903744	2	CDKAL1	A	0.170	0.14	0.17
rs80323638	2	THADA	G	0.130	0.91	0.96
rs968919	2	MIR4432HG	C	0.069	0.57	0.54
exm-rs11708067	3	ADCY5	A	0.110	0.79	0.75
exm-rs4402960	3	IGF2BP2	T	0.140	0.30	0.43
rs10513800	3	IGF2BP2	A	0.090	0.20	0.31
rs11712037	3	PPARG	C	0.130	0.87	0.88
rs35352848	3	UBE2E2	T	0.083	0.80	0.76
rs71304093	3	GSTM5P1	C	0.160	0.94	0.95
rs7428936	3	ADAMTS9-AS2	T	0.070	0.59	0.27
rs77494444	3	IGF2BP2	T	0.180	0.05	0.07
rs1046319	4	WFS1	T	0.094	0.72	0.82
rs3821943	4	WFS1	T	0.100	0.56	0.56
rs4689403	4	PPP2R2C	C	0.075	0.64	0.78
rs9986109	4	LOC107986257	A	0.076	0.39	0.42
rs28650790	5	C5orf67	T	0.100	0.19	0.15
rs1012626	6	CDKAL1	T	0.098	0.39	0.47
rs1012635	6	CDKAL1	A	0.095	0.54	0.56
rs11753041	6	CDKAL1	C	0.072	0.39	0.52
rs11759026	6	CENPW	G	0.091	0.26	0.34
rs13199286	6	CDKAL1	T	0.110	0.12	0.07
rs2206579	6	CDKAL1	A	0.073	0.69	0.74
rs4710946	6	CDKAL1	T	0.075	0.51	0.66
rs4712538	6	CDKAL1	A	0.077	0.67	0.75
rs4897178	6	CENPW	G	0.074	0.47	0.66
rs72830693	6	CDKAL1	G	0.290	0.03	0.05
rs72832325	6	CDKAL1	T	0.130	0.08	0.12
rs7451008	6	CDKAL1	C	0.170	0.27	0.26
rs9350294	6	CDKAL1	C	0.072	0.64	0.57
rs9465837	6	CDKAL1	G	0.100	0.16	0.18
exm-rs1635852	7	JAZF1	T	0.092	0.50	0.69
rs2215383	7	GTF3AP5	C	0.069	0.56	0.61
rs849327	7	JAZF1-AS1	A	0.079	0.37	0.58
exm-rs3802177	8	SLC30A8	G	0.110	0.70	0.73
rs2466295	8	SLC30A8	C	0.080	0.37	0.38
rs4350011	8	LOC105375716	G	0.092	0.57	0.71
rs62530366	8	HSF1	G	0.076	0.37	0.31

Appendix Table 4.1. CONTINUED. Characteristics of 102 SNPs associated with T2DM that were used to build GDM-GRS.

SNP name	Chromosome	Associated gene*	Risk Allele	Beta	CHILD-EAF	START-EAF
rs997313	8	LOC105375716	A	0.077	0.53	0.75
exm-rs10965250	9	CDKN2B-AS1	G	0.140	0.82	0.89
rs10965243	9	CDKN2B-AS1	A	0.160	0.90	0.91
rs1101329	9	CDKN2B-AS1	C	0.078	0.59	0.71
rs12555274	9	CDKN2B-AS1	C	0.120	0.29	0.34
rs12660618	9	CDKAL1	T	0.170	0.17	0.21
rs1333045	9	CDKN2B-AS1	C	0.071	0.52	0.52
rs78432974	9	CDKN2B-AS1	C	0.200	0.96	0.98
rs9410573	9	LOC101927502	T	0.073	0.59	0.54
exm-rs703965	10	ZMIZ1	T	0.069	0.44	0.36
exm-rs7903146	10	TCF7L2	T	0.290	0.29	0.29
rs10786048	10	IDE	C	0.099	0.59	0.50
rs10882063	10	IDE	G	0.077	0.61	0.31
rs10882064	10	IDE	T	0.110	0.76	0.55
rs10882098	10	HHEX	C	0.130	0.59	0.49
rs11187031	10	IDE	G	0.080	0.26	0.14
rs11187133	10	HHEX	G	0.130	0.75	0.59
rs11187146	10	HHEX	G	0.120	0.84	0.66
rs11196182	10	TCF7L2	C	0.150	0.86	0.88
rs11196187	10	TCF7L2	A	0.220	0.06	0.05
rs11196200	10	TCF7L2	G	0.170	0.46	0.41
rs11196213	10	TCF7L2	T	0.088	0.42	0.41
rs11257659	10	CDC123	T	0.081	0.21	0.26
rs12243578	10	TCF7L2	T	0.180	0.26	0.25
rs12259231	10	TCF7L2	C	0.100	0.79	0.90
rs17746916	10	VTI1A	T	0.150	0.06	0.03
rs2292626	10	PLEKHA1	C	0.085	0.52	0.46
rs2488073	10	HHEX	G	0.087	0.46	0.30
rs35519679	10	TCF7L2	A	0.220	0.25	0.25
rs3796398	10	PPP2R2C	C	0.080	0.50	0.56
rs61862778	10	HHEX	T	0.099	0.47	0.30
rs61872780	10	TCF7L2	A	0.370	0.01	0.01
rs61872787	10	TCF7L2	G	0.360	0.01	0.01
rs61872790	10	TCF7L2	G	0.230	0.14	0.19
rs7069881	10	TCF7L2	C	0.076	0.66	0.81
rs7079711	10	TCF7L2	G	0.170	0.85	0.89
rs7080591	10	TCF7L2	T	0.100	0.60	0.62

Appendix Table 4.1. CONTINUED. Characteristics of 102 SNPs associated with T2DM that were used to build GDM-GRS.

SNP name	Chromosome	Associated gene*	Risk Allele	Beta	CHILD-EAF	START-EAF
rs7080960	10	PLEKHA1	T	0.067	0.49	0.32
rs720784	10	TCF7L2	T	0.120	0.39	0.42
rs720785	10	TCF7L2	C	0.140	0.26	0.35
rs7901275	10	TCF7L2	C	0.120	0.45	0.52
rs810517	10	ZMIZ1	C	0.089	0.53	0.55
exm893274	11	KCNJ11	T	0.068	0.37	0.38
exm-rs2237895	11	KCNQ1	C	0.097	0.42	0.42
exm-rs2237897	11	KCNQ1	C	0.220	0.96	0.98
rs1061810	11	HSD17B12	A	0.080	0.29	0.28
rs1783598	11	FCHSD2	T	0.084	0.79	0.78
rs2283228	11	KCNQ1	A	0.150	0.94	0.96
rs233449	11	KCNQ1	G	0.089	0.71	0.77
rs76550717	11	ARAP1	A	0.096	0.84	0.83
rs4238013	12	CCND2-AS1	C	0.099	0.22	0.17
rs56348580	12	HNF1A	G	0.073	0.68	0.88
rs66947454	12	CLIC1P1	T	0.081	0.80	0.94
rs11616380	13	LOC105370275	G	0.090	0.72	0.83
rs4774420	15	VPS13C	C	0.075	0.71	0.74
rs952471	15	HMG20A	G	0.082	0.70	0.55
exm-rs1558902	16	FTO	A	0.130	0.40	0.31
exm-rs2925979	16	CMIP	T	0.074	0.29	0.28
rs1861867	16	FTO	G	0.097	0.62	0.68
rs8056223	16	CTRB2	T	0.180	0.93	0.95
rs8056814	16	CTRB1	G	0.150	0.91	0.94
rs757209	17	HNF1B	G	0.083	0.56	0.60
rs429358	19	APOE	T	0.120	0.86	0.90

Abbreviations: CHILD, Canadian Healthy Infant Longitudinal Development; EAF, estimated allele frequent of the affect allele; GDM, gestational diabetes mellitus; GRS, genetic risk score; SNPs, single nucleotide polymorphism; START, South Asian Birth Cohort; T2DM, type 2 diabetes mellitus.

*Associated genes could be genes that SNPs are found within OR closest to within <250kb base-pair.

Appendix Table 4.2. Characteristics of 77 SNPs associated with fasting glucose that were used to build FG-GRS.

SNP name	Chromosome	Associated gene*	Risk Allele	Beta	START-EAF
exm181733	2	GCKR	C	0.029	0.33
exm239600	2	NOSTRIN, SPC25	G	0.019	0.41
exm-rs560887	2	G6PC2	C	0.071	0.38
rs10497345	2	SPC25	C	0.044	0.43
rs1371614	2	DPYSL5	T	0.016	0.35
rs16856252	2	ABCB11	C	0.037	0.39
rs17540154	2	ABCB11	G	0.056	0.39
rs2068834	2	ZNF512	T	0.021	0.11
rs2178198	2	SLC4A1AP	C	0.02	0.44
rs2305929	2	BRE-AS1/BRE, RBKS	A	0.018	0.07
rs2390732	2	CERS6	A	0.015	0.19
rs3736594	2	MRPL33	A	0.017	0.32
rs3821116	2	SPC25	G	0.013	0.31
rs4665965	2	MPV17	C	0.015	0.28
rs472614	2	ABCB11	G	0.041	0.29
rs477224	2	-	C	0.036	0.09
rs780092	2	GCKR	G	0.017	0.11
rs780110	2	IFT172	A	0.019	0.24
rs937813	2	BRE	T	0.021	0.39
exm-rs11708067	3	ADCY5	A	0.023	0.34
exm-rs11715915	3	AMT	C	0.012	0.34
exm-rs7651090	3	IGF2BP2	G	0.013	0.25
rs1280	3	-	T	0.026	0.38
rs1604038	3	-	C	0.018	0.31
exm-rs4869272	5	LOC101929710, LOC107984114	T	0.018	0.15
rs9368222	6	CDKAL1	A	0.014	0.34
exm-rs11520696	7	DGKB	G	0.023	0.30
exm-rs2191349	7	DGKB	T	0.029	0.17
exm-rs2715094	7	GRB10	G	0.016	0.13
exm-rs6943153	7	GRB10	T	0.015	0.31
exm-rs6975024	7	GCK	C	0.061	0.39
rs10276674	7	DGKB	C	0.03	0.28
rs10487781	7	DGKB	A	0.012	0.15
rs17360797	7	DGKB	A	0.028	0.40
rs17544225	7	GRB10	C	0.018	0.05
rs2300584	7	GCK, LOC105375257	G	0.037	0.35
rs2908290	7	GCK, LOC105375257	A	0.027	0.30
rs4245555	7	GRB10	T	0.012	0.29

Appendix Table 4.2. CONTINUED. Characteristics of 77 SNPs associated with fasting glucose that were used to build FG-GRS.

SNP name	Chromosome	Associated gene*	Risk Allele	Beta	START-EAF
exm-rs11558471	8	LOC105375716, SLC30A8	A	0.029	0.33
rs2466299	8	LOC105375716, SLC30A8	A	0.018	0.35
rs7002551	8	LOC157273	C	0.014	0.10
rs7005140	8	LOC105375716	A	0.016	0.11
rs983309	8	LOC157273	T	0.026	0.39
exm-rs3829109	9	DNLZ	G	0.017	0.35
rs10811661	9	CDKN2B-AS1	T	0.024	0.40
rs10814916	9	GLIS3	C	0.016	0.24
rs1128905	9	GPSM1	T	0.015	0.16
exm-rs7903146	10	TCF7L2	T	0.022	0.32
rs11195502	10	-	C	0.032	0.38
exm-rs11039482	11	PTPRJ	C	0.02	0.43
exm-rs11603334	11	ARAP1	G	0.019	0.37
exm-rs1483121	11	OR4S1	G	0.018	0.43
exm-rs174570	11	FADS2	C	0.019	0.41
rs10838692	11	MADD	C	0.016	0.19
rs11020124	11	-	C	0.062	0.27
rs11038913	11	AMBRA1	T	0.019	0.43
rs11039119	11	MIR6745, PACSIN3	A	0.012	0.29
rs11039182	11	MADD	T	0.023	0.36
rs11570115	11	MYBPC3	T	0.024	0.43
rs11607883	11	SLC35C1	G	0.021	0.21
rs174576	11	FADS2	C	0.02	0.36
rs2072114	11	FADS2	A	0.023	0.03
rs2292910	11	CRY2	A	0.015	0.27
rs6483221	11	-	C	0.016	0.31
rs6485795	11	LOC100287189	G	0.015	0.26
rs7101470	11	C11orf49	A	0.022	0.02
rs7118178	11	MTCH2	G	0.018	0.33
exm-rs11619319	13	PDX1-AS1	G	0.02	0.37
exm-rs576674	13	-	G	0.017	0.07
exm-rs3783347	14	WARS	G	0.017	0.37
exm-rs4502156	15	-	T	0.022	0.24
rs6494311	15	-	C	0.012	0.28
rs7167881	15	-	C	0.021	0.36
rs11672660	19	GIPR, MIR642B	C	0.016	0.39
rs16980051	19	SYMPK	C	0.012	0.22
exm-rs6072275	20	PLCG1-AS1, TOP1	A	0.016	0.42

Abbreviations: FG, fasting glucose; GRS, genetic risk score; RAF, risk allele frequency; SNPs, single nucleotide polymorphism; START, South Asian Birth Cohort.

*Associated genes could be genes that SNPs are found within OR closest to within <250kb base-pair.

Appendix Table 4.3. Association of the GDM-GRS and gestational diabetes mellitus, fasting glucose, and $AUC_{glucose}$ by study*

	T1	T2	T3	p-value for trend	per 10 risk allele
GDM					
START cohort					
GDM-GRS score†	89 ± 5	101 ± 3	112 ± 5	-	-
n cases/ participants	28/268	37/266	44/276	-	-
Crude	1.00	1.39 (0.83, 2.37)	1.61 (0.98, 2.70)	0.082	1.28 (1.06, 1.55)
Model 1	1.00	1.68 (0.97, 2.94)	1.95 (1.15, 3.38)	0.024	1.38 (1.12, 1.70)
CHILD cohort					
GDM-GRS score†	87 ± 5	98 ± 3	110 ± 6	-	-
n cases/ participants	8/571	14/571	22/588	-	-
Crude	1.00	1.77 (0.75, 4.46)	2.74 (1.26, 6.60)	0.013	1.32 (1.06, 1.64)
Model 1	1.00	1.28 (0.50, 3.40)	2.50 (1.13, 6.08)	0.022	1.57 (1.18, 2.09)
FG					
START cohort					
GDM-GRS score†	89 ± 5	101 ± 3	112 ± 5	-	-
n participants	268	266	276	-	-
Crude	0.00	0.04 (-0.06, 0.13)	0.11 (0.02, 0.21)	0.017	0.04 (0.008, 0.08)
Model 1	0.00	0.05 (-0.04, 0.14)	0.14 (0.04, 0.23)	0.003	0.05 (0.02, 0.09)
$AUC_{glucose}$					
START cohort					
GDM-GRS score†	89 ± 5	101 ± 3	112 ± 5	-	-
n participants	268	266	276	-	-
Crude	0.00	-16.19 (-44.59, 12.22)	19.88 (-8.28, 48.04)	0.079	10.20 (-0.70, 21.10)
Model 1	0.00	-7.27 (-34.21, 19.68)	32.21 (5.52, 58.91)	0.007	14.18 (3.86, 24.50)

Abbreviations: $AUC_{glucose}$, area under the curve for glucose; CHILD, Canadian Healthy Infant Longitudinal Development; CIs, confidence intervals; FG, fasting glucose; GDM, gestational diabetes mellitus; GRS, genetic risk score; START, South Asian Birth Cohort; T, tertile.

Model 1 adjusted for age, pre-pregnancy weight, height, low diet quality, energy intake, social disadvantage index.

*T1 (reference group), T2, and T3 represent the tertiles of the GDM-GRS. For GDM, the data are expressed as OR (95% CIs) and for FG and $AUC_{glucose}$, the data are expressed as MD (95% CIs).

†GDM-GRS score reflects the number of risk alleles in each of the tertiles. The data are reported as mean ± SD.

Appendix Table 4.4. Association of the FG-GRS and fasting glucose in the START study*

	T1	T2	T3	p-value for trend	per 10 risk allele
FG-GRS score†	73 ± 4	81 ± 2	89 ± 3	-	-
n participants	268	265	278	-	-
Crude	0.00	0.07 (-0.03, 0.17)	0.15 (0.05, 0.24)	0.002	0.09 (0.03, 0.14)
Model 1	0.00	0.06 (-0.03, 0.16)	0.14 (0.05, 0.23)	0.002	0.09 (0.04, 0.14)

Abbreviations: CHILD, Canadian Healthy Infant Longitudinal Development; FG, fasting glucose; GDM, gestational diabetes mellitus; GRS, genetic risk score; MD, mean difference; OR, odds ratio; START, South Asian Birth Cohort.

Model 1 adjusted for age, prepregnancy weight, height, low diet quality, energy intake, social disadvantage index.

*T1 (reference group), T2, and T3 represent the tertiles of the FG-GRS. For FG, the data are expressed as MD (95% CIs).

†FG-GRS score reflects the number of risk alleles in each of the tertiles. The data are reported as mean ± SD.

Appendix Table 4.5. Association of carbohydrate quality and GDM risk.

	CHILD						START						CHILD + START					
	Q1 (n= 562)	Q2 (n= 562)	Q3 (n= 562)	Q4 (n= 562)	Q5 (n= 562)	p-value for trend	Q1 (n= 185)	Q2 (n= 185)	Q3 (n= 184)	Q4 (n= 185)	Q5 (n= 185)	p-value for trend	Q1 (n=747)	Q2 (n=747)	Q3 (n=746)	Q4 (n=747)	Q5 (n=747)	p-value for trend
Glycemic index																		
	45.52 ± 1.72	48.28 ± 0.52	49.81 ± 0.42	51.44 ± 0.52	54.26 ± 1.63		40.57 ± 1.90	43.73 ± 0.63	45.73 ± 0.55	47.63 ± 0.55	50.72 ± 2.09		44.29 ± 2.77	47.15 ± 2.04	48.80 ± 1.82	50.50 ± 1.73	52.38 ± 2.33	
GDM cases	8	18	17	19	20		27	26	31	25	30		35	44	48	44	50	
Crude	1.00	2.29 (1.02, 5.62)	2.16 (0.95, 5.33)	2.42 (1.09, 5.92)	2.56 (1.16, 6.21)	0.049	1.00	0.96 (0.53, 1.71)	1.18 (0.68, 2.09)	0.91 (0.51, 1.64)	1.13 (0.64, 2.00)	0.745	1.00	1.29 (0.81, 2.06)	1.42 (0.90, 2.27)	1.29 (0.81, 2.06)	1.49 (0.95, 2.36)	0.132
Model 1	1.00	2.21 (0.96, 5.50)	2.03 (0.88, 5.09)	2.34 (1.02, 5.84)	2.61 (1.14, 6.48)	0.047	1.00	1.09 (0.59, 2.00)	1.34 (0.74, 2.42)	1.13 (0.61, 2.09)	1.23 (0.68, 2.23)	0.496	1.00	1.37 (0.85, 2.22)	1.49 (0.93, 2.41)	1.40 (0.87, 2.28)	1.60 (1.00, 2.58)	0.075
Model 2	1.00	2.19 (0.90, 5.83)	2.09 (0.86, 5.58)	2.46 (1.03, 6.48)	2.55 (1.06, 6.81)	0.064	1.00	1.08 (0.59, 1.98)	1.32 (0.73, 2.40)	1.14 (0.61, 2.12)	1.27 (0.69, 2.35)	0.444	1.00	1.33 (0.82, 2.18)	1.49 (0.92, 2.42)	1.41 (0.86, 2.31)	1.60 (0.98, 2.62)	0.083
Glycemic load																		
	97.47 ± 9.84	112.80 ± 2.70	121.50 ± 2.46	129.80 ± 2.47	144.90 ± 9.74		88.29 ± 7.54	101.55 ± 2.86	109.70 ± 2.00	117.10 ± 2.46	130.90 ± 9.98		95.20 ± 10.12	110.01 ± 5.58	118.60 ± 5.61	126.60 ± 5.98	141.40 ±11.50	
GDM cases	12	20	20	14	16		32	23	32	23	29		44	43	52	37	45	
Crude	1.00	1.69 (0.83, 3.60)	1.69 (0.83, 3.60)	1.17 (0.54, 2.60)	1.34 (0.63, 2.93)	0.874	1.00	0.68 (0.38, 1.21)	1.01 (0.59, 1.73)	0.68 (0.38, 1.21)	0.89 (0.51, 1.54)	0.696	1.00	0.97 (0.62, 1.52)	1.21 (0.79, 1.86)	0.82 (0.52, 1.31)	1.02 (0.66, 1.59)	0.841
Model 1	1.00	1.74 (0.84, 3.75)	1.83 (0.89, 3.9)	1.03 (0.44, 2.40)	1.39 (0.63, 3.11)	0.893	1.00	0.74 (0.40, 1.34)	1.14 (0.65, 2.00)	0.76 (0.41, 1.38)	0.94 (0.53, 1.67)	0.877	1.00	1.04 (0.65, 1.64)	1.35 (0.88, 2.10)	0.90 (0.55, 1.44)	1.07 (0.68, 1.68)	0.894
Model 2	1.00	2.12 (0.98, 4.84)	2.06 (0.96, 4.71)	1.23 (0.51, 3.00)	1.43 (0.61, 3.47)	0.937	1.00	0.74 (0.40, 1.34)	1.16 (0.66, 2.03)	0.78 (0.42, 1.41)	0.94 (0.53, 1.66)	0.878	1.00	1.10 (0.69, 1.75)	1.43 (0.92, 2.24)	0.94 (0.57, 1.52)	1.05 (0.66, 1.67)	0.964
Total sugars (g/d)																		
	96.37 ± 13.78	122.70 ± 5.04	138.80 ± 4.44	154.60 ± 5.01	183.70 ± 19.75		63.10 ± 10.05	82.00 ± 4.02	96.59 ± 4.17	112.30 ± 5.23	144.80 ± 21.81		88.13 ± 19.34	112.65 ± 18.56	128.42 ± 18.74	144.10 ± 18.95	174.00 ± 26.34	
GDM cases	24	20	15	12	11		39	26	22	29	23		63	46	37	41	34	
Crude	1.00	0.83 (0.45, 1.51)	0.61 (0.31, 1.17)	0.49 (0.23, 0.97)	0.45 (0.21, 0.90)	0.049	1.00	0.61 (0.35, 1.05)	0.51 (0.28, 0.89)	0.70 (0.41, 1.18)	0.53 (0.30, 0.92)	0.060	1.00	0.70 (0.46, 1.04)	0.55 (0.35, 0.84)	0.61 (0.40, 0.93)	0.50 (0.32, 0.77)	0.002
Model 1	1.00	0.83 (0.44, 1.56)	0.58 (0.28, 1.15)	0.49 (0.23, 1.02)	0.45 (0.20, 0.94)	0.011	1.00	0.66 (0.37, 1.16)	0.56 (0.31, 1.00)	0.72 (0.41, 1.24)	0.60 (0.33, 1.06)	0.124	1.00	0.76 (0.50, 1.15)	0.56 (0.35, 0.87)	0.62 (0.40, 0.96)	0.54 (0.34, 0.84)	0.003
Model 2	1.00	0.78 (0.40, 1.51)	0.58 (0.28, 1.17)	0.49 (0.22, 1.03)	0.43 (0.18, 0.93)	0.014	1.00	0.63 (0.36, 1.11)	0.54 (0.30, 0.97)	0.70 (0.40, 1.21)	0.57 (0.31, 1.02)	0.101	1.00	0.71 (0.46, 1.09)	0.55 (0.34, 0.86)	0.61 (0.39, 0.94)	0.51 (0.32, 0.80)	0.003
Added sugars (g/d)																		
	46.02 ± 13.91	55.29 ± 14.82	60.11 ± 16.62	63.83 ± 19.01	69.89 ± 25.78		10.57 ± 3.62	19.34 ± 2.08	26.11 ± 2.09	34.50 ± 2.90	54.69 ± 20.38		28.68 ± 12.13	40.76 ± 12.57	49.41 ± 13.58	59.03 ± 14.43	80.16 ± 23.35	
GDM cases	19	15	9	18	21		40	29	29	16	25		59	44	38	34	46	
Crude	1.00	0.78 (0.39, 1.55)	0.46 (0.20, 1.01)	0.94 (0.49, 1.83)	1.11 (0.59, 2.10)	0.579	1.00	0.67 (0.39, 1.14)	0.68 (0.40, 1.15)	0.34 (0.18, 0.63)	0.57 (0.32, 0.97)	0.005	1.00	0.72 (0.47, 1.08)	0.61 (0.39, 0.94)	0.54 (0.34, 0.84)	0.75 (0.50, 1.13)	0.070
Model 1	1.00	0.74 (0.35, 1.51)	0.44 (0.18, 1.00)	1.10 (0.56, 2.18)	0.94 (0.47, 1.85)	0.741	1.00	0.66 (0.38, 1.14)	0.63 (0.36, 1.09)	0.38 (0.20, 0.71)	0.55 (0.30, 0.96)	0.009	1.00	0.69 (0.45, 1.06)	0.59 (0.37, 0.91)	0.61 (0.38, 0.96)	0.70 (0.45, 1.08)	0.060
Model 2	1.00	0.76 (0.35, 1.61)	0.50 (0.20, 1.16)	1.19 (0.58, 2.42)	0.97 (0.47, 1.97)	0.652	1.00	0.66 (0.38, 1.14)	0.64 (0.37, 1.11)	0.38 (0.20, 0.71)	0.54 (0.30, 0.96)	0.009	1.00	0.70 (0.45, 1.08)	0.62 (0.39, 0.96)	0.60 (0.38, 0.96)	0.68 (0.44, 1.06)	0.060

Abbreviations: CHILD, Canadian Healthy Infant Longitudinal Development; GDM, gestational diabetes mellitus; START, South Asian Birth Cohort.

*Data reported in OR (95% CIs)

Crude did not adjust for co-variates in CHILD or START. In the combined analysis, crude adjusted for cohort study.
Model 2 adjusted for Model 1, age, prepregnancy weight, height.
Model 3 adjusted for Model 2, low diet quality, energy intake, social disadvantage index.