Maternal Dietary Patterns and Birth Outcomes: A Systematic Review and Meta-Analysis

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ABSTRACT

Findings on the relations of maternal dietary patterns during pregnancy and risk of preterm birth and offspring birth size remain inconclusive. We aimed to systematically review and quantify these associations. We searched MEDLINE, Embase, CENTRAL, and CINAHL up to December 2017. Three authors independently conducted a literature search, study selection, data extraction, and quality assessment. Summary effect sizes were calculated with random effects models and studies were summarized narratively if results could not be pooled. We included 36 studies and pooled results from 25 observational studies (167,507 participants). Two common dietary patterns—"healthy" and "unhealthy"—were identified. Healthy dietary patterns—characterized by high intakes of vegetables, fruits, wholegrains, low-fat dairy, and lean protein foods—were associated with lower risk of preterm birth (OR for top compared with bottom tertile: 0.79; 95% CI: 0.68, 0.91; $I^2 = 32\%$) and a weak trend towards a lower risk of small-for-gestational-age (OR: 0.86; 95% CI: 0.73, 1.01; $I^2 = 34\%$). Only statistically data-driven healthy dietary patterns, and not dietary index-based patterns, were associated with higher birth weight (mean difference: 67 g; 95% CI: 37, 96 g; $I^2 = 75\%$). Unhealthy dietary patterns—characterized by high intakes of refined grains, processed meat, and foods high in saturated fat or sugar—were associated with lower birth weight (mean difference: −40 g; 95% CI: −61, −20 g; $I^2 = 0\%$) and a trend towards a higher risk of preterm birth (OR: 1.17; 95% CI: 0.99, 1.39; $I^2 = 76\%$). Data from observational studies indicate that greater adherence to healthy dietary patterns during pregnancy is significantly related to lower risk of preterm birth. No consistent associations with birth weight and small- or large-for-gestational-age were observed. *Adv Nutr* 2019;10:685–695.

Keywords: maternal diet, dietary pattern, diet quality, preterm birth, birth weight

Introduction

Globally, 11% of births are preterm (<37 weeks of gestation) (1), 15–20% are born low birth weight (LBW; birth weight <2500 g) (2), and the prevalence of macrosomia (birth weight >4000 g) and large-for-gestational-age (LGA; birth weight >90th percentile for gestational age) have increased by 15–25% in the last few decades (3). LBW can result from preterm birth and/or fetal growth restriction (FGR; birth weight <10th percentile of estimated birth weight), whereas small-for-gestational-age (SGA; birth weight <10th percentile for gestational age) is a common proxy for FGR (4). Being born too soon, too small, or too large are associated with neonatal mortality, morbidity, impaired development, and chronic diseases later in life (1–4).

Maternal nutrition during pregnancy is a major determinant for birth outcomes and, consequently, offspring health outcomes in later life (5). Examining dietary patterns has emerged as a more holistic approach for capturing the complex interactions among nutrients and foods—congruent with recent United States Dietary Guidelines (6). Dietary patterns can be index-based—assessed a priori with use of dietary indices to measure adherence to a predefined dietary pattern, or data-driven—assessed a posteriori where dietary patterns are statistically derived based on dietary intake reported by a population (7).

Associations between maternal dietary patterns and infant birth outcomes have been summarized in a narrative review (8) and a systematic review (9), which had only considered

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Supplemental Material 1, Supplemental Tables 1–7, and Supplemental Figures 1–2 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.

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Abbreviations used: FGR, fetal growth restriction; LBW, low birth weight; LGA, large-for-gestational-age; NOS, Newcastle-Ottawa scale; SGA, small-for-gestational-age.

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publications up to 2009. These reviews had only searched a single database, PubMed (8, 9). To our knowledge, comprehensive and up-to-date evidence has not been systematically synthesized and no meta-analysis has been performed to quantify these associations. In this study, we systematically reviewed the current literature and conducted meta-analysis on the associations of maternal dietary patterns during pregnancy with risk of preterm birth and offspring birth size among healthy pregnant women.

Methods

We followed the guidelines of preferred reporting items for systematic reviews and meta-analyses (PRISMA) (10). Literature search, study selection, data extraction, and quality assessment were independently conducted by 3 authors (A-RC and CHW or JSL). Disagreements were resolved by discussion with a fourth investigator (MF-FC).

Literature search

Literature searches in MEDLINE, Embase, CENTRAL, and CINAHL were conducted through December 2017, based on the search strategy detailed in **Supplemental Material 1**. In brief, keywords and index terms such as dietary pattern, diet quality, preterm birth, birth weight, fetal growth, and their variants were used to search for studies that examined the associations of maternal dietary patterns during pregnancy with risk of preterm birth and infant birth size. The reference list of relevant studies and reviews were also examined for additional studies. When necessary, we contacted respective authors to retrieve additional information.

Study selection

The titles and abstracts were screened and included if they were *1*) peer-reviewed publications of intervention or observational studies; *2*) studied a population of generally healthy pregnant women with no pre-existing health conditions reported; *3*) examined index-based or data-driven dietary patterns as exposure or a whole diet intervention during pregnancy; and *4*) if the outcomes of interest were related to preterm birth, LBW, FGR, SGA, LGA, macrosomia, or birth weight as a continuous variable. Studies were excluded if they focused on a single dietary component intervention (e.g., low glycemic index diet) or mixed strategies (e.g., combined diet and exercise intervention). The inclusion or exclusion criteria for the selection of studies are detailed in Supplemental Material 1. Non-English language articles were not considered as they could not be translated into English. Titles and abstracts of articles were first screened for eligibility based on (in hierarchical order) study population, exposure, and the outcome of interest. The full texts of potentially relevant articles were retrieved and evaluated to give the final included studies.

Data extraction

The following information was extracted with the use of a standardized data collection form: study characteristics, population characteristics, exposure assessment, study outcomes, maximally adjusted effect estimates, and their corresponding SE or CI, and adjusted covariates.

Assessment of study quality

We evaluated the quality of included observational studies with the Newcastle-Ottawa quality-assessment scale (NOS) (11) (**Supplemental Table 1**). Each study was given a score from 0 (low quality) to 9 (high quality), based on 3 subscales: *1*) selection, *2*) comparability, and *3*) outcome (for cohort studies) or exposure (for case-control studies). Studies that scored $\geq$7 were defined as high quality (12). The inter-rater agreement for each subscale was reasonably good (intraclass correlation coefficient values between 0.75 and 0.93) (13).

Data synthesis and analysis

Data-driven and index-based dietary patterns, regardless of their terminologies, were grouped and meta-analyzed if they shared similar constituent foods (**Supplemental Table 2**). Data-driven dietary patterns are statistically derived with methods such as principal component analysis, exploratory factor analysis, or cluster analysis, whereas index-based dietary patterns are dietary indices constructed based on multiple food-related and nutrient-related dietary components. Two common dietary patterns were identified: "healthy"—characterized by high intakes of $\geq$3 key components of the healthy eating pattern described by the 2015 United States Dietary Guidelines (6): vegetables, fruits, wholegrains, low-fat dairy, or lean protein food (i.e., seafood, lean meat/poultry, eggs, legumes, nuts/seeds, and soy products); and "unhealthy"—characterized by high intake of refined grains, processed meats, and foods high in saturated fat or sugar ($\geq$3).

If multiple healthy dietary patterns were examined in the same cohort (14–20), for example, Alternate Mediterranean diet and Alternate Healthy Eating Index for Pregnancy from the Infant Feeding Practices Study II (15), results from the publication with the largest sample size or the pattern with the most number of healthy foods (in the same publication) were chosen to be included in the main analysis. Any other patterns were then considered in sensitivity analysis by including (1 pattern at a time) their results from the same cohort. This was done similarly for unhealthy dietary patterns, such as "cheese dish, French fries, and burger" and "fried chicken, collard green, and sausages" patterns from the Pregnancy, Infection and Nutrition cohort (20).

Studies were summarized narratively if (i) reported estimates were referenced to other dietary patterns (21–23), for example, the healthy dietary pattern was compared with the "wheat products" pattern in the Osaka Maternal and Child Health Study (23); (ii) the study had unconventional outcome comparison, such as LBW with reference to infant overweight ($>$3500 g) (24); (iii) the study had dietary patterns that could not be categorized as healthy or unhealthy (19, 25–29), for example, "vegetarian" (25) and a "fruits, nuts, and Cantonese desserts" pattern (26); and (iv) the studies were based in resource-poor, low-income settings, which were not pooled because mothers were more likely to be undernourished and this may have biased the pooled estimates away from the null (30, 31). Reasons for exclusion and inclusion are detailed in Supplemental Table 2.

Random-effects models were used to calculate summary ORs and 95% CI for the association between healthy and unhealthy dietary patterns with infant birth outcomes, namely risk of preterm birth, risk of SGA/FGR/LBW, and risk of LGA; whereas regression coefficients were summarized for the association between healthy and unhealthy dietary patterns with birth weight with use of maximally adjusted effect estimates. Dietary patterns were reported either as continuous (raw or standardized), or categories of index-based scores or data-driven factor scores. To allow comparison across studies, effect estimates for each study were transformed to the same scale according to previously described methods (32, 33). The transformed estimates represent the risk or effect size in the top tertile of dietary pattern scores, compared with the bottom tertile. In a normal distribution, the means of the top and bottom tertile, quartile, and quintile lie 2.18, 2.54, and 2.80 SD apart, respectively; therefore, the log ORs or regression coefficients and corresponding SE were multiplied by (i) 2.18, for conversion from per SD to tertile, (ii) 2.18/2.54, for conversion of quartile to tertile, (iii) 2.18/2.80, for conversion of quintile to tertile, or (iv) $2.18/x$, for conversion of other categories to tertile, where x is the difference in mean dietary pattern scores (in SD units) between the highest and lowest category. To evaluate whether the conversion may have affected the results, we performed sensitivity analysis on the unconverted data.

Cochran's Q test (*P*-heterogeneity) and I^2 statistics were used to estimate the extent of heterogeneity between studies. Potential sources of heterogeneity were further explored by subgroup and meta-regression analysis by different study-level characteristics (**Table 1**) (34). Publication bias was assessed by visual inspection of a funnel plot and Egger's test (34). To evaluate the influence of an individual study on the pooled estimate, we performed sensitivity analysis by excluding 1 study at a time. We also limited the analysis to high-quality studies (NOS score ≥7) to examine the robustness of our results.

All analysis was conducted in STATA 14.0 (StataCorp) and 2-tailed P values <0.05 were considered statistically significant.

Results

Search results

The study selection process is shown in **Figure 1**. We identified 2853 unique publications from the databases and excluded 2052 after assessing titles and abstracts. Full texts of 87 potentially eligible articles were retrieved for further evaluation. We additionally identified 3 articles from the reference list of relevant studies and reviews. After detailed evaluation, 36 articles were included in this review (14–31, 35–52). Among which, there was only 1 randomized controlled trial (52), hence only observational studies were included in the meta-analysis.

Characteristics of included studies

The characteristics of observational studies are presented in **Supplemental Table 3**. They were published from 1995 to 2018 and the majority were prospective cohorts ($n = 32$) (14–27, 29, 31, 36–47, 49, 51), with the rest having case–control (35), cross-sectional (50), retrospective (28, 48), and mixed retrospective and prospective cohort design (30). Sample sizes ranged from 35 to 72,072, with participants of mean age 21–33 y and prepregnancy BMI 20–30 kg/m^2. Nineteen studies were based in Europe (16–19, 22, 24, 25, 37–40, 43–45, 48–50), 10 in America (15, 20, 21, 27–29, 42, 46, 47, 51), 4 in Asia (14, 23, 26, 41), 2 in Africa (30, 31), and 2 in Australasia (35, 36). Maternal diets were typically assessed by FFQs (number of items ranged from 29 to 360) (15–26, 28–30, 35–40, 43–50), but 6 studies used 24-h recalls or 3-d food diary (14, 27, 31, 41, 42, 51). Twenty-two studies evaluated maternal diet during the first and/or second trimester (14, 16–22, 26, 35, 37–41, 43–47), 5 in the third trimester (15, 25, 29, 50, 51), and 10 throughout pregnancy (23, 24, 27, 28, 30, 31, 36, 42, 48, 49). Twenty-one studies examined index-based dietary patterns (15–18, 24, 31, 36, 37, 41–51), whereas 15 derived dietary patterns through data-driven approaches (14, 19, 21–23, 25–30, 35, 38–40); 1 study used both approaches (20). Among studies that used data-driven dietary patterns, 8 were derived with factor analysis (14, 20–22, 28–30, 40), 4 with principal component analysis (19, 25, 35, 38), 2 with cluster analysis (23, 26), and the rest with reduced rank regression (27) and logistic regression (39). The studies are commonly adjusted for prepregnancy BMI, maternal age, and smoking during pregnancy (**Supplemental Tables 4–6**). All studies except for 5 (24, 25, 28, 48, 49) were of high quality (NOS score ≥7) (Supplemental Table 1).

Preterm birth

In total, there were 11 studies with preterm birth as outcome measure, of which 6 reported on healthy dietary patterns (114,431 observations) (20, 36, 37, 41, 44, 48) and 3 on unhealthy dietary patterns (129,092 observations) (19, 20, 38). When results were pooled, pregnant women in the top tertile of healthy dietary patterns had a lower risk of preterm birth compared to the bottom tertile (OR: 0.79; 95% CI: 0.68, 0.91; $I^2 = 32\%$; *P*-heterogeneity = 0.19; **Figure 2**). In contrast, there was a trend towards higher risk of preterm birth in the top compared with the bottom tertile of unhealthy dietary patterns (OR: 1.17; 95% CI: 0.99, 1.39; $I^2 = 76\%$; *P*-heterogeneity = 0.02; Figure 2). There was no evidence of heterogeneity between subgroups (Table 1).

In the randomized controlled trial that was not included in the meta-analysis (52), a reduction in preterm birth risk was found in the intervention group encouraged to adopt the healthy dietary pattern. Similarly, adherence to the healthy dietary pattern in a rural, low-income setting in Ethiopia was associated with lower risk of preterm birth (31).

Birth weight

Among a total of 21 studies examining birth weight as an outcome, 13 reported on healthy dietary patterns (25,499

TABLE 1 Stratified meta-analysis of maternal healthy dietary patterns and infant birth outcomes[1]

		Preterm birth					Birth weight, g					SGA				
Characteristics		***n*[2]**	**OR (95% CI)**	***I*^{2}, %**	***P*[3]**	***P*[4]**	***n*[2]**	***β* (95% CI)**	***I*^{2}, %**	***P*[3]**	***P*[4]**	***n*[2]**	**OR (95% CI)**	***I*^{2}, %**	***P*[3]**	***P*[4]**
All studies	—	6	0.79 (0.68, 0.91)	32	0.19		13	− 1.0 (−36, 34)	85	<0.001		10	0.86 (0.73, 1.01)	34	0.14	
Geographic region	—	—	—	—			—	—	—			—	—	—		
Europe	—	3	0.86 (0.77, 0.97)	14	0.31	0.12	7	16 (−34, 67)	83	<0.001	0.44	5	0.93 (0.70, 1.23)	49	0.10	0.22
Non-Europe	—	3	0.65 (0.50, 0.84)	0	0.83		6	− 22 (−74, 30)	84	<0.001		5	0.77 (0.63, 0.95)	0	0.52	
Study population	—	—	—	—			—	—	—			—	—	—		
<1000	—	1	0.69 (0.47, 1.02)	—		0.62	6	− 38 (−108, 32)	85	<0.001	0.26	4	1.12 (0.83, 1.50)	0	0.48	0.10
≥1000	—	5	0.80 (0.68, 0.94)	36	0.18		7	20 (−27, 66)	86	<0.001		6	0.77 (0.63, 0.95)	45	0.11	
Age[5], y	—	—	—	—			—	—	—			—	—	—		
<30	—	3	0.89 (0.81, 0.97)	0	0.37	0.24	5	30 (−9.1, 70)	81	<0.001	0.31	3	0.99 (0.49, 1.99)	61	0.08	0.46
≥30	—	3	0.72 (0.59, 0.87)	0	0.46		8	− 26 (−84, 32)	85	<0.001		7	0.85 (0.73, 0.98)	25	0.24	
Prepregnancy BMI[5], kg/m^2	—	—	—	—			—	—	—			—	—	—		
<25	—	5	0.80 (0.69, 0.93)	34	0.19	0.45	9	8.5 (−36, 53)	84	<0.001	0.49	7	0.89 (0.73, 1.08)	44	0.10	Ref.
≥25	—	1	0.58 (0.30, 1.13)	—			4	− 31 (−114, 52)	89	<0.001		2	0.77 (0.53, 1.13)	0	0.47	0.61
Not reported	—	—	—	—			—	—	—			1	0.49 (0.19, 1.25)	—		0.33
Pregnancy period	—	—	—	—			—	—	—			—	—	—		
1st and/or 2nd trimester	—	4	0.82 (0.70, 0.95)	38	0.18	0.37	7	11 (−31, 53)	71	0.01	Ref.	7	0.86 (0.70, 1.05)	49	0.07	Ref.
3rd trimester	—	—	—	—			3	− 20 (−154, 114)	94	<0.001	0.73	1	0.93 (0.49, 1.76)	—		0.86
Throughout	—	2	0.66 (0.47, 0.93)	0	0.66		3	− 36 (−137, 64)	87	<0.001	0.49	2	0.78 (0.40, 1.52)	40	0.20	0.87
Dietary pattern	—	—	—	—			—	—	—			—	—	—		
Data-driven	—	—	—	—			3	67 (37, 96)	75	0.02	0.04	2	0.83 (0.57, 1.20)	42	0.19	0.80
Index-based	—	6	0.79 (0.68, 0.91)	32	0.19		10	− 30 (−73, 13)	73	<0.001		8	0.87 (0.70, 1.06)	36	0.14	
Outcomes	—	—	—	—			—	—	—			—	—	—		
SGA	—	—	—	—			—	—	—			5	0.91 (0.84, 0.97)	1.4	0.40	Ref.
LBW	—	—	—	—			—	—	—			1	0.49 (0.19, 1.25)	—		0.35
FGR	—	—	—	—			—	—	—			4	0.96 (0.58, 1.58)	62	0.05	0.76
Adjustment for confounders	—	—	—	—			—	—	—			—	—	—		
Age	Yes	4	0.77 (0.61, 0.97)	48	0.12	0.88	9	− 14 (−55, 27)	81	<0.001	0.45	8	0.89 (0.80, 0.99)	6	0.38	0.72
	No	2	0.76 (0.62, 0.95)	0	0.55		4	30 (−32, 92)	83	0.001		2	1.09 (0.43, 2.76)	83	0.02	
Parity	Yes	5	0.80 (0.68, 0.94)	36	0.18	0.62	5	− 36 (−107, 36)	84	<0.001	0.32	8	0.83 (0.71, 0.97)	28	0.21	0.15
	No	1	0.69 (0.47, 1.02)	—			8	23 (−12, 59)	80	<0.001		2	1.29 (0.65, 2.55)	51	0.16	
Education	Yes	5	0.76 (0.62, 0.93)	43	0.13	0.84	3	1.3 (−37, 40)	0	0.68	0.90	7	0.93 (0.79, 1.09)	17	0.30	0.08
	No	1	0.80 (0.62, 1.03)	—			10	− 2.6 (−44, 39)	88	<0.001		3	0.70 (0.55, 0.90)	0	0.39	
Income	Yes	3	0.73 (0.61, 0.89)	0	0.56	0.43	5	0.8 (−48, 50)	65	0.02	0.87	3	0.75 (0.51, 1.11)	20	0.29	0.45
	No	3	0.81 (0.64, 1.02)	38	0.20		8	− 2.7 (−48, 43)	89	<0.001		7	0.89 (0.74, 1.06)	38	0.14	
BMI	Yes	5	0.80 (0.69, 0.93)	34	0.19	0.45	9	− 14 (−55, 27)	81	<0.001	0.45	6	0.89 (0.77, 1.01)	13	0.33	0.98
	No	1	0.58 (0.30, 1.13)	—			4	30 (−32, 92)	83	0.001		4	0.90 (0.56, 1.45)	58	0.07	
Energy intake	Yes	4	0.78 (0.63, 0.96)	48	0.13	0.83	8	− 11 (−69, 48)	88	<0.001	0.82	7	0.94 (0.78, 1.13)	27	0.22	0.07
	No	2	0.77 (0.61, 0.97)	0	0.39		5	10 (−38, 59)	81	<0.001		3	0.69 (0.54, 0.89)	0	0.74	
Physical activity	Yes	3	0.89 (0.81, 0.98)	0	0.38	0.11	3	− 22 (−54, 10)	0	0.79	0.70	2	0.80 (0.48, 1.34)	43	0.19	1.0
	No	3	0.72 (0.61, 0.86)	0	0.54		10	5.8 (−34, 46)	86	<0.001		8	0.86 (0.68, 1.07)	34	0.16	
Alcohol	Yes	1	0.76 (0.42, 1.35)	—		0.94	2	8.0 (−36, 52)	0	0.52	0.80	2	1.01 (0.68, 1.50)	0	0.74	0.50
	No	5	0.78 (0.66, 0.92)	45	0.13		11	− 3.8 (−43, 35)	87	<0.001		8	0.83 (0.68, 1.02)	47	0.07	

[1] Stratification is based on the characteristics of the included studies to provide sufficient statistical power for each subgroup analysis. FGR, fetal growth restriction; LBW, low birth weight; SGA, small-for-gestational-age.

[2] *n* represents the number of studies in the subgroup analysis.

[3] *P* values for heterogeneity within a subgroup from Cochran's Q test.

[4] *P* values for differences between groups from meta-regression.

[5] If data were not available, classification was based on the majority of the population (>50%).

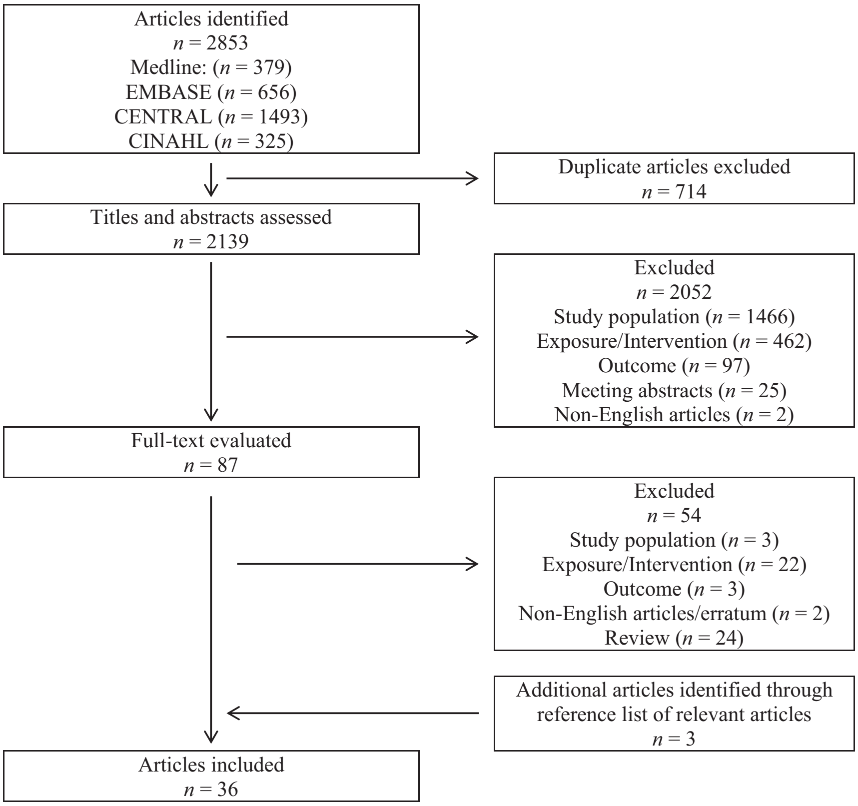

FIGURE 1 Flowchart of study selection.

observations) (15, 17, 25, 28, 39, 41–43, 46, 49, 51) and 3 reported on unhealthy dietary patterns (13,900 observations) (25, 28, 29). Adherence to healthy dietary patterns during pregnancy was not significantly associated with birth weight (mean difference in birth weight comparing the top with the bottom tertile of mothers: −1.0 g; 95% CI: −36, 34 g; $I^2 = 85\%$; P-heterogeneity <0.001; **Figure 3**), but unhealthy dietary patterns was associated with lower infant birth weight (mean difference: −40 g; 95% CI: −61, −20 g; $I^2 = 0\%$; P-heterogeneity = 0.90; Figure 3).

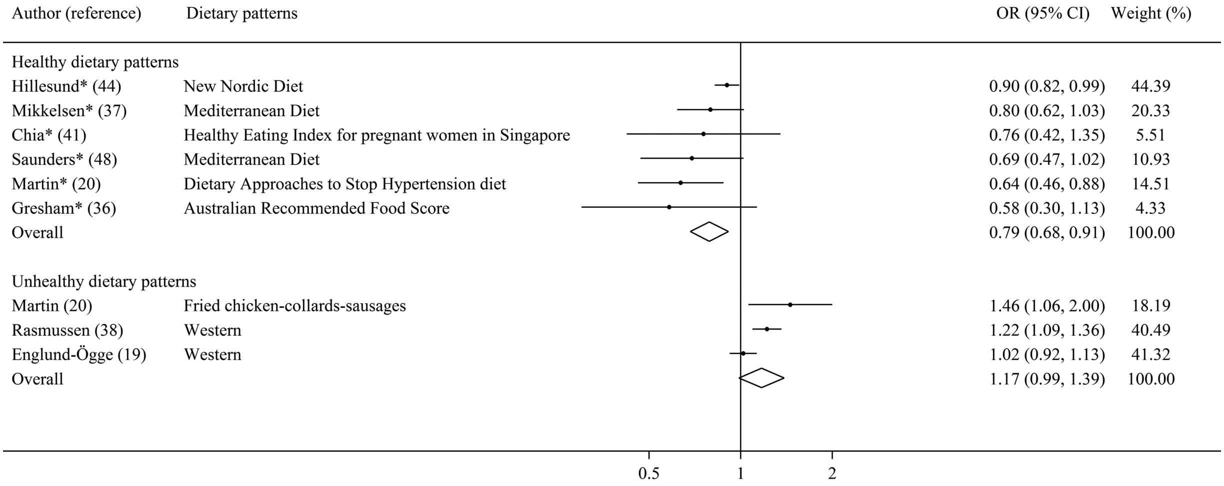

FIGURE 2 Associations between maternal dietary patterns and the risk of preterm birth. Black dots denote study-specific effect estimates comparing the lowest and highest tertiles of dietary patterns, horizontal lines denote 95% CI, diamonds indicate the pooled effect estimates with their corresponding 95% CI, and asterisks indicate index-based dietary patterns. Descriptions of dietary patterns are detailed in Supplemental Table 2.

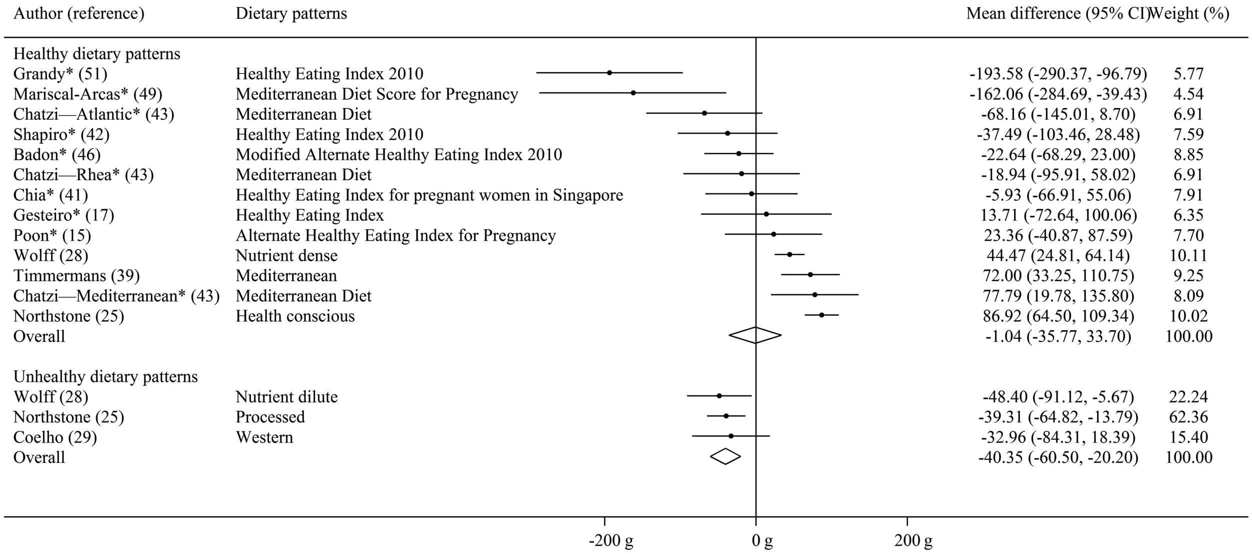

FIGURE 3 Associations between maternal dietary patterns and birth weights of offspring. Black dots denote study-specific effect estimates comparing the lowest and highest tertiles of dietary patterns, horizontal lines denote 95% CI, diamonds indicate the pooled effect estimates with their corresponding 95% CI, and asterisks indicate index-based dietary patterns. Descriptions of dietary patterns are detailed in Supplemental Table 2.

When we performed subgroup analysis to examine potential sources of heterogeneity, we detected differences in pooled effect estimates based on methods used to derive dietary patterns (P-difference = 0.04), such that significant direct association with birth weight was only observed in healthy dietary patterns that were data-driven (mean difference: 67 g; 95% CI: 37, 96 g; I^2 = 75%; P-heterogeneity = 0.02) but not for index-based dietary patterns (mean difference: −30 g; 95% CI: −73, 13 g; I^2 = 73%; P-heterogeneity <0.001) (Table 1). There is a suggestion of missing studies to the bottom right of the funnel plot (**Supplemental Figure 1**; Egger's test P = 0.004). However, it is unlikely that studies in the positive direction (i.e., a healthy dietary pattern increases birth weight) would not be published.

In 2 studies that were not included in the meta-analysis, the healthy dietary pattern in Japan (compared with the "wheat products" pattern—bread, confectionaries, juices, and soft drinks) was associated with higher birth weight (23). In contrast, the healthy dietary pattern in the United States (compared with the unhealthy dietary pattern) was not associated with birth weight (21).

Small-for-gestational-age/low birth weight/fetal growth restriction

Eighteen studies examined SGA/FGR/LBW as an outcome, of which 10 reported on healthy dietary patterns (77,308 observations) (14, 15, 35, 36, 43, 45, 47, 48). There was a weak trend towards lower risk of SGA/FGR/LBW in the top compared with the bottom tertile of healthy dietary patterns (OR: 0.86; 95% CI: 0.73, 1.01; I^2 = 34%; P-heterogeneity = 0.14; **Figure 4**). No evidence was detected of heterogeneity between subgroups (Table 1) and publication bias (**Supplemental Figure 2**; Egger's test P = 0.53). Only 1 study has investigated the association between unhealthy dietary pattern and SGA; they observed no significant association (35).

In 5 studies that were not pooled, the healthy dietary pattern in Spain was associated with lower risk of LBW with reference to infant overweight (24). Similarly in other studies, healthy dietary patterns—in comparison to the "wheat products" pattern in Japan, and unhealthy dietary pattern in Denmark—were associated with lower risk of SGA (22, 23). Adherence to healthy dietary patterns was associated with lower risk of LBW in resource-poor, low-income settings (30, 31).

Large-for-gestational-age

Five studies examined LGA as an outcome, of which 4 reported on healthy dietary patterns (70,190 observations) (14, 15, 45, 47). Adherence to healthy dietary patterns during pregnancy was not significantly associated with risk of LGA (OR: 1.03; 95% CI: 0.78, 1.38; I^2 = 70%; P-heterogeneity = 0.02; **Figure 5**). No studies have investigated the association with unhealthy dietary patterns.

Sensitivity analysis

Similar estimates were observed when we restricted our analysis to high-quality studies (NOS score $\geq$7) or omitting 1 study at a time. Alternately, including similar dietary patterns from the same cohort (14–20) or using unconverted data did not change our results significantly. The summary ORs ranged from 0.72 (95% CI: 0.61, 0.84) to 0.87 (95% CI: 0.80, 0.95) for healthy dietary patterns and risk of preterm birth when the various sensitivity analyses were performed. (**Supplemental Table 7**).

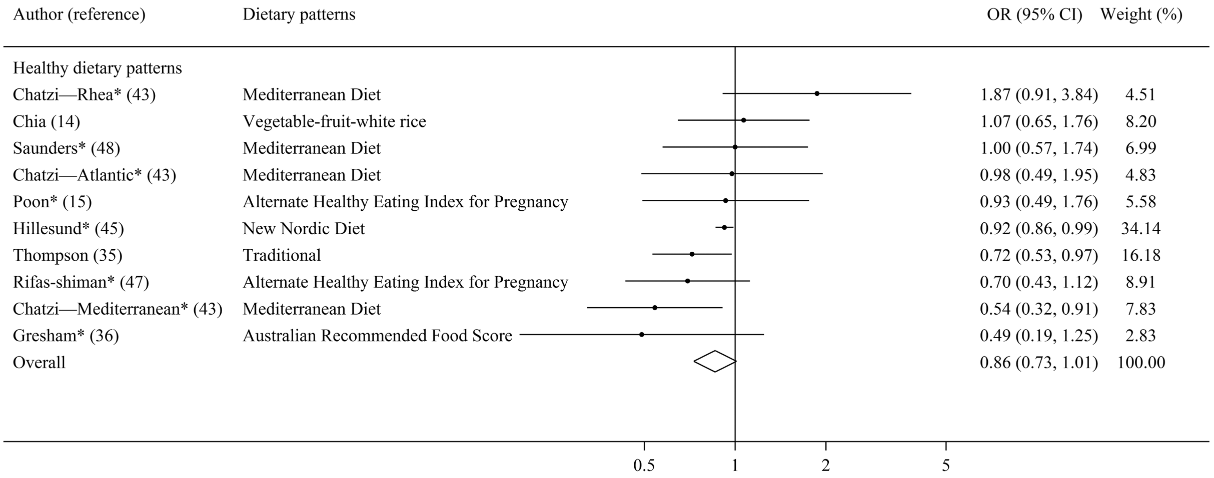

FIGURE 4 Associations between maternal healthy dietary patterns and the risk of small-for-gestational-age/fetal growth restriction/low birth weight. Black dots denote study-specific effect estimates comparing the lowest and highest tertiles of dietary patterns, horizontal lines denote 95% CI, diamonds indicate the pooled effect estimates with their corresponding 95% CI, and asterisks indicate index-based dietary patterns. Descriptions of dietary patterns are detailed in Supplemental Table 2.

Results of other dietary patterns

Higher adherence to the traditional pattern in Norway (potatoes and fish) was associated with lower risk of preterm birth (19). The vegetarian pattern in England (meat substitutes, pulses, nuts, and herbal tea) was associated with lower infant birth weight (25), whereas the protein-rich pattern (dairy desserts, low fat meat, and processed meats) (28), prudent pattern (dairy products, fruits, cracker, and meat) (29), and the eggs, starchy vegetables, fruits, and non-wholegrains pattern in the United States (27), fruits, nuts, and Cantonese desserts and varied patterns in China (compared with the traditional Cantonese pattern—cereals, eggs, and Cantonese soups) (26) were associated with higher birth weight.

Discussion

In this systematic review and meta-analysis of observational studies including 167,507 participants, we showed that adherence to “healthy” dietary patterns during pregnancy was associated with lower risk of preterm birth and a weak trend towards lower risk of SGA/FGR/LBW. Healthy dietary patterns that were data-driven, but not those index-based, were associated with higher birth weight. On the other hand, “unhealthy” dietary patterns (all data-driven) were associated with a lower birth weight and a trend towards higher risk of preterm birth. No significant associations were observed between dietary patterns and risk of LGA. To our knowledge, this is the first study to quantify the associations between maternal dietary patterns and birth outcomes with a meta-analysis and is also the most up-to-date and comprehensive systematic review on this topic.

We found that the top tertile of healthy dietary patterns was associated with a 21% lower risk of preterm birth, when compared with the bottom tertile. Inversely, there was a trend towards higher risk of preterm birth (17%) in the top compared with the bottom tertile of unhealthy dietary patterns. A previous meta-analysis on specific nutrients

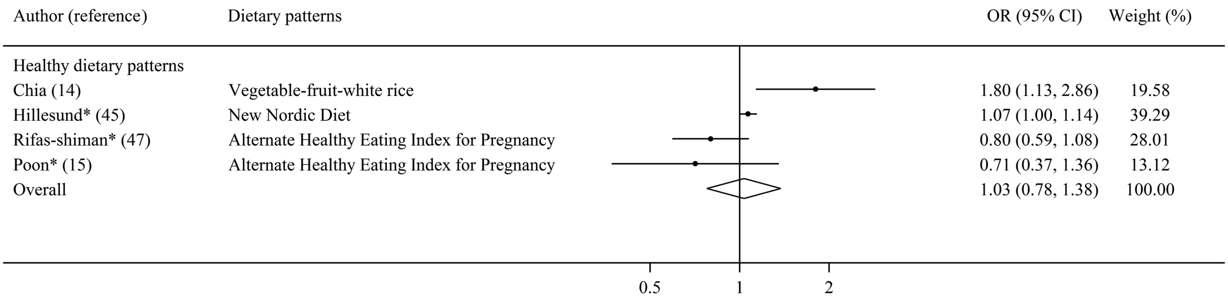

FIGURE 5 Associations between maternal healthy dietary patterns and the risk of large-for-gestational-age. Black dots denote study-specific effect estimates comparing the lowest and highest tertiles of dietary patterns, horizontal lines denote 95% CI, diamonds indicate the pooled effect estimates with their corresponding 95% CI, and asterisks indicate index-based dietary patterns. Descriptions of dietary patterns are detailed in Supplemental Table 2.

showed an 11% lower risk of preterm birth for a 1 SD increase in vitamin B-12 (53), whereas zinc supplementation resulted in a 14% reduction of preterm birth (primarily in low-income women) (54). With regards to the benefits of other vitamins (55–59), minerals (60, 61), multiple micronutrients (62), or energy and protein supplementation (63) on preterm birth, there is presently no current convincing supporting evidence. Our results suggest that the approach of examining whole diet patterns, beyond individual nutrients, may have substantial cumulative influence on risk of preterm birth.

Although the causes of preterm birth are multifactorial, many of the mechanisms are associated with increased inflammation (64, 65). Healthy dietary patterns characterized by high intake of foods with antioxidative and anti-inflammatory properties such as vegetables, fruits, wholegrains, fish, legumes and pulses, thus have the potential to reduce inflammation contributing to premature rupture of membranes that subsequently reduce risk of preterm birth (65, 66). On the contrary, foods from the unhealthy dietary patterns—processed meats, foods high in saturated fat or sugar—are associated with inflammation and preterm birth (67–69). Given the established associations of preterm birth with adverse health outcomes later in life (1), the shift from unhealthy to healthy eating patterns has important clinical significance.

With birth size, greater adherence to healthy dietary patterns derived through use of a data-driven approach, but not an index-based approach, was associated with higher birth weight. In contrast, unhealthy dietary patterns (all data-driven) were associated with lower birth weight. Commonly used data-driven methods such as factor analysis and principal component analysis may be more strongly related to birth weight than the index-based dietary patterns because they aim to maximize the explained variance in food intakes (70, 71). Furthermore, if certain dietary components of the index-based dietary pattern are not relevant to birth weight (72) or if most people are not meeting dietary recommendations, the association between the given index and birth weight could be attenuated (73).

Birth weight is influenced both by duration of gestation and rate of fetal growth (74). Given that maternal dietary patterns were associated with preterm birth, we recognize that the association between maternal dietary patterns and birth weight could be mediated by gestational age. The weak trends between maternal diet with risk of SGA/FGR and inconclusive association with LGA (because of high heterogeneity), which have considered the impact of gestational age in outcome definitions, further support this hypothesis.

To our knowledge, no meta-analysis has examined the association between dietary patterns and the risk of SGA. Previous nutrient-focused meta-analyses, which were mostly conducted in rural or low-income populations, showed that multiple micronutrients (62) or balanced protein energy supplementation (i.e., food/supplements in which protein provides <25% of energy) resulted in a reduction in risk of SGA whereas 1 trial of high-protein supplementation (>35% of energy from protein) was associated with an increased risk of SGA (63). In a meta-analysis of 6 multicenter trials, marine oil (ω-3 fatty acids) supplementation showed no effect on SGA in high-risk pregnancies (75). As we have excluded studies on high-risk pregnancies (see Study selection) and mothers with low nutritional status (see Supplemental Table 2), it precludes our ability to compare our results with these previous meta-analyses. Whether or not specific nutrients or general dietary patterns play a greater role on infant birth size warrants further investigation.

In the investigation of the extent of heterogeneity between studies, statistical heterogeneity was low for preterm birth ($I^2 = 32\%$) and SGA/FGR/LBW ($I^2 = 34\%$), but substantially high for birth weight ($I^2 = 85\%$) and LGA ($I^2 = 70\%$). Through meta-regression and subgroup analysis, none of the covariates were able to explain the observed heterogeneity. Therefore, the validity of the pooled estimates for birth weight and LGA is uncertain, as individual study results were inconsistent.

Some limitations are worth noting. First, although dietary patterns were grouped based on matching of similar constituent foods, clinical heterogeneity may be present because of differences in methods used to derive dietary patterns as well as the cultural differences in dietary habits. Defining dietary patterns with the same a priori scoring or employing confirmatory factor analysis to further establish the validity of the patterns derived with exploratory factor analysis could assist future research to obtain more consistent results (76). Second, the small number of studies for some associations (i.e., $n = 3$ studies on unhealthy dietary patterns and preterm birth and $n = 4$ studies on healthy dietary patterns and LGA) did not allow us to perform stratified analysis or meta-regression to examine potential sources of heterogeneity on our pooled results. Third, we did not consider conference abstracts and non-English language articles, which might have reduced the comprehensiveness of our search. However, studies have shown that language restrictions have little effect on summary estimates (77). Fourth, SGA, FGR, and LBW were treated as a single outcome to represent infants who were born small although they have slightly different definitions. However, there was no evidence of heterogeneity when the analysis was stratified based on study outcomes (SGA, FGR, or LBW). Fifth, we recognized that our findings are based on mainly observational studies and no definite causal inferences can be drawn. Last, although the majority of the studies adjusted for potential confounders rather comprehensively, residual and unmeasured confounding cannot be ruled out.

Conclusion and recommendations

Overall, we demonstrated that adherence to healthy dietary patterns—characterized by high intake of vegetables, fruits, wholegrains, low-fat dairy, and lean protein foods—during pregnancy was significantly associated with lower risk of preterm birth, whereas unhealthy dietary patterns—characterized by high intake of refined grains, processed meat, foods high in saturated fat or sugar—were associated with lower birth weight and a trend towards higher risk of preterm birth.

Given that the healthy dietary pattern described here is similar to current dietary recommendations in various countries including the United Kingdom (78), United States (6), Canada (79), and China (80), the results of this meta-analysis provide relevant information to policy makers and health professionals both locally and internationally. Considering current efforts to standardize dietary pattern methodology across various population-based cohorts, this study represents an alternative approach to examining current data and identifying gaps for future research. This is particularly critical for life-course research, including pregnancy, in which there is a lack of studies and in which randomized trials can be challenging and controversial to perform.

This study marks a step forward in use of dietary patterns as an approach to inform public health recommendations and dietary guidelines. Although presently recognized by the 2015 United States Dietary Guidelines Advisory Committee (6), this can be expanded internationally, because dietary guidelines form the cornerstone for national food and nutrition policies and the basis of evidence-based advice for public health recommendations.

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