

Associations between Maternal Dietary Patterns and Perinatal Outcomes: A Systematic Review and Meta-Analysis of Cohort Studies

Shima Abdollahi,¹ Sepideh Soltani,² Russell J de Souza,^{3,4} Scott C Forbes,⁵ Omid Toupchian,¹ and Amin Salehi-Abargouei^{6,7}

¹ School of Public Health, North Khorasan University of Medical Sciences, Bojnurd, Iran; ²Yazd Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran; ³ Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada; ⁴ Population Health Research Institute, Hamilton, Ontario, Canada; ⁵ Department of Physical Education, Faculty of Education, Brandon University, Brandon, Manitoba, Canada; ⁶ Nutrition and Food Security Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran; and ⁷ Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran;

ABSTRACT

The aim was to systematically review and meta-analyze prospective cohort studies investigating the relation between maternal dietary patterns during pregnancy with pregnancy and birth outcomes. PubMed, Scopus, and ISI Web of Science were searched from inception until October 2019 for eligible studies. Studies reporting relative risk, ORs, or incidences (for binary data) or means \pm SDs or B-coefficients (for continuous outcomes) comparing the highest and lowest adherence with maternal dietary patterns were included. Dietary patterns were categorized as "healthy," "unhealthy," or "mixed." No language restrictions were applied. Study-specific effect sizes with SEs for outcomes of interest were pooled using a random-effects model. Quality of evidence was assessed using Grading of Recommendations Assessment, Development, and Evaluation (GRADE). Sixty-six relevant publications were included. A higher maternal adherence to a healthy diet was associated with a reduced risk of gestational hypertension (14%, P < 0.001), maternal depression (40%, P = 0.004), low birth weight (28%, P = 0.001), pretern birth (56%, P < 0.001), higher gestational weight gain (Hedges' g: 0.15; P = 0.01), and birth weight (Hedges' g: 0.19; P = 0.001), pretern birth (56%, P < 0.001), higher mixed diet was associated with higher odds of gestational hypertension (23%, P < 0.001 for unhealthy, and 8%, P = 0.01 for mixed diet). In stratified analyses, a higher healthy eating index was associated with reduced odds of being large based on gestational age (31%, P = 0.02) and a higher head circumference at birth (0.23 cm, P = 0.02). The Mediterranean and "prudent" dietary patterns were related to lower odds of being small based on gestational age (46%, P = 0.04) and pretern birth (52%, P = 0.03), respectively. The overall GRADE quality of the evidence for most associations was low or very low, indicating that future high-quality research is warranted. This study was registered at http://www.crd.york.ac.uk/PROSPERO as CRD4201

Keywords: dietary patterns, pregnancy outcomes, perinatal outcomes, systematic review, meta-analysis

Introduction

Modifiable factors such as smoking, weight gain, and diet affect pregnancy and neonatal outcomes (1-5). The "Barker hypothesis" proposed in 1990 by the British epidemiologist David Barker (1938–2013) posits that, in humans, intrauterine growth retardation, low birth weight (LBW), and premature birth have a causal relation to the origins of hypertension, cardiovascular disease, and type 2 diabetes in middle aged adults (6-8).

Several investigations have examined the relation between maternal intake of nutrients, foods, and food groups with pregnancy outcomes (9-13). An important conceptual shift in the field of nutrition has been a movement away from studies investigating single foods or nutrients in favor of

studies examining the entire diet (14–17). Evaluating the entire diet is more informative since associations between individual foods or nutrients with diseases are difficult to detect due to small effect sizes and biological interactions (18, 19). Dietary pattern analyses overcome these limitations possibly by having larger effect sizes, absorbing interaction effects among nutrients, and importantly, reflecting "real world" eating habits (20). Moreover, dietary patterns can easily inform public health recommendations. Several approaches have been developed and used extensively to derive dietary patterns. These include a posteriori methods that benefit from the use of statistical analyses, such as factor analysis, cluster analysis, and reduced rank regression, and a priori approaches that evaluate overall diet quality compared with recommended diets [e.g., The Healthy Eating Index-2010, Dietary Approaches to Stop Hypertension (DASH) diet score, and Mediterranean diet score] (20, 21).

Several studies have attempted to establish associations between maternal dietary patterns and perinatal outcomes; however, results are inconsistent. For instance, in a Norwegian prospective cohort study, Brantsæter et al. (15) found that a "vegetable" dietary pattern (characterized by high intake of vegetables, plant foods, and vegetable oils) reduces the risk of pre-eclampsia, whereas adherence to a "Western" dietary pattern, characterized by a high consumption of processed meat, white bread, sugar-sweetened drinks, and salty snacks, increases the risk. In contrast, in the Generation R study (Netherlands), no associations were found between pregnancy dietary pattern and pre-eclampsia (22). Another prospective cohort study performed in Denmark showed that maternal adherence to a "Mediterranean-like" dietary pattern was associated with reduced risk of preterm delivery (23). In addition, several prospective cohort studies found that a healthier dietary pattern in pregnancy is associated with higher birth weight (24-26), whereas others found no association despite similar study methodology (27-31).

Previous meta-analyses have explored the associations between maternal diet and cognitive and behavioral outcomes in children (32), risk of allergic disease (33) or asthma (34), risk of hypospadias and birth weight (35), birth outcomes (36), glycemic outcomes, and other pregnancy outcomes (37). However, these studies assessed limited outcomes, were not exhaustive in their selection of diets, and had methodological limitations. Notably, in most of these syntheses, prospective and cross-sectional (34, 35, 37, 38) or interventional (39) associations were pooled together. Since, well-designed and conducted prospective cohort studies are the strongest observational methodological approach to examine the relation between diet and health (40), we conducted this systematic review to summarize the evidence from prospective cohort studies examining the associations between maternal dietary patterns and perinatal (maternal and neonatal) outcomes and synthesize these results, where appropriate, using meta-analytic techniques.

Methods

The current study is in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (41) and was registered in an international prospective registry of systematic reviews (http://www.crd.york.ac.uk/PROSPERO; registration no.: CRD42018089756).

Search strategy and selection criteria

A systematic search for relevant published articles was conducted using PubMed, Scopus, and ISI Web of Science databases from inception to 25 October 2019. There was no language restriction. A combination of keywords relevant to dietary patterns, pregnancy, and study design were used to identify potential studies. Furthermore, the reference lists of identified articles were reviewed manually to find any other related studies. Details about the search strategy are provided in **Supplemental Table 1**.

Titles and abstracts of all retrieved articles were evaluated independently by 2 reviewers (OT and SS), and potentially eligible studies underwent a full-text review for inclusion according to the following criteria: 1) prospective cohort or nested case-control studies and 2) assessment of the association between dietary patterns of adult mothers (≥ 18 y) regardless of the methods used to define dietary patterns and all events that occur for the mother or offspring (perinatal outcomes). Cross-sectional, case-control, clinical trials, and review studies were excluded. We also excluded studies if they evaluated an individual nutrient or food group. Furthermore, studies that included women with pre-existing diseases, twins or higher-order multiple pregnancies, and induced pregnancy were also excluded. If duplicate publications of the same cohort were found, the most complete data were included in the meta-analysis. Discrepancies in the application of these criteria were resolved by discussion with another author (AS-A).

Definition of dietary patterns

For this review, we grouped the dietary patterns (or scores) into 3 categories based on constituent foods of each diet: healthy, unhealthy, and mixed patterns. Foods in each diet were selected based on the dietary recommendations for the prevention of chronic diseases (42, 43). Accordingly, a healthy diet was characterized by high intakes of fruits, vegetables, whole grains, low-fat dairy products, vegetable oils, and fish. An unhealthy diet was characterized by refined grains, foods high in saturated fats, red meat, processed meat, fast foods, and high sugary foods, which are related to a range of chronic diseases, such as cardiovascular diseases, cancer, and diabetes (44, 45). A combination of both healthy and unhealthy foods was labeled as mixed. If studies reported ≥ 2 healthy or unhealthy dietary patterns, we selected the pattern that most clearly fulfilled the predetermined healthy or unhealthy criteria. When both a priori and a posteriori dietary patterns were reported in the same population, the

Supported by the North Khorasan University of Medical Sciences, Bojnurd, Iran (grant number 98p1334).

Author disclosures: RJ de Souza has served as an external resource person to the World Health Organization's Nutrition Guidelines Advisory Group on *trans* fats, saturated fats, and polyunsaturated fats. The WHO paid for his travel and accommodation to attend meetings from 2012–2017 to present and discuss this work. He has also done contract research for the Canadian Institutes of Health Research's Institute of Nutrition, Metabolism, and Diabetes, Health Canada, and the World Health Organization for which he received remuneration. He has received speaker's fees from the University of Toronto, and McMaster Children's Hospital. He has held grants from the Canadian Institutes of Health Research, Canadian Foundation for Dietetic Research, Population Health Research Institute, and Hamilton Health Sciences Corporation as a principal investigator, and is a co-investigator on several funded team grants from Canadian Institutes of Health Research that examine maternal and infant health. He serves as an independent director of the Helderleigh Foundation (Canada). All the other authors report no conflicts of interest.

Supplemental Tables 1–25 and Supplemental Figures 1 and 2 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances.

Address correspondence to AS-A (e-mail: abargouei@ssu.ac.ir; abargouei@gmail.com). Abbreviations used: DASH, Dietary Approaches to Stop Hypertension; FFQ, food-frequency questionnaire; FGR, fetal growth restriction; GDM, gestational diabetes mellitus; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IUGR, intrauterine growth restriction; LBW, low birth weight; LGA, large for gestational age; ROBINS-E, Risk of Bias IN observational Studies of Exposures; RR, risk ratio; SGA, small for gestational age; WMD, weighted mean difference.

priori dietary pattern was preferred, due to lower researcher involvement in diet identification. Any disagreements with respect to categorization were discussed and resolved by discussion with the senior author (AS-A).

Data extraction

The eligible studies were reviewed and the following information was extracted: first author's name, publication year, name of the cohort (or study), country, timing of dietary assessment (i.e., gestational week), total number of participants, dietary assessment tool, name of dietary pattern, outcome ascertainment, and variables that entered into the multivariable model as potential confounders. Effect sizes with 95% CIs were also extracted for the categories of diet adherence. When multiple estimates were reported in the article, we used the results with adjustment for the highest number of confounders (i.e., the "most" multivariableadjusted model). Data extraction was completed by 2 separate authors, working independently (OT and SS), and entered in duplicate. Inconsistencies were resolved through discussion with a third author (AS-A).

Study quality assessment

Two researchers (SA and SS) independently assessed the methodological quality of included articles using the Risk Of Bias IN observational Studies of Exposures (ROBINS-E) tool (46). The articles were rated from low risk of bias to critical risk of bias based on 7 domains (confounding, selection bias, classification of interventions, deviations from intended interventions, missing data, measurement bias, and selection of reported results). Articles with low risk of bias for all criteria were judged as low risk of bias; if at least 1 criterion was moderate, serious, or critical risk of bias, the overall quality of study was regarded as moderate, serious, and critical risk of bias, respectively (47).

Quality of meta-evidence

We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to assess certainty of evidence for each exposure-outcome association based on the major domains of study limitations (48, 49). The quality of evidence derived from prospective observational studies begins as low quality (50). Then, the quality was downgraded based on 5 criteria. Scores were downgraded for risk of bias (if most of the studies showed serious critical risk of bias) (46), inconsistency [serious ($I^2 = 50\%$ to 75%) or very serious ($I^2 = 75\%$ to 100%) heterogeneity] (51), indirectness (when the results of most studies were not generalizable or did not directly measure the exposure and outcome of interest) (52), imprecision (we did not downgrade for this factor because of the large sample sizes of the included studies) (53), and publication bias (as assessed by funnel plots and Egger's and Begg's tests) (54).

Data synthesis

We conducted meta-analyses when at least 3 studies provided data for a given outcome. The included studies reported a measure of association or difference along with an estimate

of the variance (e.g., SE or CI). The effect size was the natural logarithm of the observed OR or risk ratio (RR) comparing the highest versus lowest exposure category (for binary outcomes) and the summary mean differences between the highest and lowest exposure category for continuous outcomes. All estimates were pooled as ORs. The few studies that reported RRs were treated as ORs, which resulted in a conservative estimate of the RR. When the number of events in each category was reported, the OR was calculated using events in the highest exposure versus reference level and the total number of participants in each category. The effect sizes were standardized using Hedges' g if all the studies in the meta-analysis did not use the same scale to assess the continuous outcomes (55), including gestational weight gain and birth weight. Associations were considered small if Hedges' g was ≤ 0.2 , medium if Hedges' g was between 0.2 and 0.8, and large if Hedges' g was ≥ 0.8 (56). When studies reported data separately by ethnicity or BMI categories in the same population, we pooled the estimates using a fixedeffects meta-analysis before including the study estimate in the analysis. The overall associations were derived using the DerSimonian and Laird random-effects model. Statistical heterogeneity between studies was assessed using Cochran's *Q* test and quantified by the I^2 statistic (51). When eligible studies did not report data in a form that could be included in the meta-analysis, they were included in the systematic review and narratively summarized.

We performed subgroup analyses to compare the associations of dietary patterns with health outcomes based on the following classification: 1) prudent dietary pattern, 2) New Nordic diet, 3) DASH diet, 4) Mediterranean diet, 5) Healthy Eating Index, 6) diet diversity, 7) plant-based diet, and 8) other healthy diets. Our primary sensitivity analysis approach was to remove each single study from the metaanalyses and recalculate the summary effect (the "leave-oneout" approach). An influential outlier was considered a study whose removal either pushed the significance level of the overall effect from <0.05 to ≥ 0.05 (or vice versa) or altered the effect size by $\geq 10\%$. An additional sensitivity analysis was also conducted in which we removed unadjusted effect sizes and recalculated the summary estimate. Publication bias was evaluated when at least 10 studies were available for an outcome by inspection of Begg's funnel plots, and the statistical asymmetry was checked by using Egger's regression asymmetry test and Begg's adjusted rank correlation test. When there was evidence of publication bias, Duval and Tweedie's "trim and fill" method was used to correct funnel plot asymmetry (57). All data analyses were implemented using STATA version 11 (StataCorp), and P values <0.05 were considered statistically significant.

Results

Study search and characteristics of included studies

The flow of study selection is provided in **Figure 1**. The primary search identified 20,276 articles; 193 full-text articles were retrieved and assessed for eligibility. Finally, 113 publications from 51 cohort studies met the inclusion criteria

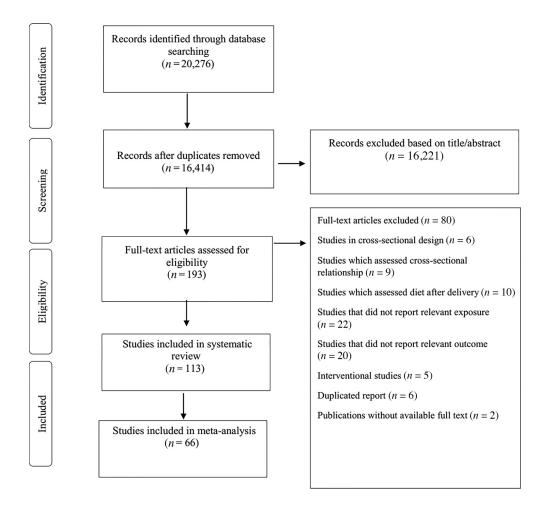


FIGURE 1 Flow diagram of study selection procedures.

and were included in the systematic review (15, 22–31, 58– 159). The most common reasons for exclusion were related to failure to report relevant exposure or outcomes. The complete list of reasons for exclusion of articles is presented in **Supplemental Table 2**.

All publications assessed diet during pregnancy, except for 13 (6 cohort studies) which examined the prepregnancy diet (63, 74-76, 86, 88, 101, 105, 135, 136, 144, 145, 155). One study pooled the prepregnancy and pregnancy dietary data in the same analysis (90). The included studies were conducted in the United States (29 publications from 13 cohorts) (28, 29, 31, 61-63, 74, 78, 85, 86, 88, 89, 106, 113, 114, 118, 128-130, 132, 133, 137, 139, 141, 144, 145, 155, 157, 159), European countries (34 publications from 11 cohorts) (15, 22, 23, 25–27, 30, 58, 64–66, 79, 80, 94, 95, 97, 98, 103, 105, 107, 117, 120-122, 126, 127, 134, 138, 140, 142, 143, 147, 148, 151), Spain (10 publications from 4 cohorts) (24, 67, 70, 75, 76, 84, 87, 116, 131, 146), Canada (3 publications from 6 cohorts) (83, 99, 158), and Brazil (7 publications from 3 cohorts) (59, 60, 73, 81, 119, 149, 150). An additional 22 publications (13 cohorts) were from Asia (14, 71, 72, 77, 91-93, 96, 100, 102, 108–112, 115, 123, 124, 152, 156, 159), 3 from Australia (90, 135, 136), and 3 from Africa (68, 153, 154). Three publications pooled the data from different countries

(69, 101, 125). The dietary patterns derived from the eligible studies as well as their categorization for the present study are provided in **Supplemental Table 3**.

In total, 66 publications were included in the analyses to assess the association of dietary patterns with maternal outcomes, including cesarean delivery (14, 59, 87, 91, 137, 139, 141), depression (68, 100, 123), gestational weight gain (14, 24, 26, 27, 31, 60, 61, 78, 81, 87, 113, 137, 139, 141, 142, 154, 157), gestational diabetes mellitus (GDM) (24, 62, 63, 75–77, 88, 90, 92, 93, 95, 96, 101, 112, 113, 119, 129, 133, 136, 137, 145, 148, 155–157), and gestational hypertensive disorders (14, 15, 22, 66, 69, 78, 88, 90, 92, 95, 97, 137, 144, 147, 157) or offspring outcomes, including LBW (26, 30, 78, 90, 91, 104, 154), preterm birth (23, 25, 29–31, 59, 78, 90, 91, 95, 154, 157), stillbirth (86, 91, 154), fetal growth restriction (FGR) (69, 131), obesity (24, 30, 58, 74), and birth-size parameters (24–28, 30, 31, 59, 66, 69, 71, 78, 87, 125, 128, 131, 137, 139, 143, 154, 157).

Risk of bias of included studies

The risk of bias of included studies was assessed using the ROBINS-E tool. **Supplemental Table 4** shows the details on the scores for each study. Most studies were at high risk of bias due to uncontrolled/residual confounding. Another

source of bias was risk of bias due to outcome assessment methods, where studies mostly relied on medical record data or self-report, which might lead to measurement bias. Finally, a validated food-frequency questionnaire (FFQ) was the most common dietary measurement method (60/66; 90.9%), which, although economical for large-scale epidemiology studies, is known to be biased because responses are selfreported from memory and are often subject to individual variation in perception of portion sizes (160).

Most studies that examined the association between maternal diet and cesarean delivery (14, 87, 91, 92, 137, 139, 141), gestational hypertensive disorders (14, 66, 69, 88, 90, 97, 137, 144, 157), gestational weight gain (14, 24, 27, 31, 61, 81, 87, 113, 137, 141, 154, 157), GDM (24, 63, 75–77, 88, 90, 93, 95, 112, 113, 136, 137, 145, 157), birth weight (24–27, 31, 71, 87, 137, 139, 154), LBW (26, 90, 91, 104, 154), and stillbirth (91, 154) were at high risk of bias.

Association between maternal diet and maternal outcomes

Meta-analysis.

The meta-analysis of cohort studies investigating the association between dietary patterns and the odds of maternal outcomes is reported in **Table 1** and **Supplemental Figure 1**.

GDM.

Twenty-seven articles investigated the association between dietary pattern and GDM (Supplemental Table 5). Two publications could not be included in the quantitative synthesis because the data were not appropriate for the statistical approach (73, 135). We pooled the 17 studies that reported the association between a healthy dietary pattern and GDM (24, 62, 75-77, 92, 93, 95, 101, 112, 119, 129, 133, 136, 145, 148, 156, 157). We found no significant association between higher adherence to a healthy diet and odds of GDM (17 studies, 121,558 participants; OR: 0.89; 95% CI: 0.75, 1.06; P = 0.2). Similarly, higher adherence to an unhealthy (8 studies, 25,148 participants; OR: 1.08; 95% CI: 0.81, 1.43; P = 0.59) or a mixed (7 studies, 24,826 participants; OR: 1.17; 95% CI: 0.95, 1.44; P = 0.13) dietary pattern was not associated with the incidence of GDM (Table 1). The subgroup meta-analysis also found no significant association between types of healthy dietary patterns and odds of GDM (Table 1).

Gestational hypertensive disorders.

Fifteen articles investigated the association between dietary pattern and gestational hypertensive disorders (**Supplemental Table 6**) (14, 15, 22, 66, 69, 78, 88, 90, 92, 95, 97, 137, 144, 147, 157). Two articles were excluded from analyses because results were not presented as highest versus lowest categories of diet adherence (73, 99). We pooled the outcomes of gestational hypertension (14, 69, 88, 90, 97, 144, 157) and pre-eclampsia (15, 22, 66, 78, 92, 95, 147) in the same analysis. One study reported number of participants with gestational hypertension and also participants with pre-eclampsia in quartiles of the diet score (137). We estimated effect size using the sum of the 2 numbers.

Higher adherence to a healthy diet was associated with a 14% lower odds of hypertensive disorders during pregnancy (12 studies, 195,916 participants; OR: 0.86; 95% CI: 0.81, 0.91; P < 0.001). Higher adherence to an unhealthy diet was associated with a 23% higher odds of hypertensive disorders during pregnancy (5 studies, 81,144 participants; OR: 1.23; 95% CI: 1.14, 1.34; P < 0.001); and higher adherence to a mixed diet was associated with an 8% higher odds of these disorders (5 studies, 83,475 participants; OR: 1.08; 95% CI: 1.01, 1.16; P = 0.01) (Table 1). In stratified analyses, higher adherence to the Healthy Eating Index was associated with a reduced odds of gestational hypertensive disorders comparing with the lowest category (3 studies, 23,048 participants; OR: 0.85; 95% CI: 0.74, 0.99; P = 0.03) (Table 1).

Gestational weight gain.

Seventeen articles reported the association between dietary patterns and gestational weight gain, 10 of which were included in the meta-analysis (**Supplemental Table 7**) (24, 27, 31, 81, 87, 113, 137, 142, 154, 157).

The meta-analysis showed that the highest adherence to a healthy dietary pattern was significantly associated with more weight gain when compared with the lowest adherence; however, the association was weak (9 studies, 9803 participants; Hedges' g: 0.15; 95% CI: 0.03, 0.28; P = 0.01) (Table 1), although there was no significant association with the odds of excessive gestational weight gain (as a dichotomous outcome) comparing extreme categories of healthy dietary pattern (26, 61, 78, 139, 141, 142) (6 studies, 71,719 participants; OR: 0.87; 95% CI: 0.73, 1.04; P = 0.13) (**Supplemental Table 8**, Table 1).

Inadequate gestational weight gain in relation to maternal dietary pattern was reported in 9 articles, of which 5 were included in the meta-analysis (61, 78, 95, 139, 142) (**Supplemental Table 9**). These analyses revealed no significant association between healthy diet and the odds of inadequate gestational weight gain (5 studies, 71,390 participants; OR: 0.98; 95% CI: 0.83, 1.17; P = 0.88). In subgroup analyses, there was no significant association between healthy dietary patterns and the odds of inadequate gestational weight gin (Table 1). There were insufficient data to conduct analyses of unhealthy or mixed diets in this regard.

Maternal depression.

We pooled the results from 3 studies to evaluate the association between dietary pattern during pregnancy and maternal depression (**Supplemental Table 10**) (68, 100, 123). A higher adherence to a healthy dietary pattern was associated with a 40% reduced odds of maternal depression (3 studies, 5092 participants; OR: 0.60; 95% CI: 0.42, 0.85; P = 0.004) (Table 1).

Cesarean delivery.

Eight studies investigated the association between dietary pattern in pregnancy and cesarean delivery (14, 59, 73, 87, 91, 137, 139, 141), of which 5 were included in the meta-analysis (**Supplemental Table 11**) (14, 87, 91, 137, 139).

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			Meta-analysis	ysis		Heterogeneity	neity	
Study group	Studies, <i>n</i> [reference(s)]	Participant, <i>n</i>	OR (95% CI)	P-effect	Q statistic	<i>P</i> -within group	μ ² , %	P-between group
Gestational diabetes mellitus Healthy dietary pattern	17 (24, 62, 75, 77, 92, 93, 95, 101, 112, 119,	121,558	0.89 (0.75, 1.06)	0.2	49.33	< 0.001	67.6	0.001
Unhealthy dietary pattern Mixed dietary pattern	1.29, 133, 130, 145, 145, 146, 130, 137, 8 (75, 77, 92, 96, 112, 119, 136, 155) 7 (63, 77, 92, 93, 112, 119, 156)	25,148 24,826	1.08 (0.81, 1.43) 1.17 (0.95, 1.44)	0.59 0.13	17.59 13.05	0.01 0.04	60.2 54.0	
Healthy diet subgroups Prudent dietary pattern Mediterranean diet Healthy Eating Index New Nordic diet score DASH score Diet quality	6 (77, 92, 93, 129, 148, 155) 6 (24, 75, 101, 113, 136, 145) 5 (62, 88, 133, 148, 157) 1 (26) 1 (145) 1 (88)	19,639 32,698 27,586 21,376 21,376	0.81 (0.59, 1.13) 0.83 (0.64, 1.09) 0.74 (0.51, 1.07) 1.43 (1.17, 1.77) 0.66 (0.53 0.82) 0.68 (0.53 0.85)	0.22 0.19 0.01 0.001 0.001	13.38 14.71 14.62 0.0 0.0	0.02 0.01 0.006	62.6 66.0 72.6	<0.001
Dietary diversity Plant-based foods The Australian recommended food score Other healthy diets	1 (88) 4 (63, 90, 136, 156) 1 (90) 4 (76, 119, 136, 137)	21,312 23,210 1902 9957	1.00 (0.78, 1.26) 0.91 (0.79, 1.05) 1.70 (0.71, 4.06) 0.67 (0.41, 1.09)	1.00 0.22 0.23 0.11	0.0 1.56 0.0 0.01	0.67 0.01	— 0.0 72.5	
Gestational hypertensive disorders Healthy dietary pattern Unhealthy dietary pattern Mixed dietary pattern	12 (22, 69, 78, 90, 92, 95, 97, 137, 144, 157) 5 (15, 66, 72, 92, 97) 5 (15, 22, 72, 92, 97)	195,916 81,144 83,475	0.86 (0.81, 0.91) 1.23 (1.14, 1.34) 1.08 (1.01, 1.16)	<0.001 <0.001 0.01	10.88 2.32 1.37	0.45 0.67 0.84	0.0 0.0	< 0.001
Healthy diet subgroups Prudent dietary pattern Mediterranean diet Healthy Eating Index New Nordic diet score DASH score DIET quality DIET quality DIET dA AN	2 (92, 147) 4 (22, 69) 3 (78, 88, 157) 2 (95, 97) 1 (144) 1 (144) 1 (188) 1 (88) 2 (15, 97) 2 (15, 97)	29,004 6462 23,048 127,211 54,588 19,917 78,562 78,562 7904	0.70 (0.53, 0.91) 0.82 (0.50, 1.34) 0.85 (0.74, 0.99) 0.89 (0.83, 0.95) 0.83 (0.73, 0.93) 0.83 (0.73, 0.93) 0.83 (0.72, 1.05) 0.87 (0.72, 1.05) 0.87 (0.72, 1.05) 0.40 (0.19, 0.85)	0.01 0.65 0.03 0.003 0.162 0.48 0.48	1.24 0.65 0.00 0.00 0.00 0.00 0.00 0.00 0.00	0.26 0.88 0.64 0.31 	19:4 0.0 94.4 1	60000
Uther heatry diet Inadequate gestational weight gain Healthy dietary pattern Unhealthy dietary pattern	1 (137) 5 (26, 61, 78, 139, 142) 1 (142)	1808 71,390 1917	0.98 (0.69, 1.61) 0.98 (0.69, 1.40) 0.98 (0.69, 1.40)	0.9 0.88 0.91	0.00 8.3 0.00	0.0	51.8	0.84
Healthy dier subgroups Prudent dietary pattern Healthy Eating Index New Nordic diet score Plant-based diet	1 (142) 4 (61, 78, 139, 142) 1 (26) 1 (142)	1917 4793 66,597 1917	0.84 (0.58, 1.22) 1.01 (0.75, 1.35) 0.94 (0.91, 0.98) 0.85 (0.58, 1.24)	0.358 0.180 0.003 0.4	0.00 7.44 0.00 0.00	0.05	59.7	0.67

(Continued)

(Continued)
TABLE 1

			Meta-analysis	sis		Heterogeneity	neity	
Study group	Studies, <i>n</i> [reference(s)]	Participant, <i>n</i>	OR (95% Cl)	P-effect	Q statistic	<i>P</i> -within group	μ ² , %	P-between group
Excessive gestational weight gain		1			0		c c L	
Healthy dietary pattern	6 (26, 61, 78, 139, 141, 142)	/1//9	0.8/ (0./3, 1.04)	0.13	11.99	0.03	58.3	0.02
Unhealthy dietary pattern	2 (60, 142)	2076	1.43 (1.06, 1.92)	0.01	0.04	0.85	0.0	
Mixed dietary pattern	1 (60)	159	0.74 (0.31, 1.71)	0.48	0.0			
Healthy diet subgroups								
Prudent dietary pattern	1 (142)	1917	1.06 (0.76, 1.47)	0.73	0.0	0.0	0.0	0.15
Healthy Eating Index	5 (61, 78, 139, 141, 142)	5222	0.83 (0.66, 1.03)	0.1	7.59	0.1	47.3	
New Nordic diet score	1 (26)	66,597	0.97 (0.92, 1.03)	0.4	0.0	0.0	0.0	
Other healthy diets	1 (142)	1917	1.09 (0.77, 1.53)	0.62	0.0	0.0	0.0	
Maternal depression								
Healthy dietary pattern	3 (68, 100, 123)	5092	0.60 (0.42, 0.85)	0.004	3.54	0.171	43.4	0.04
Unhealthy dietary pattern	2 (68, 123)	1394	0.87 (0.57, 1.33)	0.515	1.01	0.315	1.0	
Healthy diet subgroups								
Prudent dietary pattern	2 (68, 123)	1394	0.72 (0.39, 1.30)	0.274	1.67	0.197	40.0	0.17
Dietary diversity	1 (100)	3698	0.52 (0.44, 0.62)	<0.001	0.0			
Cesarean delivery								
Healthy dietary pattern	5 (59, 87, 91, 137, 139)	3921	0.83 (0.68, 1.00)	0.06	0.86	0.93	0.0	0.26
Unhealthy dietary pattern	3 (14, 59, 91)	1922	1.16 (0.81, 1.67)	0.39	0.49	0.78	0.0	
Mixed dietary pattern	3 (14, 59, 91)	1922	0.91 (0.68, 1.22)	0.54	1.82	0.4	0.0	
Healthy diet subgroups								
Prudent dietary pattern	2 (59, 91)	666	0.80 (0.55, 1.18)	0.27	0.0	0.98	0.0	0.82
Mediterranean diet	1 (87)	35	0.18 (0.007, 4.89)	0.31	0.0	0.0		
Healthy Eating Index	2 (87, 139)	1114	0.86 (0.63, 1.17)	0.34	0.79	0.37	0.0	
Other healthy diet	1 (137)	1808	0.84 (0.61, 1.15)	0.29	0.0	0.0		
Gestational weight gain (Hedges' g)								
Healthy dietary pattern	9 (24, 27, 31, 81, 87, 113, 142, 154, 157)	9803	0.15 (0.03, 0.28) ²	0.01	55.31	<0.001	85.5	0.09
Unhealthy dietary pattern	2 (81, 142)	3356	0.00 (—0.09, 0.09) ²	0.99	0.74	0.39	0.0	
Mixed dietary pattern	1 (31)	764	0.19 (0.01, 0.36) ²	0.03	0.0			
Healthy diet subgroups								
Prudent dietary pattern	3 (31, 81, 142)	4120	0.27 (—0.10, 0.65) ²	0.15	26.72	<0.001	92.5	< 0.001
Mediterranean diet	4 (24, 27, 87, 113)	3040	0.04 (-0.09, 0.17) ²	0.32	5.61	0.13	46.5	
Healthy Eating Index	3 (87, 142, 157)	5462	- 0.002 (-0.08, 0.07) ²	0.95	1.34	0.51	0.0	
Dietary diversity	1 (154)	374	0.26 (0.06, 0.46) ²	0.001	0.00	00.0		
Other healthy diets	2 (137, 142)	4966	- 0.02 (-0.10, 0.05) ²	0.49	1.41	0.23	28.8	
¹ DASH Diatany Anoroschas to Ston Hymortansion								

¹ DASH, Dietary Approaches to Stop Hypertension. ² Values are Hedges' *g* (95% CI). A healthy diet tended to be associated with decreased odds of caesarean delivery (5 studies, 3921 participants; OR: 0.83; 95% CI: 0.68, 1.00; P = 0.06), but there were no associations between unhealthy (3 studies, 1922 participants; OR: 1.16; 95% CI: 0.81, 1.67; P = 0.39) or mixed (3 studies, 1922 participants; OR: 0.91; 95% CI: 0.68, 1.22; P = 0.54) dietary patterns (Table 1).

Association between maternal diet and offspring outcomes

The meta-analysis of cohort studies investigating the association between maternal dietary patterns and the odds of offspring outcomes is reported in **Table 2** and **Supplemental Figure 2**.

Birth weight.

Thirty-one eligible studies provided an estimate of the association between maternal diet and birth weight, of which 19 studies were included in the meta-analysis (24–28, 30, 31, 66, 69, 71, 78, 87, 125, 128, 131, 137, 139, 143, 154). Other studies were excluded from the analyses because data did not compare highest versus lowest adherence to diets (72, 73, 79, 83, 109, 111, 116, 122, 124, 141, 158, 159) (**Supplemental Table 12**).

A higher maternal adherence to a healthy diet was strongly associated with higher birth weights compared with lower adherence (15 studies, 75,041 participants; Hedges' g: 0.91; 95% CI: 0.05, 0.32; P = 0.007) (Table 2). There were no associations for unhealthy (2 studies, 1585 participants; Hedges' g: -0.10; 95% CI: -0.33, 0.11; P = 0.35) or mixed (3 studies, 2659 participants; Hedges' g: 0.37; 95% CI: -0.24, 0.99; P = 0.24) dietary patterns and birth weight. There were no significant subgroup findings (Table 2).

Birth length.

Thirteen studies explored the association between maternal dietary pattern and birth length (14, 27, 30, 64, 69, 72, 78, 87, 124, 131, 139, 141, 159) and 7 (9 effect sizes) were included in the quantitative syntheses (27, 30, 69, 78, 87, 131, 139). (Supplemental Table 13).

The meta-analysis revealed no significant associations between a healthy dietary pattern and birth length [9 effect sizes, 7227 participants; weighted mean difference (WMD): 0.08 cm; 95% CI: -0.06, 0.23; P = 0.26]. There were no significant subgroup findings (Table 2).

Head circumference.

Ten studies (12 effect sizes) examined the association between maternal healthy diet and head circumference at birth (27, 30, 69, 78, 83, 124, 131, 139, 143, 159). Three studies could not be included in the quantitative synthesis because of inappropriate data (83, 124, 159) (**Supplemental Table 14**).

There was no significant association between healthy diet and head circumference (9 effect sizes, 10,303 participants; WMD: 0.09 cm; 95% CI: -0.03, 0.22; P = 0.14). In subgroup analyses, infants born to mothers with higher adherence to the Healthy Eating Index during pregnancy had 0.23-cm higher birth head circumference compared with infants born to mothers with lower adherence (4 studies, 3810 participants; WMD: 0.23 cm; 95% CI: 0.03, 0.43; P = 0.02) (Table 2).

LBW.

Seven eligible studies reported the association between maternal diet and LBW (26, 30, 78, 90, 91, 104, 154) (**Supplemental Table 15**).

The meta-analysis indicated that higher maternal adherence to a healthy diet during pregnancy was associated with 28% lower odds of having an LBW infant (7 studies, 70,662 participants; OR: 0.72; 95% CI: 0.53, 0.97; P = 0.001) (Table 2).

Preterm birth.

Seventeen studies were identified that examined the association between maternal dietary pattern and odds of preterm birth, of which 12 contributed to the quantitative synthesis (23, 25, 29–31, 59, 80, 90, 91, 95, 154, 157) (**Supplemental Table 16**).

Mothers with the highest adherence to a healthy diet during pregnancy had a 56% lower odds of a preterm birth (10 studies, 39,415 participants; OR: 0.44; 95% CI: 0.31, 0.62; P < 0.001). In subgroup analysis, the prudent dietary pattern was associated with lower preterm birth incidence (5 studies, 71,554 participants; OR: 0.48; 95% CI: 0.25, 0.93; P = 0.03). No significant associations were found for unhealthy (4 studies, 70,144 participants; OR: 2.05; 95% CI: 0.85, 4.91; P = 0.1) and mixed (4 studies, 68,411 participants; OR: 0.67; 95% CI: 0.32, 1.39; P = 0.28) dietary patterns (Table 2).

Large for gestational age.

Results from 6 articles were used to evaluate the association of maternal diet and large for gestational age (LGA) (26, 59, 78, 128, 137, 157). Five studies were excluded from quantitative syntheses because of inappropriate data (14, 79, 109, 118, 158) (**Supplemental Table 17**).

There was no significant difference in odds of LGA among mothers who had the highest adherence to a healthy diet compared with lowest adherence (6 studies, 72,499 participants; OR: 0.89; 0.95% CI: 0.67, 1.19; P = 0.45). In subgroup analyses, there was a 31% lower odds of LGA in mothers with higher adherence to the Healthy Eating Index (3 studies, 3906 participants; OR: 0.69; 0.95% CI: 0.5, 0.94; P = 0.02) (Table 2).

Small for gestational age.

Fifteen articles investigated the association between maternal dietary pattern and small for gestational age (SGA), 8 of which were included in the meta-analysis (26, 59, 66, 78, 128, 137, 143, 157) (**Supplemental Table 18**).

There was no evidence of association between maternal healthy dietary patterns and incidence of SGA (7 studies, 75,706 participants; OR: 0.8; 0.95% CI: 0.57, 1.11; P = 0.19). Pooling the results of 3 studies, higher adherence to a

Churden second	[[]][]]]	Participants,	WMD (95% CI),	to all other		P-within	12 oc	P-between
	oranies, II [reference(s)]	"	IJ		ל זומווזנו	dhuig	0/ 1	dnoiß
Birth weight (Hedges' <i>g</i>)								
Healthy dietary pattern	15 (24, 26–28, 30, 69, 78, 87, 128, 137, 139, 143, 154)	75,041	0.19 (0.05, 0.32)	0.007	324.69	<0.001	95.7	< 0.001
Unhealthy dietary pattern	2 (71, 125)	1585	- 0.10 (-0.33, 0.11)	0.35	2.37	0.09	63.4	
Mixed dietary pattern	3 (31, 66, 71)	2659	0.37 (-0.24, 0.99)	0.24	76.31	<0.001	97.4	
Healthy diet subgroups								
Prudent dietary pattern	1 (31)	764	0.14 (-0.03, 0.31)	0.11	0.00			< 0.001
Mediterranean diet	8 (24, 25, 27, 69, 87, 143)	35,345	0.04 (-0.03, 0.12)	0.24	11.27			
Healthy Eating Index	7 (28, 30, 78, 87, 128, 131, 139)	8271	0.25 (-0.08, 0.59)	0.11	188.19			
New Nordic diet score	1 (26)	56,629	0.06 (0.04, 0.08)	< 0.001	0.00			
Dietary diversity	1 (154)	374	1.31 (1.09, 1.54)	< 0.001	0.00			
Other healthy diet	1 (137)	1807	0.15 (0.02, 0.28)	0.01	0.00			
Birth length (cm)								
Healthy dietary pattern	9 (27, 30, 69, 78, 87, 131, 139)	7227	0.08 (-0.06, 0.23)	0.26	10.35	0.24	22.7	
Healthy diet subgroups								
Mediterranean diet	5 (27, 69, 87)	3382	0.10 (-0.15, 0.35)	0.43	5.48	0.24	27.1	0.7
Healthy Eating Index	5 (30, 78, 87, 131, 139)	3845	0.08 (-0.05, 0.22)	0.43	4.78	0.31	16.3	
Birth head circumference (cm)								
Healthy dietary pattern	9 (27, 30, 69, 78, 131, 139, 143)	10,303	0.09 (-0.03, 0.22)	0.14	18.21	0.02	56.1	
Healthy diet subgroups								
Mediterranean diet	5 (27, 69, 143)	6493	0.004 (-0.08, 0.09)	0.93	4.3	0.36	7.0	0.004
Healthy Eating Index	4 (30, 78, 131, 139)	3810	0.23 (0.03, 0.43)	0.02	5.69	0.12	47.3	
Low birth weight								
Healthy dietary pattern	7 (26, 30, 78, 90, 91, 104, 154)	70,662	0.72 (0.53, 0.97) ²	0.001	4.09	0.66	0.0	0.04
Unhealthy dietary pattern	1 (91)	812	2.91 (0.97, 8.74) ²	0.05	0.00			
Mixed dietary pattern	1 (91)	812	0.60 (0.27, 1.34) ²	0.21	0.00			
Healthy diet subgroups								
Prudent dietary pattern	1 (91)	812	0.59 (0.19, 1.81) ²	0.36	0.00			0.63
Healthy Eating Index	2 (30, 78)	1944	0.69 (0.32, 1.45) ²	0.33	1.13	0.28	11.1	
New Nordic diet score	1 (26)	66,597	0.77 (0.62, 0.97) ²	0.02	0.00			
Dietary diversity	2 (104, 154)	494	0.51 (0.26, 1.00) ²	0.05	0.43	0.51	0.0	
The Australian recommended food score	1 (90)	1897	0.40 (0.12, 1.33) ²	0.13	0.00			
Preterm birth								
Healthy dietary pattern	10 (23, 25, 29–31, 59, 90, 91, 154, 157)	39,415	0.44 (0.31, 0.62) ²	<0.001	25.01	0.003	64.0	<0.001
Unhealthy dietary pattern	4 (29, 59, 80, 91)	70,144	2.05 (0.85, 4.91) ²	0.1	60.28	< 0.001	95.0	
Mixed dietary pattern	4 (31, 59, 80, 91)	68,411	0.67 (0.32, 1.39) ²	0.28	23.05	< 0.001	87.0	
Healthy diet subgroups								
Prudent dietary pattern	5 (29, 31, 59, 80, 91)	71,554	0.48 (0.25, 0.93) ²	0.03	46.73	< 0.001	93.1	<0.001
Mediterranean diet	2 (23, 25)	28,240	0.64 (0.40, 1.01) ²	0.06	0.13	0.72	0.00	

(Continued)

TABLE 2 Meta-analysis of maternal dietary patterns and offspring outcomes (all analyses were conducted using a random-effects model)¹

(Continued)
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Herby End plots 2.04 (57) 351 0.60 (0.40 (0.5) 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07 0.73 0.07	Study group	Studies, <i>n</i> [reference(s)]	Participants, <i>n</i>	WMD (95% CI), cm	P-effect	Q statistic	<i>P</i> -within group	I ² , %	P-between group
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$									
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Healthy Eating Index	2 (30, 157)	3351	0.60 (0.40, 0.92) ²	0.02	0.07	0.79	0.0	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	New Nordic diet score	1 (95)	72.037	0.91 (0.80 1.03) ²	0 14	000			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		(00)	3143	0 50 (0 40 0 86) ²	9000				
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$					0.000	0.00			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Dietary diversity	1 (154)	3/3	0.22 (0.11, 0.43) ²	<0.00	0.00			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	The Australian recommended food score	1 (90)	1897	0.50 (0.21, 1.17) ²	0.11	0.00			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Large for gestational age								
en 1(5) 1(5) 1(5) 1(5)	Healthy dietary pattern	6 (26, 59, 78, 128, 137, 157)	72,499	0.89 (0.67, 1.19) ²	0.45	13.13	0.02	61.9	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Unhealthy dietary pattern	1 (59)	188	4.13 (1.302, 13.14) ²	0.01	0.00			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Healthy diet subgroups								
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Prudent dietary pattern	1 (59)	188	1.84 (0.74, 4.53) ²	0.18	0.0			0.007
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Healthy Eating Index	3 (78, 128, 157)	3906	0.69 (0.50, 0.94) ²	0.02	1.1	0.57	0.0	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	New Nordic diet score	1 (26)	66,597	1.11 (1.05, 1.19) ²	<0.001	0.0			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Other healthy diet	1 (137)	1808	0.81 (0.54, 1.21) ²	0.3	0.0			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Small for gestational age								
then $2(59, 66)$ 105 $0.83 (0.34, 202)^2$ 0.69 1.29 0.25 222 $1(59)$ 1(59) 1035 0.100 $1.14)^2$ 0.08 1.29 0.06 710 $1(59)$ 1(13) 105 1030 1030 0.23 (0.25, 2.14)^2 0.19 0.00 $$ 10 3(66, 128, 143) 3(66, 128, 143) 3(66, 128, 123) 0.02 0.04 15 0.03 604 3(68, 128, 133) 3(66, 128, 123) 3060 0.03 0.020 0.020 0.01 $$ 1 in head $1(133)$ 12.4 (0.33, 2.09)^2 0.02 0.000 $$ 1 in head $1(133)$ 12.4 (0.33, 2.09)^2 0.02 0.000 $$ 1 in $4(69, 131)$ $2(60, 131)$ $0.96 (0.57, 161)^2 0.89 631 0.000 1in head 1(131) 1(131) 1(131) 1(131) 128, 0.12, 0.29 0.03 0.000 1in 4(69, 131) 1(131) 1(131) 128, 0.124^2 0.36 0.92^2 0.030 0.000 1in weight 1(131) 1(131) 128, 0.28(0.58, 1.24)^2 0.31 0.030 0.000 1in weight 1(69, 131) 128, 0.28(0.58, 1.24)^2 0.31 0.030 0.000$	Healthy dietary pattern	<u> </u>	75,706	0.80 (0.57, 1.11) ²	0.19	19.24	0.004	68.8	0.02
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Unhealthy dietary pattern		1035	0.83 (0.34, 2.02) ²	0.69	1.29	0.25	22.2	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Mixed dietary pattern	2 (59, 66)	1035	0.31 (0.08, 1.14) ²	0.08	3.45	0.06	71.0	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Healthy diet subaroups	~ ~							
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Prudent dietary nattern	1 (59)	188	0.23 (0.026.2.14) ²	0 19	000			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			0001		100	2000	000	F 0 7	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		5 (00, 126, 145)	4079	0.04 (0.29, 0.99)	0.04	00.0	0.00	00.4	Č
$1(26)$ $1(26)$ $66,597$ 0.22 0.02 0.00 $ 4(69,131)$ $1(31)$ $1(30)$ $1.24(0,73,209)^2$ 0.42 0.00 $ 4(69,131)$ $0.96(0,57,161)^2$ 0.89 6.31 0.09 52.4 $3(69)$ $1(13)$ 23284 $1.19(0.81,174)^2$ 0.36 0.33 0.66 0.00 $1(131)$ 787 $0.4(0.17,0.92)^2$ 0.33 0.00 $ 4(69,131)$ $0.85(0.58,1.24)^2$ 0.41 0.55 0.49 0.78 0.00 $3(69)$ 3369 32384 $0.87(0.57,1.33)^2$ 0.55 0.91 0.78 0.00 $1(131)$ $3(69)$ 33284 $0.78(0.3,1.58)^2$ 0.33 1463 0.002 795 $4(69,131)$ 23284 $0.57(0.3,1.58)^2$ 0.33 1463 0.002 795 $3(59)$ 3284 $0.57(0.41,2.18)^2$ 0.31 772	Healthy Eating Index	3 (/8, 128, 15/)	3906	0.89 (0.52, 1.53) ²	0.69	4.15	0.12	9.13	0.01
$1(137)$ $1(137)$ $1(24(0.73, 2.09)^2$ 0.42 0.00 $ 4(69, 131)$ 4071 $0.96(0.57, 1.61)^2$ 0.89 6.31 0.09 524 $3(69)$ $3(89)$ 3284 $1.19(081, 174)^2$ 0.36 0.00 $ 4(69, 131)$ 787 $0.4(0.17, 092)^2$ 0.03 0.00 $ 4(69, 131)$ 787 $0.4(0.17, 092)^2$ 0.03 0.00 $ 3(69)$ 787 $0.4(0.17, 092)^2$ 0.36 0.30 $ 1(131)$ 4071 $0.85(0.58, 1.24)^2$ 0.41 0.78 0.78 0.00 $3(69)$ 713 0.7132^2 0.53 0.79^2 0.78 0.00 $1(131)$ 787 $0.78(0.3, 1.58)^2$ 0.53 0.79 0.78 0.00 $ 3(69)$ 7131^2 0.55 0.91 772 0.02 741 $ 1(131)$	New Nordic diet score	1 (26)	66,597	0.92 (0.86, 0.99) ²	0.02	0.00			
4 (69, 131) 4071 $0.96 (0.57, 1.61)^2$ 0.89 6.31 0.09 52.4 3 (69) 3.1 3.19 $1.19 (0.81, 1.74)^2$ 0.36 0.33 0.66 0.00 1 (131) 787 $0.4 (0.17, 0.92)^2$ 0.03 0.00 $$ $$ 4 (69, 131) 787 $0.36 (0.58, 1.24)^2$ 0.41 0.55 0.9 0.00 3 (69) 787 $0.38 (0.53, 1.24)^2$ 0.41 0.55 0.9 0.00 1 (131) 787 $0.87 (0.57, 1.33)^2$ 0.53 0.49 0.78 0.00 4 (69, 131) 787 $0.38 (0.3, 1.79)^2$ 0.53 0.49 0.78 0.00 3 (69) 787 $0.78 (0.3, 1.58)^2$ 0.33 1.463 0.002 795 3 (69) 787 $0.26 (0.3, 1.58)^2$ 0.91 7.72 0.002 795 3 (69) 771 $0.56 (0.41, 2.18)^2$ 0.91 7.72 0.002 795 1 (131) 787 $0.24 (0.1, 0.56)^2$ 0.01 0.00 $$	Other healthy diet	1 (137)	1808	1.24 (0.73, 2.09) ²	0.42	0.00			
4 (69, 131) 4 (71 0.96 (0.57 , 1.61) ² 0.89 6.31 0.09 52.4 3 (69) 1 (131) 787 0.4 (0.17 , 0.92) ² 0.38 0.66 0.00 1 (131) 787 0.4 (0.17 , 0.92) ² 0.37 0.33 0.66 0.00 4 (69, 131) 4071 0.85 (0.58 , 1.24) ² 0.41 0.55 0.9 0.00 3 (69) 3 (69) 787 0.78 (0.57 , 1.33) ² 0.53 0.49 0.78 0.00 1 (131) 787 0.78 (0.33 , 1.79) ² 0.55 0.99 0.78 0.00 4 (69, 131) 6.9 (1.7 (1.96) 0.53 (1.58) ² 0.53 0.49 0.78 0.00 3 (69) 787 0.78 (0.57 , 1.33) ² 0.53 0.49 0.78 0.00 4 (69, 131) 6.9 (1.7 (1.58) ² 0.53 0.38 14.63 0.002 795 3 (69) 787 0.24 ($0.1, 0.56$) ² 0.01 0.00 -1 -1 1 (131) 772 0.91 772 0.02 74.1	Fetal growth restriction in head								
$4(69, 131)$ 4071 $0.96(0.57, 1.61)^2$ 0.89 6.31 0.09 524 $3(59)$ $1(131)$ 3284 $1.19(0.81, 1.74)^2$ 0.36 0.03 0.66 0.00 $4(69, 131)$ 787 $0.4(0.17, 0.92)^2$ 0.36 0.83 0.66 0.00 $4(69, 131)$ 787 $0.4(0.17, 0.92)^2$ 0.36 0.33 0.69 0.78 0.00 $3(59)$ 3284 $0.85(0.58, 1.24)^2$ 0.41 0.55 0.9 0.00 $3(69)$ $1(131)$ 787 $0.387(0.57, 1.33)^2$ 0.53 0.49 0.78 0.00 $1(131)$ 787 $0.78(0.3, 1.79)^2$ 0.53 0.79 0.00 $$ $$ $4(69, 131)$ 809 $0.78(0.3, 1.58)^2$ 0.31 0.31 0.91 7.72 0.002 795 $3(69)$ $3(69)$ $0.24(01, 0.56)^2$ 0.21 0.91 7.72 0.022 741 $1(131)$ 787 $0.24(01, 0.56)^2$ 0.91 7.71 0.022 741	circumference								
$3(6)$ $3(6)$ 3284 $1.19(081, 1.74)^2$ 0.36 0.83 0.66 0.00 $1(131)$ 787 $0.4(0.17, 0.92)^2$ 0.03 0.00 $$ $ 4(69, 131)$ 4071 $0.85(0.58, 1.24)^2$ 0.41 0.55 0.9 0.00 $3(69)$ 3.284 $0.87(0.57, 1.33)^2$ 0.53 0.49 0.78 0.00 $3(69)$ 787 $0.78(0.33, 1.79)^2$ 0.55 0.49 0.78 0.00 $4(69, 131)$ 4071 $0.69(0.3, 1.58)^2$ 0.38 1463 0.002 795 $3(69)$ 3.284 $0.95(0.41, 2.18)^2$ 0.31 172 0.002 795 $3(69)$ 3.284 $0.95(0.41, 2.18)^2$ 0.91 7.72 0.002 795 $3(69)$ 787 $0.24(01, 0.56)^2$ 0.01 0.00 $$ $-$	Healthy dietary pattern	4 (69, 131)	4071	0.96 (0.57, 1.61) ²	0.89	6.31	0.09	52.4	
$3(69)$ 3284 $1.19 (081, 1.74)^2$ 0.36 0.06 0.00 $1(131)$ 787 $0.4 (0.17, 0.92)^2$ 0.03 0.66 0.00 $4(69, 131)$ 787 $0.4 (0.17, 0.92)^2$ 0.03 0.00 $$ $ 4(69, 131)$ 4071 $0.85 (0.58, 1.24)^2$ 0.41 0.55 0.9 0.00 $3(69)$ 3.284 $0.87 (0.57, 1.33)^2$ 0.53 0.49 0.78 0.00 $1(131)$ 787 $0.78 (0.33, 1.79)^2$ 0.55 0.9 0.00 $4(69, 131)$ 4071 $0.69 (0.3, 1.58)^2$ 0.38 14.63 0.002 795 $3(69)$ 3.284 $0.95 (0.41, 2.18)^2$ 0.31 772 0.002 795 $3(69)$ 777 0.31 0.01 0.00 $$ $ 1(131)$ 787 $0.24 (0.1, 0.56)^2$ 0.31 0.72 795 795 $3(69)$ 717 0.001 0.001 0.00 $$ $ -$	Healthy diet subgroups								
$1(131)$ 787 $0.4(0.17, 0.92)^2$ 0.03 0.00 $ 4(69, 131)$ $4(6, 131)$ 4071 $0.85(0.58, 1.24)^2$ 0.41 0.55 0.9 0.00 $3(69)$ $3(69)$ 3284 $0.87(0.57, 1.33)^2$ 0.53 0.49 0.78 0.00 $3(6)$ $1(131)$ 787 $0.78(0.3, 1.79)^2$ 0.55 0 0 0 $4(6, 131)$ 787 $0.78(0.3, 1.79)^2$ 0.53 0.49 0.78 0.00 $4(6, 131)$ 787 $0.56(0.3, 1.58)^2$ 0.38 14.63 0.002 79.5 $3(69)$ 3284 $0.95(0.41, 2.18)^2$ 0.91 7.72 0.022 79.5 $3(69)$ 787 $0.24(0.1, 0.56)^2$ 0.001 0.002 74.1	Mediterranean diet	3 (69)	3284	1.19 (0.81. 1.74) ²	0.36	0.83	0.66	0.00	0.01
4 (6, 131) 4 (6, 131) 4 (6, 131) 0.85 (0.58, 1.24) ² 0.41 0.55 0.9 0.00 3 (6) 3 (6) 3 (6) 3 (6) 3 (6) 0.78 0.78 0.078 0.00 1 (131) 787 0.78 (0.33, 1.79) ² 0.55 0.49 0.78 0.00 4 (6, 131) 787 0.59 (0.3, 1.58) ² 0.38 14.63 0.002 79.5 3 (6) 3 (6) 3 (6) 0.34 (0.3, 0.56) ² 0.38 14.63 0.002 79.5 3 (6) 3 (6) 787 0.55 (0.41, 2.18) ² 0.91 7.72 0.02 74.1 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00	Healthy Eating Index	1 (131)	787	0.4 (0.17, 0.92) ²	0.03	0.00		I	
4 (69, 131) 4 (69, 131) 0.55 (0.58, 1.24) ² 0.41 0.55 0.9 0.00 3 (69) 3 (69) 3 (69) 3 (69) 0.78 0.78 0.78 0.00 1 (131) 787 0.78 (0.33, 1.79) ² 0.55 0 0 0 0 4 (69, 131) 787 0.78 (0.3, 1.58) ² 0.38 14.63 0.002 79.5 3 (69) 3 (69) 3284 0.95 (0.41, 2.18) ² 0.91 7.72 0.022 79.5 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00 - - -	Fetal growth restriction in length								
3 (6) 3 (6) 3 (6) 3 (6) 0.57, 1.33) ² 0.53 0.49 0.78 0.00 1 (131) 787 0.78 (0.33, 1.79) ² 0.55 0 - - - 4 (6), 131) 787 0.56 (0.3, 1.58) ² 0.38 14.63 0.002 79.5 3 (6) 3 (6) 3284 0.95 (0.41, 2.18) ² 0.91 7.72 0.02 74.1 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00 - - -	Healthy dietary pattern	4 (69, 131)	4071	0.85 (0.58, 1.24) ²	0.41	0.55	0.9	0.00	
3 (6) 3 (6) 3 2 2 4 0 87 (0.57, 1.33) ² 0.53 0.49 0.78 0.00 1 (131) 7 87 0.78 (0.33, 1.79) ² 0.55 0 - - - 4 (69, 131) 787 0.58 (0.3, 1.58) ² 0.38 14.63 0.002 79.5 3 (69) 3 2 2 4 0.95 (0.41, 2.18) ² 0.91 7.72 0.02 74.1 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00 - - -	Healthy diet subgroups								
1 (131) 787 0.78 (0.33, 1.79) ² 0.55 0 4 (69, 131) 4 (071 0.69 (0.3, 1.58) ² 0.38 14.63 0.002 79.5 3 (69) 3284 0.95 (0.41, 2.18) ² 0.91 7.72 0.02 74.1 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00	Mediterranean diet	3 (69)	3284	0.87 (0.57, 1.33) ²	0.53	0.49	0.78	0.00	0.81
4 (69, 131) 4 (69, 131) 4 (071 0.69 (0.3, 1.58) ² 0.38 14,63 0.002 79.5 3 (69) 3 (69) 3284 0.95 (0.41, 2.18) ² 0.91 7.72 0.02 74.1 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00 - - -	Healthy Eating Index	1 (131)	787	0.78 (0.33, 1.79) ²	0.55	0		I	
n 4 (69, 131) 4 0/1 0.69 (0.3, 1.58) ² 0.38 14,63 0.002 79.5 3 (69) 3 (69) 3284 0.95 (0.41, 2.18) ² 0.91 7.72 0.02 74.1 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00 - - -	Fetal growth restriction in weight								
3 (69) 3284 0.95 (0.41, 2.18) ² 0.91 7.72 0.02 74.1 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00	Healthy dietary pattern	4 (69, 131)	4071	0.69 (0.3, 1.58) ²	0.38	14.63	0.002	79.5	
3 (69) 3284 0.95 (0.41, 2.18) ² 0.91 7.72 0.02 74.1 1 (131) 787 0.24 (0.1, 0.56) ² 0.001 0.00 — — —	Healthy diet subgroups								
1 (131) 787 0.24 (0.1, 0.56) ² 0.001	Mediterranean diet	3 (69)	3284	0.95 (0.41, 2.18) ²	0.91	7.72	0.02	74.1	0.00
	Healthy Eating Index	1 (131)	787	0.24 (0.1, 0.56) ²	0.001	0.00			

(Continued)

Study group	Studies, <i>n</i> [reference(s)]	Participants, n	WMD (95% Cl), cm	P-effect	Q statistic	<i>P</i> -within group	I ² , %	P-between group
Stillbirth								
Healthy dietary pattern	3 (86, 91, 154)	17,135	0.74 (0.29, 1.85) ²	0.52	11.71	0.003	82.9	
Unhealthy dietary pattern	1 (91)	812	57.97 (3.52, 955.99) ²	0.005	0.00			
Mixed dietary pattern	1 (91)	812	0.33 (0.22, 0.50) ²	<0.001	0.00			
Obesity in offspring								
Healthy dietary pattern	4 (30, 58, 74, 84)	39,436	0.96 (0.83, 1.12) ²	0.65	0.53	0.91	0:0	
Macrosomia								
Healthy dietary pattern	3 (26, 30, 78)	68,541	1.67 (0.46, 5.98) ²	0.42	48.67	< 0.001	95.9	
¹ DASH, Dietary Approaches to Stop Hypertension; WMD, weighted mean difference. ² Values are ORs (95% CIs).	ion; WMD, weighted mean difference.							

Mediterranean diet was associated with a 46% reduction in the odds of SGA (3 studies, 4829 participants; OR: 0.54; 0.95% CI: 0.29, 0.99; P = 0.04) (Table 2).

FGR in weight, height, and head circumference.

Two articles reported the association between a healthy diet and FGR in offspring (69, 131) (Supplemental Table 19). These studies reported the results of the INfancia y Medio Ambiente—(Environment and Childhood) Project (INMA) cohort consortium in the Atlantic, Mediterranean (69), and Valencia areas of Spain (131), and the Rhea mother-child study in Crete, Greece (69). The study by Saunders et al. (134) could not be included in the analyses because linear associations were presented.

There was no significant association when considering the extreme categories of a healthy diet for FGR in weight, height, and head circumference (4 studies, 4071 participants; OR: 0.69, 0.95% CI: 0.3, 1.58; *P* = 0.38, for FGR in weight; OR: 0.85, 0.95% CI: 0.58, 1.24; *P* = 0.41, for FGR in length; OR: 0.96, CI: 0.57, 1.61; P = 0.89, for FGR in head circumference). There were no significant subgroup findings (Table 2).

Stillbirth.

Meta-analysis based on 3 studies (86, 91, 154) (Supplemental Table 20) showed no evidence of an association between higher maternal adherence to a healthy diet and stillbirth (3 studies, 17,135 participants; OR: 0.74; 0.95% CI: 0.29, 1.85; P = 0.52) (Table 2).

Obesity in offspring.

Five studies investigated the association between maternal diet and obesity in offspring (30, 58, 74, 84, 114) (Supplemental Table 21). One study was not included in the analysis because it did not present a suitable association measure (114). There was no evidence of an association between maternal diet and obesity in offspring (4 studies, 39,436 participants; OR: 0.96; 0.95% CI: 0.83, 1.12; *P* = 0.65).

Macrosomia.

Three studies explored the association of maternal diet during pregnancy and odds of fetal macrosomia (26, 30, 78) (Supplemental Table 22). No significant association was observed (3 studies, 68,541 participants; OR: 1.67; 0.95% CI: 0.46, 5.98; P = 0.42).

Narrative syntheses

Supplemental Table 23 shows the characteristics of studies that were not suitable for quantitative synthesis.

Allergic disease in offspring.

Six studies (n = 12,311 participants) evaluated the association of maternal diet with allergic diseases in offspring (70, 102, 108, 117, 120, 138) (Supplemental Table 23). Chatzi et al. (70) reported that a high Mediterranean diet score was associated with reduced odds of atopy at age 6.5 y (OR: 0.55; 95% CI: 0.31, 0.97). Loo et al. (108) reported similar results for a "seafood and noodles" dietary pattern (characterized

TABLE 2 (Continued

by higher intakes of noodles, seafood, and soya sauce–based gravies and low intakes of curry and ethnic bread) (OR: 0.7; 95% CI: 0.5, 0.9). Another study showed that diet with higher intakes of baked and sugary products during pregnancy was associated with a higher prevalence of food allergies in the offspring (OR: 1.51; 95% CI: 1.01, 2.14) (102). An additional 3 studies, however, found no significant association between maternal diet and allergic diseases in offspring (117, 120, 138).

Asthma in offspring.

Three studies (n = 10,421 participants) examined linear associations of maternal diet and asthma in the offspring (Supplemental Table 23) (106, 120, 138). No evidence of an association between maternal diet and asthma symptoms in offspring was observed in any study.

Eczema in offspring.

Six studies (n = 13,960 participants) investigated the association between maternal dietary patterns and eczema in the offspring (67, 106, 108, 115, 120, 138) (Supplemental Table 23). No significant associations were observed in any study.

Wheeze in offspring.

Five studies (n = 11,362 participants) measured the association of maternal dietary pattern with wheezing in the offspring (67, 106, 108, 115, 138) (Supplemental Table 23). All but one study found no significant association. Miyake et al. (115) found that higher adherence to a Western dietary pattern was associated with reduced odds of wheezing in childhood (OR: 0.59; 95% CI: 0.35, 0.98).

Pregnancy loss.

Two studies (n = 11,884 participants) investigated the associations between maternal diet and pregnancy loss (86, 91). Neither reported significant associations between maternal diet and the odds of pregnancy loss.

Maternal anxiety.

Two studies (n = 3883 participants) investigated the association between maternal diet and anxiety symptoms (Supplemental Table 23). In one study, a high maternal dietary diversity score was negatively associated with anxiety status (OR: 0.75, 95% CI: 0.62, 0.91) (100). In another study, the common Brazilian diet (characterized by higher intake of rice, beans, meats and eggs, and vegetable spices) (β : -1.2; 95% CI: -2.22, -0.18) and a healthy dietary pattern (β : -1.2; 95% CI: -2.43, -0.13) were associated with fewer anxiety symptoms (150).

Difficulty conceiving.

One study (n = 458 participants) reported that higher adherence to a Mediterranean diet was associated with a lower risk of difficulty getting pregnant (i.e., improved fertility; OR: 0.56, 95% CI: 0.35, 0.95) (Supplemental Table 23) (146).

Postpartum overweight.

One study (n = 186 participants) observed no significant association between maternal diet and being overweight during postpartum (Supplemental Table 23) (60).

Postpartum weight retention.

Two studies (n = 47,197 participants) measured the association between maternal diet and postpartum weight retention. One study suggested no significant association (60). Another study found that a higher Healthy Eating Index score was inversely associated with weight retention 6 mo after delivery (OR: 0.94; 95% CI: 0.91, 0.96) (Supplemental Table 23) (151).

Child emotional dysregulation.

One study (n = 7814 participants) found that a maternal unhealthy dietary pattern was associated with child emotional dysregulation at 2 y of age (correlation coefficient: 0.024; $P \le 0.05$) (Supplemental Table 23) (127).

Forearm fracture in offspring.

One study (n = 53,922 participants) found no association between maternal dietary pattern in pregnancy and first forearm fracture in offspring (Supplemental Table 23) (126).

Hypospadias.

One study (n = 7928 participants) found that women who identified as vegetarian were more likely to give birth to a boy with hypospadias compared with omnivores (OR: 4.99; 95% CI: 2.10, 11.88) (Supplemental Table 23) (121).

Internalizing and externalizing problems in offspring.

Three studies (n = 53,653 participants) investigated the associations between maternal diet and internalizing and externalizing problems in the offspring (Supplemental Table 23). One study (n = 23,020 participants) indicated that higher intake of unhealthy foods during pregnancy was associated with increased child externalizing behaviors (intercept factor: 0.03, slope factor: -0.002; P < 0.01) (98). In another study (n = 3104 participants), maternal Mediterranean diet was negatively associated (OR: 0.90; 95% CI: 0.83, 0.97) and the traditional Dutch diet was positively associated (OR: 1.11; 95% CI: 1.03, 1.21) with child externalizing problems (140). Finally, Borge et al. (65) (n = 27,529 participants) reported that higher maternal diet quality score was inversely associated with child developmental outcomes.

Intrauterine growth restriction.

Two studies (n = 4019 participants) examined the association between maternal diet and intrauterine growth restriction (IUGR) (Supplemental Table 23). Hajianfar et al. (91) reported that higher adherence to a healthy dietary pattern (OR: 2.35; 95% CI: 1.54, 3.6) and Western dietary pattern (OR: 0.18; 95% CI: 0.11, 0.29) was associated with higher and lower incidences of IUGR, respectively. Timmermans et al. (143) reported that higher maternal adherence to a Mediterranean diet was associated with lower incidences of IUGR (OR: 0.34; 95% CI: 0.2, 0.6).

Low birth length and low birth head circumference.

One study (n = 812 participants) reported no association between maternal diet pattern (Western, traditional, and healthy) and low birth length and low birth head circumference (Supplemental Table 23) (91).

Neurodevelopmental disorders in offspring.

One study (n = 80,743 participants) found no association of maternal vegetarian diet during pregnancy and risk of neurodevelopmental disorders in the offspring (Supplemental Table 23) (107).

Rhinitis in offspring.

One study (n = 622 participants) found no association between maternal dietary pattern during pregnancy and odds of rhinitis in the offspring (Supplemental Table 23) (108).

Respiratory infection in offspring.

One study (n = 1376 participants) found no significant association between maternal diet during pregnancy and risk of respiratory infections in the offspring at age 3 (Supplemental Table 23) (106).

Substance-use disorders among adolescent offspring.

One study (n = 5228 participants) found that a "health conscious" diet during pregnancy was associated with increased risk of cannabis use (OR: 1.29; 95% CI: 1.14, 1.47), and a maternal vegetarian diet was associated with increased risk of alcohol (OR: 1.28; 95% CI: 1.17, 1.41), cannabis (OR: 1.42; 95% CI: 1.3, 1.55), and tobacco use (OR: 1.21; 95% CI: 1.1, 1.33) in offspring at the age of 15 years old (Supplemental Table 23) (94).

Publication bias and sensitivity analysis

Funnel plots were suggestive of publication bias in the analyses of dietary pattern and GDM, which was confirmed by Egger's test (P = 0.03). However, the trim-and-fill method was applied and results remained stable (OR: 0.51; 95% CI: 0.82, 1.23).

The sensitivity analysis revealed that the study by Tielemans et al. (142) was responsible for the heterogeneity for inadequate gestational weight gain ($I^2 = 51.8\%$) and removal of this study changed the estimates from nonsignificant to significant for the association between maternal healthy dietary pattern and lower risk of inadequate gestational weight gain (OR: 0.94, 95% CI: 0.9, 0.98; P = 0.003; $I^2 = 0.0\%$, *P*-heterogeneity = 0.48). Exclusion of studies by Zerfu et al. (154) and Navarro et al. (30) for the association between maternal healthy dietary pattern and birth weight in the offspring reduced heterogeneity ($I^2 =$ from 95.7% to 40.0%, *P*-heterogeneity = 0.06), with stability in the significance of pooled estimates; however, the association was weak (Hedges' g: 0.05, 95% CI: 0.01, 0.09).

Additionally, the results for preterm birth and hypertensive disorders of pregnancy were consistently significant when we restricted the meta-analysis to adjusted effect sizes only. The association between higher adherence to a healthy

Certainty of evidence

The GRADE certainty of evidence was moderate for obesity in offspring ($\oplus \oplus \oplus \bigcirc$); low ($\oplus \oplus \bigcirc \bigcirc$) for cesarean delivery, excessive and inadequate gestational weight gain, maternal hypertensive disorders, maternal depression, and FGR in length; and very low ($\oplus \bigcirc \bigcirc$) for all others (**Table 3**).

Discussion

In this comprehensive systematic review of prospective observational studies, we have summarized the evidence for associations between dietary patterns in pregnancy and adverse outcomes in mothers and offspring. Significant associations were found between higher adherence to a healthy diet and reduced risk of gestational hypertensive disorders, maternal depression, LBW, preterm birth, and higher gestational weight gain and birth weight. Higher maternal adherence to an unhealthy and a mixed diet was associated with a higher risk of gestational hypertension. The stratified analyses based on the types of healthy diet revealed that a higher Healthy Eating Index score was associated with a greater head circumference and reduced odds of LGA. Mediterranean and prudent dietary patterns were also associated with a reduced risk of SGA and preterm birth, respectively.

There have been previous meta-analyses investigating the effects of maternal diet in pregnancy and related outcomes (13, 32-37). A meta-analysis (2016) of 21 studies concluded that adherence to a healthy diet during pregnancy is significantly associated with a 22% lower odds of preeclampsia and GDM and a 25% lower risk of preterm birth (37). A meta-analysis (2017) of 25 studies showed that a healthy maternal diet is associated with higher birth weight and lower risk of preterm birth, while unhealthy diets were associated with lower birth weight (36). A recent metaanalysis showed that vegan mothers were more likely to give birth to LBW infants compared with omnivorous mothers (35). A vegetarian diet may not provide some of the nutrients, such as vitamin B-12 and zinc, that are associated with LBW infants (161), although most of the included studies were from low-income countries, which may impact diet quality. Furthermore, gestational weight gain and maternal BMI are important predictors of birth weight and were not considered in the study. Our meta-analysis extends these findings to synthesize prospective associations of both maternal diet and maternal and offspring outcomes. The importance of dietary exposures in early pregnancy for maternal and fetal health is generally well accepted (162,

Outcome	Studies, <i>n</i> (reference)	Risk of bias ²	Inconsistency ³	Indirectness ⁴	Imprecision ⁵	Publication bias	Certainty <mark>5</mark>
Maternal outcomes							
Cesarean delivery	7 (14, 59, 87, 91, 137, 139, 141)	Very serious	Not serious	Not serious	Not serious	Not assessed ⁶	@ @ O Low
Excessive gestational weight gain	7 (26, 60, 61, 78, 139, 141, 142)	Serious	Serious ⁴	Not serious	Not serious	Not assessed ⁶	@ @ O Low
Gestational diabetes mellitus	25 (24, 62, 63, 75–77, 87, 90, 92, 93, 95, 96, 101, 112,	Very serious	Very serious	Serious	Not serious	Serious ⁷	OOO Very low
Gestational hypertensive disorders	1.5, 1.9, 1.29, 1.50, 1.50, 1.50, 1.45, 1.46, 1.52–1.57 17 (14. 15. 22. 66, 69. 78. 88. 90. 92. 95. 97. 137.	Serious	Not serious	Serious	Not serious	Not serious	@⊕⊖⊖ Low
	144, 147, 157))
Gestational weight gain	10 (24, 27, 31, 82, 87, 113, 137, 142, 154, 157)	Very serious	Very serious ⁴	Not serious	Not serious	Not serious	@OOO Very low
Inadequate gestational weight gain	5 (26, 61, 78, 139, 142)	Serious	Serious	Not serious	Not serious	Not assessed ⁶	@ @ O Low
Maternal depression	3 (68, 100, 123)	Serious	Serious	Not serious	Not serious	Not assessed ⁶	@ @ O Low
Offspring outcomes							
Birth weight	21 (24–28, 30, 31, 66, 69, 71, 78, 87, 125, 128, 131,	Very serious	Serious ⁴	Serious	Not Serious	Not serious	⊕⊖⊖⊖ Very low
	137, 139, 143, 154)						
Birth length	9 (27, 30, 69, 78, 87, 131, 139)	Serious	Serious	Serious	Not serious	Not assessed ⁶	@OOO Very low
Birth head circumference	9 (27, 30, 69, 78, 131, 139, 143)	Serious	Serious	Serious	Not serious	Not assessed ⁶	@OOO Very low
Fetal growth restriction in weight	3 (69, 131)	Serious	Very serious	Serious	Not serious	Not assessed ⁶	@OOO Very low
Fetal growth restriction in length	3 (69, 131)	Serious	Not serious	Serious	Not serious	Not assessed ⁶	⊕⊕⊖⊖ Low
Fetal growth restriction in head circumference	3 (69, 131)	Serious	Serious	Serious	Not serious	Not assessed ⁶	@OOO Very low
Large for gestational age	6 (26, 59, 78, 128, 137, 157)	Serious	Very serious	Serious	Not serious	Not assessed ⁶	@ OOO Very low
Preterm birth	12 (23, 25, 29–31, 59, 80, 90, 91, 95, 154, 157)	Serious	Very serious	Not serious	Not serious	Not serious	@ OOO Very low
Low birth weight	7 (26, 30, 78, 90, 91, 104, 154)	Very serious	Not serious	Serious	Not serious	Not assessed ⁶	@OOO Very low
Small for gestational age	8 (26, 59, 66, 78, 128, 137, 143, 157)	Serious	Very serious	Serious	Not serious	Not assessed ⁶	@OOO Very low
Stillbirth	3 (86, 91, 154)	Very serious	Very serious	Serious	Not serious	Not assessed ⁶	@ OOO Very low
Obesity in offspring	4 (30, 58, 74, 84)	Serious	Not serious	Not serious	Not serious	Not assessed ⁶	⊕⊕⊕⊖ Moderate

TABLE 3 GRADE evidence profile for prospective cohort studies of maternal dietary pattern and perinatal outcomes¹

Very low quality: We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect. GRADE, Grading of Recommendations Assessment, Development and Evaluation; ROBINS-E, Risk limited; the true effect may be substantially different from the estimate of the effect.

Of Bias IN observational Studies of Exposures.

²Risk of bias assessed using ROBINS-E tool. Possibility of residual confounding always must be considered in observational studies. Main study limitations included incomplete adjustment for confounders and measurement bias related to outcome assessment. Downgrade 2 levels when > 75% of included studies for each outcome rated serious risk of bias.

 3 Downgrade 1 level if l^2 was 50% to 75%, and 2 levels if l^2 was 75% to 100%.

⁴Downgrade 1 level when most of the studies did not directly measure the outcomes.

 5 No downgrade for imprecision because of >2000 participants for each outcome.

No downgrade for publication bias, as publication bias could not be assessed due to lack of power for assessing funnel plot asymmetry and small study effects (< 10 cohorts included in our meta-analysis). ^{$^{\prime}$}Downgrade 1 level for publication bias (P = 0.03). 163). Maternal dietary pattern, an overall measurement of food and nutrient intake, influences the health of offspring (162). It is well documented that dietary patterns emphasizing higher amounts of fruits, vegetables, whole grains, and fish and de-emphasizing intakes of processed foods and high-fat and high sugary foods are associated with lower incidences of chronic diseases, inflammation, and cardiovascular diseases (164, 165). A diet rich in antioxidants is associated with lower homocysteine concentrations, which is a known risk factor for pre-eclampsia (166). Furthermore, dietary patterns rich in vitamins and antioxidants may protect against postpartum depression through attenuating inflammatory markers in the brain (68). Such antiinflammatory diets can also improve blood glucose control and antioxidant capacity (167) that are related to preterm birth (168, 169).

Our results revealed that high adherence to a healthy diet is associated with greater gestational weight gain and lower risk for both excessive and inadequate gestational weight gain. This result is in contrast with some previous findings (24, 142, 157, 170). We interpret this finding to mean that healthy diets likely promote gestational weight gain within recommended ranges. Alternatively, prepregnancy BMI was lower among those women with the highest adherence to a healthy diet (31, 113, 157). Therefore, it is plausible that women who eat healthier are leaner, and although they gain more absolute weight during pregnancy, their gestational weight gain remains within Institute of Medicine recommendations.

High adherence to healthy diets during pregnancy was associated with higher birth weights, which may be due to higher fat-free mass accrual (171–174). Previous studies have shown that poor diet quality during pregnancy is associated with higher neonatal adiposity, independent of maternal weight and energy intake (132, 139). Although we could not specify if this higher birth weight would consistently result in a classification of LGA, the lack of association with macrosomia or LGA suggests that the infants' mass accrual is within the normal range. However, more research is needed to fully understand these results.

As with any review of observational studies, an important issue in our study is separating associations of diet from those induced by residual confounders. In our sensitivity analysis, which only included the most-adjusted models (13 studies), the associations between maternal healthy diet and risk of GDM were stronger. Maternal age, BMI, physical activity, and familial history of diabetes are known risk factors for GDM (175, 176). These factors were taken into account in most studies that reported adjusted effect sizes. The results of the sensitivity analysis for gestational hypertensive disorders and preterm birth were the same as those without adjustments, which indicates that maternal diet is associated with these events independent of measured confounders.

Our review has several strengths. First, we have evaluated the methodological quality of the studies and assessed the certainty of evidence for these associations using GRADE. Second, we have limited this review to prospective studies, which ensures that diet reporting is not influenced by adverse events, therefore minimizing recall bias. Third, a comprehensive search strategy was developed; thus, we are confident that we captured all relevant studies. Fourth, the wide range of ethnicities with large sample sizes increases the generalizability of our results.

Our study also has some limitations. First, diet is a set of several exposures that are strongly intercorrelated. For instance, individuals who adhere to a healthy diet are typically more active, leaner, and engage in several healthy behaviors, which makes it difficult to ascribe an effect to a specific behavior. Second, we were limited by the handful of dietary patterns described/derived by the included studies. Thus, we must acknowledge that what is defined as a "healthy" or "prudent" pattern based on current knowledge is likely to evolve as knowledge of nutrition and health expands. Thus, these labels are subjective. Third, we can never rule out that our findings are due to residual confounders measured or unmeasured. However, we were unable to directly adjust our complete set of analyses for a standard set of confounders, which would have been an approach to deal with this limitation. Moreover, it should be noted that, although adjustment for multiple tests are not routinely used in systematic reviews and not recommended in general, issues of multiplicity might be important in systematic reviews as much as other research types. It is recommended that planning of the statistical testing of hypotheses (including any adjustments for multiple testing) should be done at the design stage of original articles. However, this is difficult for systematic reviews when it is not clear which outcomes and which measures will be available from eligible studies, such as the present review. It is important to note that one in 20 independent statistical tests will be statistically significant at the 5% significance level. Therefore, the statistically significant findings should be interpreted with caution. A fourth major limitation of the present study is that we subjectively categorized diet as "healthy," "unhealthy," and "mixed" dietary patterns, as described and presented by the primary study. Since this classification is highly researcher-specific, variability in classification of diets may lead to misclassification, thus biasing our results towards the null. Finally, in dietary pattern analyses, the names chosen for the diet are user-generated and may not be comparable from study to study. Although a diet is judged by the degree of adherence to the overall diet, not a specific food, loading unhealthy foods into a healthy diet can also alter the findings.

Although observational studies cannot provide highquality evidence for a causal relation, we used the GRADE framework to assess our confidence in the evidence for a causal relation between exposures of an outcome. Overall, 5% of associations were rated as moderate confidence, 31.5% as low, and 63% as very low. A common limitation that lowered our confidence in findings due to comparability issues included failure to account for demographic factors as potential confounders. It is well established that sociodemographic and other behavioral factors, such as physical activity, smoking, and maternal obesity, among others, are associated with adverse events of pregnancy (177–179). Some studies controlled for several confounders using regression-based approaches, whereas others simply counted the number of events or means in categories of the diet adherence, without adjustment. In addition, exposure measurement bias-derived from imprecise exposure measurement tools-may be present. Most of the reviewed studies relied on FFQs to assess the dietary intakes (60 out of 66 studies). The FFQ has been extensively used in nutrition epidemiology studies and has been shown to be a reliable and valid tool in general adult populations (180). However, this tool is subject to measurement error because it fails to collect detailed information about food preparation and cooking methods and is dependent on memory-based recall (181), which reduced the overall quality of studies. Novel technology methods such as web-based dietary assessment tools (182) or image-based dietary food records may provide more detailed information and have advantages over the traditional methods (183).

We observed high between-studies heterogeneity for many analyses, which remained after sensitivity analysis. We acknowledge that some degree of heterogeneity is to be expected because of diverse baseline characteristics of the participants, various approaches of dietary pattern identification, varying outcome assessment methods (selfreported or medical records, and/or measured), and different cutoffs for definition of outcomes, such as GDM, gestational hypertension, and preterm birth. However, we were not able to perform subgroup analyses based on several prespecified effect modifiers, some of which may have influenced the estimates of association (e.g., maternal age, ethnicity, and prepregnancy weight) and downgrade the evidence for inconsistency. Serious indirectness was observed in some analyses because the outcome was measured indirectly in most of the studies, although we did not downgrade the evidence for imprecision due to the large number of included participants. All of these limitations led to a moderate to very low certainty of evidence; this means that the observed associations may differ if high-quality studies were included in the analysis.

Conclusions

Overall, a healthy maternal diet was associated with a lower incidence of gestational hypertension, maternal depression, LBW, preterm birth, and with increased gestational weight gain and birth weight. A maternal unhealthy diet was associated with increased risk of gestational hypertension. As the quality of evidence was low or very low for all outcomes, it is recommended that future studies examine the effect of maternal dietary patterns on adverse events using rigorous methodological approaches.

Acknowledgments

The authors' responsibilities were as follows—AS-A and SS: conceived the study idea; SA, SS, and OT: conducted the

literature search and performed data extraction and quality assessment; SA and AS-A: analyzed the data; SA: wrote the first draft of the manuscript; RJdS and SCF: provided critical review; AS-A: had primary responsibility for final content; and all authors: read and approved the final manuscript.

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