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## **Impact of dietary inflammatory index on gestational diabetes mellitus in normal and overweight women: a systematic review and meta-analysis of observational studies**

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**Running title:** A review of DII and GDM

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## ABSTRACT

**Background and Objectives:** To systematically investigate the association between the dietary inflammatory index (DII) and gestational diabetes mellitus (GDM), with a focus on the role of BMI in this relationship. **Methods and Study Design:** A comprehensive search was conducted in PubMed, Embase, Web of Science, The Cochrane Library, Medline, CINAHL Complete, Chinese Periodical Full-text Database, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, and China Wanfang Database for relevant observational studies published up to August 2023. The quality of the included studies was assessed using the Newcastle-Ottawa Scale. The pooled effect size was calculated using a random-effects model. Subgroup and meta-regression analyses were performed to explore potential sources of heterogeneity. **Results:** The study included 54,058 participants from 10 studies. Pregnant women with a higher DII, indicating a pro-inflammatory diet, had a significantly increased risk of GDM compared to those with a lower DII, indicating an anti-inflammatory diet (pooled OR: 1.17, 95% CI: 1.01-1.36;  $I^2=70%$ ,  $p <0.001$ ). Subgroup analyses revealed a stronger association in normal weight stratification (OR: 1.25, 95%CI: 1.04-1.51), case-control studies (OR: 1.45, 95%CI: 1.03-2.05), Asia (OR: 1.26, 95%CI: 1.10-1.43), Europe (OR: 1.27, 95%CI: 1.09-1.48), 3-day dietary record as a dietary assessment tool (OR: 1.30, 95%CI: 1.16-1.46), physical activity adjustment (OR: 1.28, 95%CI: 1.13-1.46), and energy intake adjustment (OR: 1.33, 95%CI: 1.19-1.48). Meta-regression analysis confirmed that geographical region significantly influenced heterogeneity between studies ( $p <0.05$ ). **Conclusions:** An elevated DII is independently linked to a higher risk of GDM, especially in women of normal weight.

**Key Words:** dietary inflammatory index, BMI stratification, gestational diabetes mellitus, meta-analysis, pregnancy

## INTRODUCTION

Gestational diabetes mellitus (GDM) is a metabolic disorder that first manifests during pregnancy.<sup>1</sup> The International Diabetes Federation reports that 16.7% of pregnant women worldwide will experience hyperglycemia, with GDM accounting for 80.3% of these cases in 2021.<sup>2</sup> GDM poses significant short- and long-term health risks for both the mother and the unborn child. Mothers face increased risks of gestational hypertension, pre-eclampsia, hydramnios, and further type II diabetes,<sup>3</sup> while the fetus is more likely to macrosomia,

hyperinsulinemia, delayed fetal lung maturation, and intrauterine death.<sup>4</sup> As a result, the prevention and treatment of GDM are gaining increased attention in clinical practice.

Current research suggests that persistent maternal inflammation may have a role in the onset and progression of GDM, and inflammatory marker alterations may be favorably related to the emergence of GDM.<sup>5</sup> Dietary components are known to influence inflammatory processes and affect inflammatory biomarkers, such as C-reactive protein (CRP) and tumor necrosis factor (TNF).<sup>6,7</sup> The dietary patterns that are internationally recognized and linked to inflammation levels in the population under investigation include the typical Western diet, which is associated with increased inflammatory factors, as well as the Mediterranean diet and the Dietary Approaches to Stop Hypertension (DASH), which are associated with reduced inflammatory factors.<sup>8,9</sup> Therefore, it is necessary to explore the association that the DII measures as a tool for evaluating the dietary inflammatory potential in relation to GDM.

The dietary inflammatory index (DII) is a tool for assessing the inflammatory potential of an individual's diet by evaluating the intake of macronutrients and micronutrients through a food frequency questionnaire (FFQ). The DII was developed by public health expert Cavicchia at the University of South Carolina in 2009.<sup>10</sup> Shivappa et al. updated the DII by assigning values to 45 dietary components or nutrients based on studies conducted between 2007 and 2010.<sup>11</sup> The DII comprises 45 dietary components, 36 of which have anti-inflammatory effects and 9 of which have pro-inflammatory effects.<sup>11</sup> Components that increase levels of pro-inflammatory markers, such as interleukin (IL)-1 $\beta$ , IL-6, TNF- $\alpha$ , and CRP, are assigned a score of +1, those that decrease levels of anti-inflammatory markers, such as IL-4 and IL-10, are assigned a score of -1, and components with no discernible effect are assigned a score of 0. The individual's DII is calculated by adding the assigned scores of all dietary components consumed by them. The DII score above 0 is defined as a pro-inflammatory diet, while a score below 0 indicates an anti-inflammatory diet. Thus, a higher DII score indicates a more pro-inflammatory diet, characterized by higher consumption of foods such as red meat, processed foods, and sugary beverages. Conversely, a lower DII score reflects an anti-inflammatory diet, including higher intake of fruits, vegetables, whole grains, and omega-3 fatty acids. The DII has been shown to correlate well with established markers of inflammation, including IL-1 $\beta$ , IL-4, IL-6, IL-10, TNF- $\alpha$ , and CRP, highlighting its utility in assessing the inflammatory potential of diets.<sup>12</sup> Recent observational studies have shown that a diet's pro-inflammatory potential may increase the risk of unfavorable health outcomes, including cardiovascular disease, cancer, cognitive impairment, diabetes, GDM, and even unfavorable pregnancy outcomes.<sup>13-17</sup>

Although recent epidemiological studies have suggested an association between DII and GDM, their results remain controversial.<sup>17, 18</sup> An increased risk of developing GDM has been associated with the pro-inflammatory potential of the diet, as measured by DII,<sup>17, 19, 20</sup> while other studies have found no association.<sup>15, 18</sup> Meanwhile, some studies suggest that pre-pregnancy BMI may influence the effect of the diet's pro-inflammatory potential on the development of GDM.<sup>17, 21, 22</sup> In addition, the interaction between pre-pregnancy BMI and a pro-inflammatory diet may play a crucial role in the development of GDM, as individuals with a higher BMI may have an enhanced inflammatory response to such diets in early pregnancy,<sup>23</sup> thereby increasing their risk of developing GDM. Given the conflicting findings in the literature regarding the relationship between DII and GDM, this study conducted a meta-analysis to systematically evaluate this relationship. We also further stratified by pre-pregnancy BMI, geographical region, and other potential confounders to provide a more nuanced understanding of this relationship.

## **MATERIALS AND METHODS**

### ***Search Strategy and Selection***

The meta-analysis was carried out following the PRISMA guidelines.<sup>24</sup> Two investigators independently searched PubMed, Embase, Web of Science, Cochrane Library, Medline, CINAHL Complete, Chinese Periodical Full-text Database, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, and China Wanfang Database, from inception to August 1, 2023. To ensure the comprehensiveness and currency of our meta-analysis, an updated literature search was conducted up to April 1, 2024. The search terms included (dietary inflammatory index or inflammatory potential of diet or inflammatory diet or anti-inflammatory diet or pro-inflammatory diet or dietary inflammatory potential or DII) and (diabetes, gestational or diabetes, pregnancy-induced or pregnancy-induced diabetes or gestational diabetes or gestational diabetes mellitus or diabetes mellitus, gestational or GDM) (Supplementary Table 1). References to relevant articles were also searched for other potential studies. The systematic review was submitted to PROSPERO and assigned the registration number: CRD42023435054.

### ***Inclusion and exclusion criteria***

These were the criteria for inclusion: (1) the study population was pregnant women; (2) a case-control or cohort study; (3) the exposure factor was pro-inflammatory DII or anti-inflammatory DII (4) the study outcome was GDM; (5) the study reported either odds ratios

(ORs), hazard ratios (HRs), or risk ratios (RRs) accompanied by their respective 95% confidence intervals (CIs) or provided adequate information to calculate these effect measures. These were the criteria for exclusion: (1) duplicate publications; (2) studies focusing on other diseases or dietary patterns; (3) unpublished data and gray literature, including conference abstracts, papers, and patents.

### ***Data extraction***

Data were extracted independently by two researchers, and any discrepancies in the extraction process were resolved by discussion with a third researcher. The extracted information from the primary studies included: the primary author's name, year of publication, location, study design, sample size, dietary assessment tool, DII classification, diagnostic criteria for GDM, OR/RR with the 95% CI, and covariate adjustment.

### ***Quality assessment***

Two investigators assessed the quality of the literature using the Newcastle-Ottawa Scale (NOS) independently.<sup>25</sup> The NOS comprises three aspects: selection, comparability, and outcome (for cohort studies) or exposure (for case-control studies). The highest possible score is 9, with a score of  $\leq 3$  indicating low quality, 4 to 6 indicating medium quality, and  $\geq 7$  indicating high quality. Any discrepancies in the quality assessment were resolved through discussion with a third researcher.

### ***Statistical analysis***

Stata17.0 was used to analyze the data from all included studies. The results are presented in a descriptive manner, describing the search process and study characteristics. We assessed the association between DII (higher versus lower categories) and GDM using the pooled OR and 95% CI in the meta-analysis. Both RRs and HRs were considered as comparable OR estimators and were combined with ORs to create a pooled OR.<sup>26</sup> Given the expected clinical heterogeneity, we used the random effects model to calculate the pooled OR with 95% CI. The degree of heterogeneity between included studies is measured by the  $I^2$  metric.  $I^2$  values of 25%, 50%, 75% and  $>75\%$  indicate no, moderate, substantial and considerable heterogeneity, respectively.<sup>27</sup>

We investigated the causes of heterogeneity through subgroups. Subgroup analyses were performed based on the following: the pre-pregnancy BMI, study design, region, dietary assessment tool, physical activity adjustment, and energy intake adjustment. Additionally, we

used study design, region, dietary assessment tool, physical activity adjustment, and energy intake adjustment as covariates in the meta-regression. Sensitivity analyses were performed using a stepwise literature exclusion method to assess the reliability of the findings. A funnel plot was built for visual examination, and Egger's test was employed to evaluate the possibility of publication bias.<sup>28</sup>

## RESULTS

### *Study search and characteristics*

A total of 458 studies were found by searching the electronic database. After removing duplicates, 330 articles remained. 312 irrelevant articles were excluded after further reading the titles and abstracts. Eventually, only 10 studies met the criteria. Figure 1 displays the specific details of the literature screening process. The 10 studies were published between 2016-2022 and involved a total of 54,058 participants, including Spain (one study),<sup>29</sup> Finland (one study),<sup>20</sup> Iran (two studies),<sup>18, 19</sup> USA (two studies),<sup>15, 22</sup> China (three studies),<sup>17, 30, 31</sup> and Japan (one study).<sup>21</sup> Regarding study design, two studies used a case-control design,<sup>18, 30</sup> and eight studies used a cohort study.<sup>15, 17, 18, 20-22, 29, 31</sup> Eight studies used the FFQ,<sup>15, 17, 18, 20-22, 29, 30</sup> and two studies used a 3-day dietary record as a dietary assessment tool.<sup>20, 31</sup> All studies used the method developed by Shivappa,<sup>11</sup> to calculate DII scores. Nine studies analyzed DII as a categorical variable,<sup>15, 17-19, 21, 22, 29-31</sup> while one study treated it as a continuous variable.<sup>20</sup> Details of the included studies are given in Table 1.

### *Quality assessment*

The mean NOS score for the literature's quality evaluation was 7.2. The methodological quality of nine investigations was high while one was medium, as assessed by the NOS (Supplementary Table 2).

### *DII and risk of GDM*

As shown in Figure 2, The DII scores showed a positive correlation with the occurrence of GDM (pooled OR: 1.17, 95% CI: 1.01~1.36) with moderate heterogeneity ( $I^2=70.0\%$ ,  $p<0.001$ ) (Five studies indicated a significant link between an elevated DII score and a higher prevalence of GDM. Conversely, one study found an association between an pro-inflammatory diet and a reduced risk of GDM, while the others found no significant association). The result indicated a pro-inflammatory diet raised the risk of GDM in pregnant women more than an anti-inflammatory diet.

### ***Subgroup analysis and meta-regression***

Subgroup and meta-regression analyses were conducted to explore potential sources of heterogeneity in the included studies. Subgroup analyses based on pre-pregnancy BMI, study design, region, dietary assessment tool, and adjustment variables (physical activity and energy intake during pregnancy) are presented in Table 2.

As demonstrated in Figure 3, stratifying by pre-pregnancy BMI reduced heterogeneity between studies. The association between DII and GDM was more pronounced among normal weight participants (pre-pregnancy BMI < 25) with a pooled OR of 1.25 (95% CI: 1.04-1.51;  $I^2 = 37.2%$ ,  $p = 0.203$ ) compared to overweight participants (pre-pregnancy BMI  $\geq 25$ ) with a pooled OR of 1.08 (95% CI: 0.79-1.50;  $I^2 = 77.8%$ ,  $p = 0.004$ ).

Stratification by study design indicated a stronger association between high DII and GDM in case-control studies (pooled OR: 1.45, 95% CI: 1.03-2.05;  $I^2 = 30.4%$ ,  $p = 0.231$ ). Regional stratification revealed more significant associations in Asia (pooled OR: 1.26, 95% CI: 1.10-1.43;  $I^2 = 39.5%$ ,  $p = 0.142$ ) and Europe (pooled OR: 1.27, 95% CI: 1.09-1.48;  $I^2 = 0$ ,  $p = 0.937$ ). Stratification by assessment tool showed notable differences between studies using FFQs (pooled OR: 1.13, 95% CI 0.92-1.39;  $I^2 = 71.8%$ ,  $p = 0.001$ ) and dietary records (pooled OR: 1.30, 95% CI 1.16-1.46;  $I^2 = 0$ ,  $p = 0.691$ ). Additionally, subgroup analyses demonstrated a stronger association in studies adjusted for physical activity (pooled OR: 1.28, 95% CI: 1.13-1.46;  $I^2 = 0$ ,  $p = 0.465$ ) and energy intake (pooled OR: 1.33, 95% CI: 1.19-1.48;  $I^2 = 0$ ,  $p = 0.560$ ) (Supplementary Figure 1-5).

Stratified analyses indicated that factors such as pre-pregnancy BMI, study design, geographical region, dietary assessment tool, and adjustments for physical activity and energy intake might be sources of heterogeneity in this study. In addition, meta-regression analysis provided further evidence that geographical region significantly contributed to the observed heterogeneity between studies ( $p < 0.05$ ) (Supplementary Table 3).

### ***Sensitivity analysis and publication bias***

The sensitivity analysis presented in Supplementary Figure 6 showed that no single study had a significant impact on the overall pooled results. In addition, the funnel plot in Figure 4 and Egger's test ( $t = 0.05$ ,  $p = 0.962$ ) presented in Supplementary Figure 6 both indicated the absence of publication bias, further supporting the robustness of our findings.



## DISCUSSION

Our meta-analysis systematically searched published studies that examined the relationship between DII and GDM risk, resulting in the inclusion of ten studies with 54,058 participants. The results showed that pregnant women with a higher pro-inflammatory potential in their diet (high DII scores) had a 17% higher incidence of GDM compared to those with an anti-inflammatory diet (lower DII scores). Subgroup analyses showed that the association between DII and GDM risk was stronger in case-control studies, especially in the Asian and European regions. The association was also stronger when 3-day dietary records were used to assess diet and in studies that adjusted for physical activity and energy intake. Notably, the effect of DII on GDM risk was more significant in normal weight women (BMI < 25) compared with overweight or obese women. In addition, our meta-regression analysis showed that both geographical region and pre-pregnancy BMI contributed to the heterogeneity between studies, suggesting that these factors may influence the relationship between DII and GDM risk.

The results showed a positive association between DII and the risk of developing GDM. This finding is consistent with previous meta-analyses showing an association between a higher DII and an increased risk of diabetes.<sup>32, 33</sup> For instance, one meta-analysis showed that those who consumed a more pro-inflammatory diet were 32% more likely to develop diabetes.<sup>32</sup> Motamed et al. also found that the pooled effect sizes of high-quality studies showed a significant association between a higher DII and the incidence of type 2 diabetes.<sup>33</sup> Therefore, healthcare professionals should evaluate a diet quality by using the DII score for assessing the inflammatory potential of the diet, and counsel accordingly the provided DII scores.

The mechanism of action by which a pro-inflammatory diet may increase the risk of developing GDM has been explained in several ways. Primarily, specific dietary components may influence the development of chronic inflammation. A pro-inflammatory diet can increase levels of inflammatory cytokines, leading to dysfunction and structural impairment of pancreatic islet  $\beta$ -cells and insulin resistance, all of which contribute to the onset of GDM.<sup>5, 34, 35</sup> In addition, dietary effects on body weight, BMI, and fat mass can further exacerbate the inflammatory response,<sup>36</sup> thereby increasing the risk of GDM through these interrelated physiological mechanisms. Studies have indicated that diets high in refined grains, red meat and meat products, different forms of confectionary, and sugary drinks can raise the blood levels of inflammatory substances including CRP, TNF- $\alpha$ , and IL-6, which raises the body's degree of inflammation.<sup>37-39</sup> Additionally, research has shown that the consumption of both unprocessed and processed meats before pregnancy is associated with a higher risk of GDM,

even after adjusting for BMI.<sup>40, 41</sup> This has been linked to the high levels of saturated fatty acids, trans fatty acids, nitrosamines, and other elements in processed meat products, which have been implicated in oxidative stress, insulin resistance, and damage to pancreatic islet  $\beta$ -cells.<sup>42, 43</sup>

The influence of gut microorganisms is another potential mechanism. Diet can affect the balance of the gut microbiota, and nutrients can either promote or inhibit the growth and reproduction of microbiota.<sup>44</sup> For example, Zheng et al. conducted a study examining the relationship between the DII and gut microbiota and found that individuals with the most pro-inflammatory diets had higher levels of *Ruminococcus torques*, *Eubacterium nodatum*, *Acidaminococcus intestini*, and *Clostridium leptum*, while those with the most anti-inflammatory diets had increased levels of *Akkermansia muciniphila*.<sup>45</sup> This suggests a direct link between diet-induced inflammation and changes in the composition of the gut microbiota.

Additionally, evidence from a randomized controlled trial showed that the anti-inflammatory diet significantly improved the inflammatory state of the participants while reducing body weight and visceral adiposity, suggesting that dietary components with anti-inflammatory potential may also have an indirect effect on the gut microbiota.<sup>46</sup>

The gut microbiota plays a key role in regulating metabolism, including the function of insulin. When the balance of the gut microbiota is disturbed, it can lead to reduced insulin receptor sensitivity and increased insulin resistance, both of which are factors in the onset of GDM.<sup>47</sup> Furthermore, the composition of the gut microbiota is influenced not only by diet, including anti-inflammatory dietary components, but also by other environmental factors such as pollution, antibiotic residues, and xenobiotics.<sup>48</sup> It is important to understand the relationship between dietary factors, gut microbiota, and GDM risk in order to develop effective prevention and management strategies.

In the subgroup analysis, we observed a notable finding: in normal-weight pregnant women, the association between the DII and GDM was stronger than that in overweight pregnant women. This finding suggests that a pro-inflammatory diet may increase the risk of GDM in women with normal BMI, while for overweight women, the influence of pro-inflammatory diet on GDM was not significant. This may be because higher BMI is a stronger predictor of insulin sensitivity in pregnancy than a pro-inflammatory diet.<sup>49</sup> Pregnant women with a higher BMI already have a higher risk of GDM.<sup>50</sup> On the other hand, pregnant women who are overweight or obese could adopt a high-quality dietary pattern that is rich in anti-inflammatory components, such as phenolic compounds, vitamins, and polyunsaturated fatty

acids during pregnancy.<sup>51</sup> This dietary management strategy could aim to reduce inflammation in pregnant women with GDM.<sup>52</sup> Alternatively, there could be a bias in dietary recall, where participants are more likely to report a healthier diet. Therefore, these findings highlight the importance of including BMI when assessing the relationship between diet and health outcomes, particularly in the context of GDM. Future research should investigate the interaction between BMI and dietary inflammation in determining the risk of GDM, with the aim of elucidating the underlying mechanisms of this relationship.

According to the subgroup analysis, the case-control study showed a more substantial correlation between high DII scores and the likelihood of developing GDM than the cohort study. This could be because there were more cohort studies included, which increased within-group heterogeneity. Recollection bias,<sup>53</sup> which happens when cases in case-control studies have outcomes of interest and are maybe more deliberate or inquisitive when examining earlier exposures compared to controls, may also be connected to this result. Furthermore, the subgroup analysis findings stratified by region indicated that the correlations were greater for studies conducted in Asia and Europe than in North America. Inter-study heterogeneity was significantly reduced by regional stratification. The studies included were mostly focused on Asia, and as dietary habits and patterns vary greatly among races and nations, further research should be conducted in more regions to give greater support. Stronger associations were found in studies that used food diaries than in those that used the FFQ. The possible explanation for the difference in results is that dietary assessment tools may influence the DII score. The FFQ is currently the most widely used dietary assessment tool and provides a more comprehensive view of participants' dietary habits and intake over time.<sup>54</sup> In contrast, food diaries require participants to record their dietary intake in real time, providing a more detailed and accurate reflection of their consumption.<sup>54</sup> This level of detail may allow for a more accurate assessment of dietary patterns and their inflammatory potential, leading to a more accurate calculation of the DII. This suggests that the choice of dietary assessment tool plays a crucial role in the assessment of diet-health relationships and highlights the importance of considering this factor when interpreting study results.

Subgroup analysis showed that elevated DII increased the risk of GDM, even after controlling for variables such as physical activity and energy intake. Physical exercise is a protective factor for GDM, and moderate exercise can increase insulin sensitivity and reduce insulin resistance.<sup>55, 56</sup> In addition, Wirth et al. found that total dietary energy intake significantly influenced the accuracy of DII assessments.<sup>57</sup> Therefore, we stratified these

variables to increase the reliability of our results, recognizing that levels of physical activity and energy intake significantly influence the risk of GDM.

The meta-analysis has several limitations. First, most of the study participants in this analysis were Asian, so caution should be taken in generalizing these findings to diverse populations. Second, DII scores may be affected by variability in the nutrients included in different studies. Additionally, the use of different categorical cut-off points for DII scores (such as quartiles and tertiles) complicates comparisons in our analysis. Although these methods are commonly used in epidemiological studies,<sup>58</sup> they may obscure subtle but important differences.<sup>59</sup> Furthermore, there was significant heterogeneity in the association between studies. However, through subgroup and meta-regression analyses, we found that the heterogeneity was mainly explained by factors such as BMI status, study design, region, assessment tools and variable adjustment. Future research should focus on addressing these sources of heterogeneity. Finally, the inclusion of only ten studies resulted in pooled ORs with marginal statistical significance. More rigorous methods are needed in future studies to clarify the strength of the association between DII scores and GDM.

### ***Conclusion***

This meta-analysis shows a statistically significant association between higher DII and an increased risk of GDM, especially in normal weight participants. This finding highlights the potential impact of a pro-inflammatory diet, as opposed to an anti-inflammatory diet, in increasing the risk of GDM in pregnant women. However, it is important to note that these findings are based on a relatively small number of studies. Therefore, future research with larger sample sizes, more diverse populations, and more rigorous methodologies is crucial to elucidate the mechanisms by which DII influences GDM risk.

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## CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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**Table 1.** Main characteristics of the eligible studies

Author, Year	Country	Study design	Study period	Dietary assessment tool	Sample size	Type of DII Data and comparison	Diagnosis criteria
Zhang et al. 2021	China	Prospective cohort	2013-2016	FFQ	2639	Categorical Tertile 3 vs. Tertile 1	IADPSG
Sen et al. 2016	USA	Prospective cohort	1999-2002	FFQ	2128	Categorical Tertile 4 vs. Tertile 1	ADA
Kyozuka et al. 2022	Japan	Prospective cohort	2011-2014	FFQ	45213	Categorical Quartile 4 vs. Quartile 1	JSOG
Wu et al. 2021	China	Case-control	2019-2020	FFQ	164 (cases:82, controls:82)	Categorical High vs. Low	IADPSG
Soltani et al. 2021	Iran	Prospective cohort	2015-2016	FFQ	812	Categorical Quartile 4 vs. Quartile 1	ADA/IAPDSG
Zhao et al. 2018	China	Prospective cohort	2014-2015	3-day dietary record	336	Categorical Tertile 3 vs. Tertile 1	IADPSG
Pajunen et al. 2021	Finland	Prospective cohort	2013-2017	3-day dietary record	351	Continuous	ACOG
McCullough 2017	USA	Prospective cohort	2009-2011	FFQ	1057	Categorical Quartile 4 vs. Quartile 1	Self-reporting
Shivappa et al. 2019	Iran	Case-control	—	FFQ	388 (cases:121, controls:266)	Categorical Tertile 3 vs. Tertile 1	ADA
Casas et al. 2022	Spain	Prospective cohort	2017-2020	FFQ	970	Categorical Tertile 3 vs. Tertile 1	ADA

Author, Year	Overall and stratified OR	Food parameters	Adjustment factors
Zhang et al. 2021	Overall: 1.43 (1.05-1.95) BMI < 25: 1.45 (1.00-2.10) BMI ≥ 25: 2.2 (1.03-4.6)	26	Age, pre-pregnancy BMI, socioeconomic status, education level, physical activity, smoking status, alcohol use, multivitamin intake, family history of diabetes.
Sen et al. 2016	Overall: 0.78 (0.65-0.95) BMI ≥ 25: 0.57 (0.36-0.91)	28	Age, pre-pregnancy BMI, education level, parity, race/ethnicity, smoking status, and household income.
Kyozuka et al. 2022	Overall: 1.02 (0.82-1.26) BMI < 25: 1.01 (0.76-1.36) BMI ≥ 25: 1.07 (0.87-1.32)	30	Age, conception method, hypertension, education level, smoking status
Wu et al. 2021	Overall: 1.334 (1.132-1.564)	17	Age, pre-pregnancy BMI, pregnancy history
Soltani et al. 2021	Overall: 1.04 (0.72-1.48)	29	Age, pre-pregnancy BMI, socioeconomic status, education level, physical activity, adverse obstetric history
Zhao et al. 2018	Overall (BMI < 25): 1.33 (1.13-1.56)	20	Age, pre-pregnancy BMI, education level, family history of diabetes, CRP, parity, energy intake
Pajunen et al. 2021	Overall (BMI ≥ 25): 1.27 (1.08-1.49)	27	Age, pre-pregnancy BMI, education level, physical activity, smoking status, hypertension, history of GDM, energy intake
McCullough 2017	Overall: 0.94 (0.47-0.1.88)	27	Age, pre-pregnancy BMI, race/ethnicity, household income, smoking status
Shivappa et al. 2019	Overall: 2.1 (1.02-4.34)	32	Age, physical activity, smoking status, family history of diabetes, multivitamin intake
Casas et al. 2022	Overall: 1.24 (0.7-2.2)	33	Age, pre-pregnancy BMI, education level, smoking status, alcohol use, physical activity, drug use, hypertension, history of autoimmune disease, adverse obstetric history

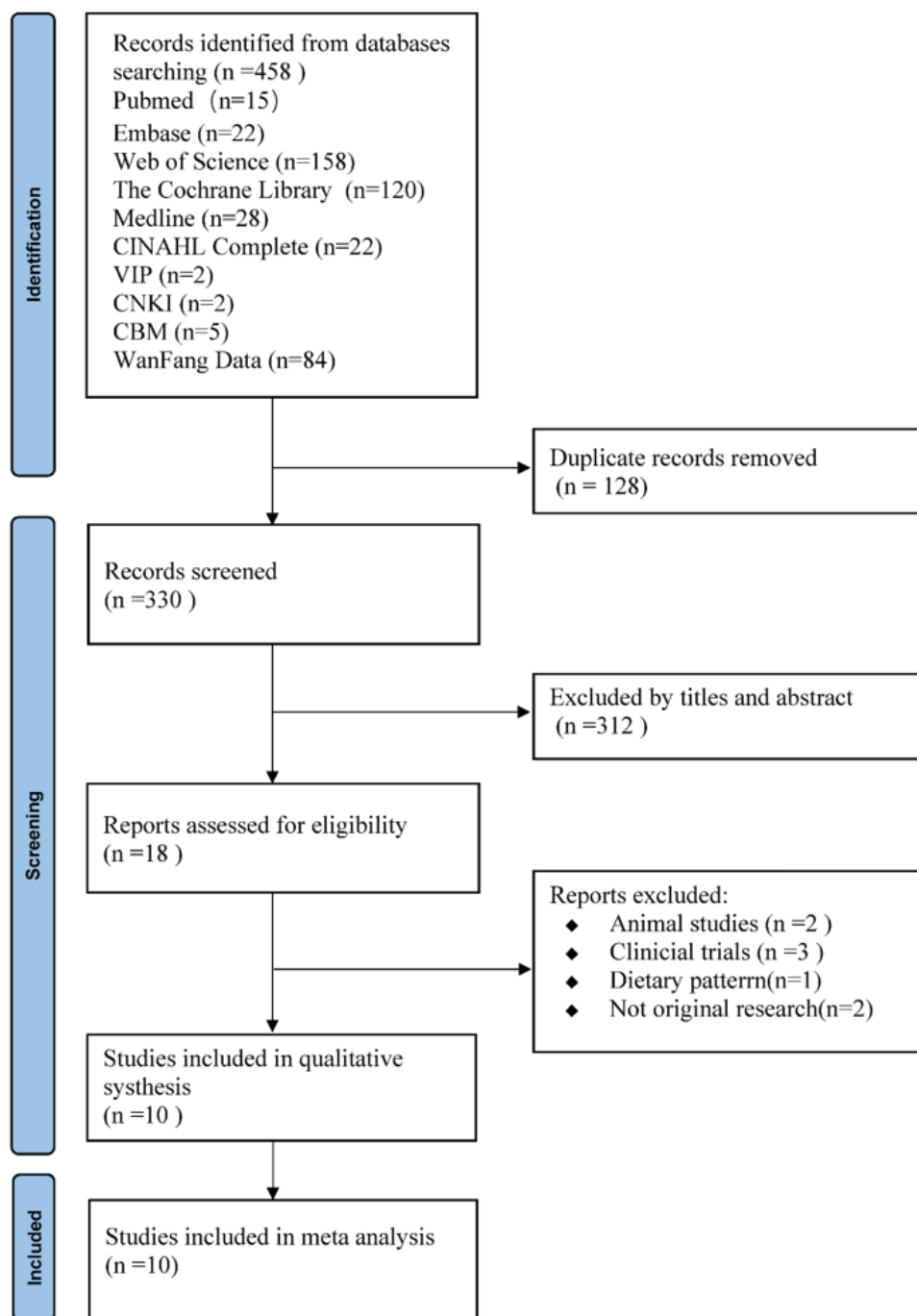
DII, dietary inflammatory index; FFQ, food frequency questionnaire; IADPSG, International Association of Diabetes and Pregnancy Study; ADA, American Diabetes Association; JSOG, Japan Society of Obstetrics and Gynaecology; ACOG, American Academy of Obstetricians and Gynecologists.

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**Table 2.** Stratified analyses on the association between DII and the risk of GDM

Subgroup	Number of study	OR (95%CI)	Heterogeneity	
			$I^2$ (%)	$p$
Total	10	1.17(1.01, 1.36)	70	< 0.001
Pre-pregnancy BMI (kg/m <sup>2</sup> )				
< 25	3	1.25(1.04, 1.51)	37.2	0.203
≥25	4	1.08(0.79, 1.50)	77.8	0.004
Study design				
Cohort	8	1.12(0.94, 1.33)	71.2	0.001
Case-control	2	1.45(1.03, 2.05)	30.4	0.231
Region				
Asia	6	1.26(1.10, 1.43)	39.5	0.142
Europe	2	1.27(1.09, 1.48)	0	0.937
North America	2	0.79(0.66, 0.95)	0	0.611
Dietary assessment tool				
FFQ	8	1.13(0.92, 1.39)	71.8	0.001
Dietary record	2	1.30(1.16, 1.46)	0	0.691
Adjustment for physical activity				
Yes	5	1.28(1.13, 1.46)	0	0.465
No	5	1.08(0.86, 1.37)	83.2	< 0.001
Adjustment for energy intake				
Yes	4	1.33(1.19, 1.48)	0	0.560
No	6	1.17(1.01, 1.30)	70	< 0.001

FFQ, food frequency questionnaire



**Figure 1.** Flow chart of included studies.

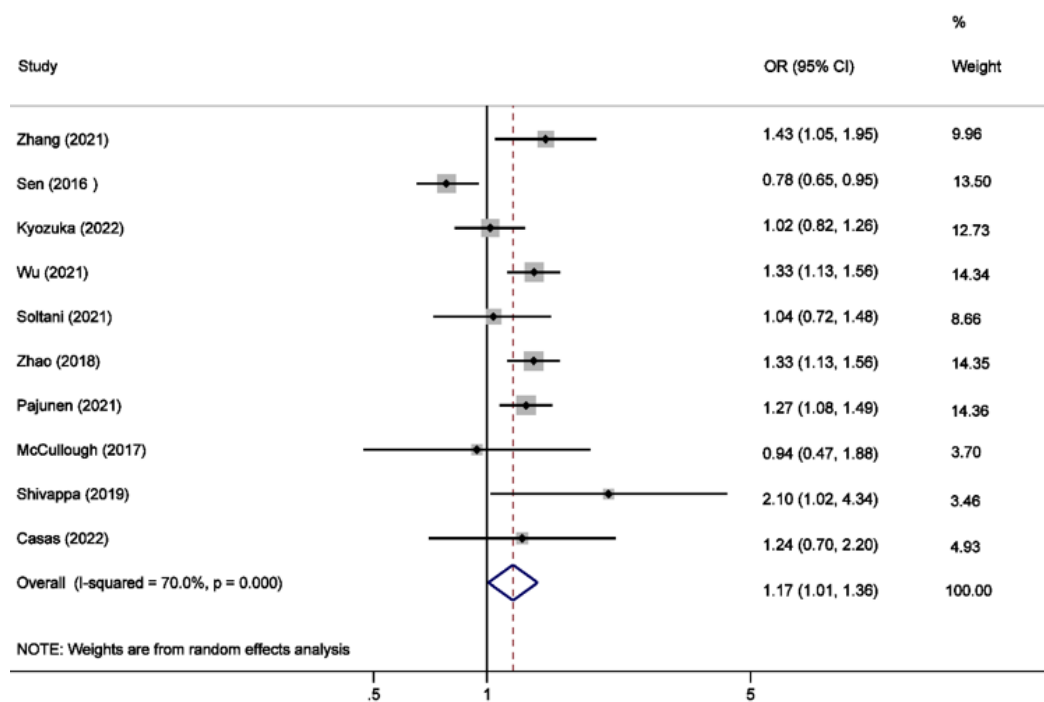


Figure 2. Forest plot of associations between DII and the risk of GDM

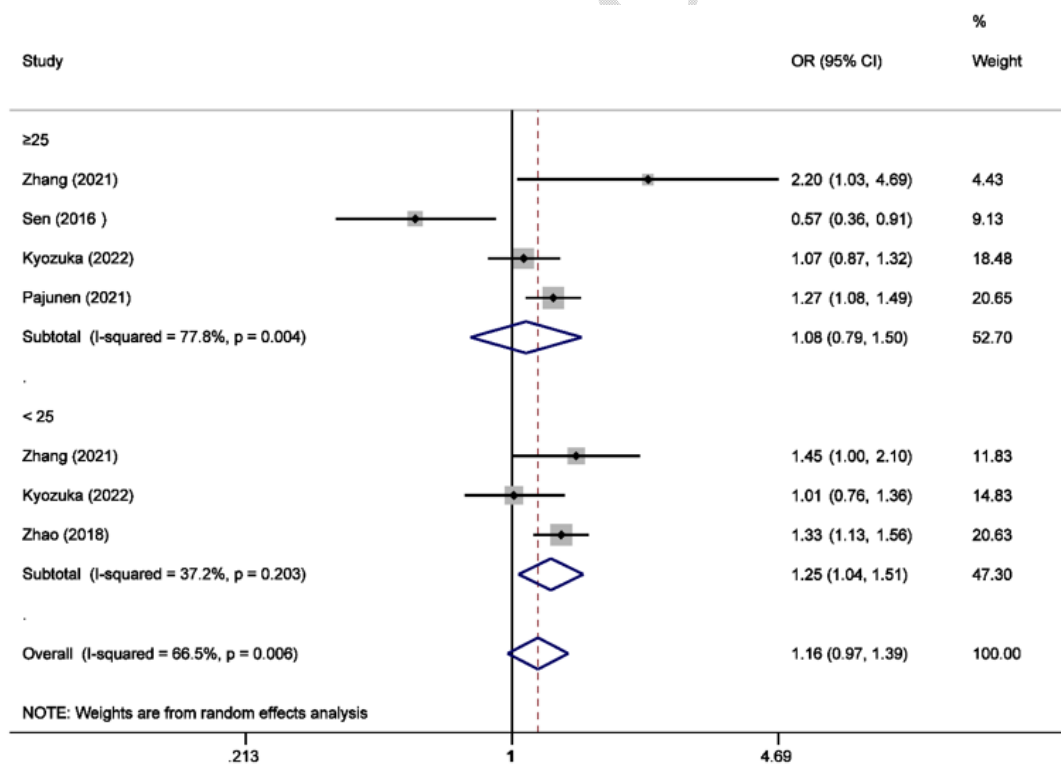


Figure 3. Subgroup analyses stratified by pre-pregnancy BMI

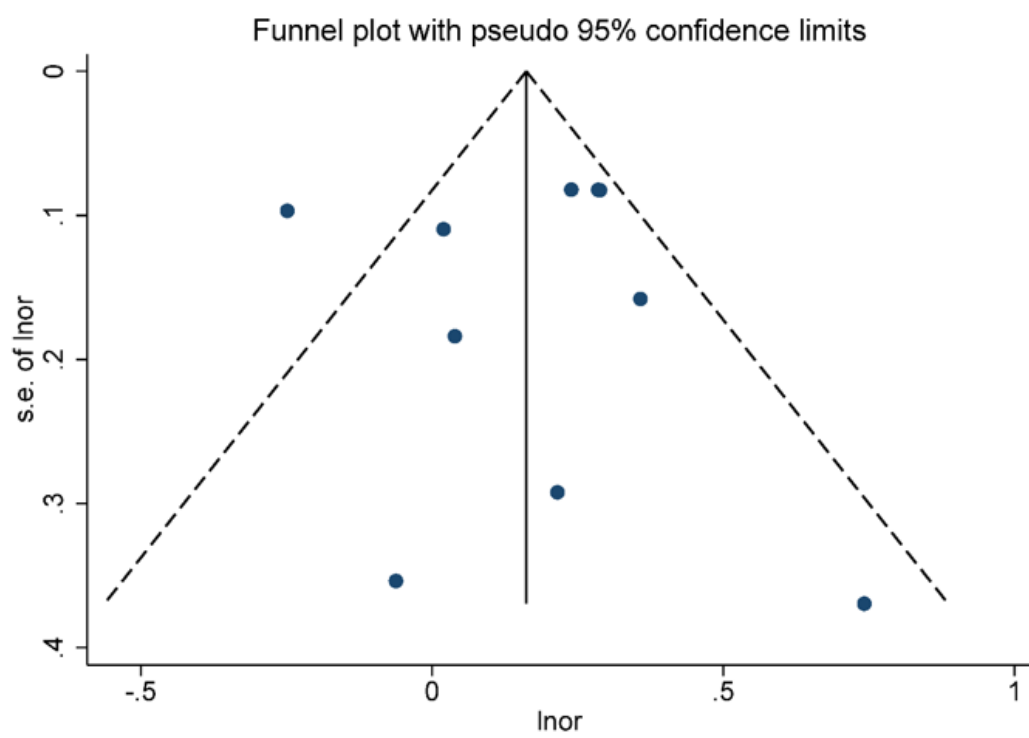


Figure 4. Funnel plot for publication bias

**Supplementary Table 1.** Main characteristics of the eligible studies

Database	Search strategy
PubMed	#1 dietary inflammatory index[Title/Abstract] OR inflammatory potential of diet[Title/Abstract] OR inflammatory diet[Title/Abstract] OR anti-inflammatory diet [Title/Abstract] OR pro-inflammatory diet[Title/Abstract] OR dietary inflammatory potential[Title/Abstract] OR DII[Title/Abstract] #2 diabetes, gestational[MeSH Terms] #3 diabetes, gestational[Title/Abstract] OR diabetes, pregnancy-induced[Title/Abstract] OR pregnancy-induced diabetes[Title/Abstract] OR gestational diabetes[Title/Abstract] OR gestational diabetes mellitus [Title/Abstract] OR diabetes mellitus, gestational [Title/Abstract] OR GDM[Title/Abstract] #4 #2 OR #3 #5 #1 AND #4
Embase	#1 'dietary inflammatory index ':ti,ab,kw OR 'inflammatory potential of diet ':ti,ab,kw OR 'inflammatory diet ':ti,ab,kw OR 'anti-inflammatory diet ':ti,ab,kw OR 'pro-inflammatory diet ':ti,ab,kw OR 'dietary inflammatory potential ':ti,ab,kw OR 'DII ':ti,ab,kw #2 'pregnancy diabetes mellitus'/exp #3 'diabetes, gestational':ti,ab,kw OR 'diabetes, pregnancy-induced':ti,ab,kw OR 'pregnancy-induced diabetes':ti,ab,kw OR 'gestational diabetes':ti,ab,kw OR 'gestational diabetes mellitus':ti,ab,kw OR 'diabetes mellitus, gestational':ti,ab,kw OR 'GDM':ti,ab,kw #4 #2 OR #3 #5 #1 AND #4
Web of Science	#1 Topic: (dietary inflammatory index or inflammatory potential of diet or inflammatory diet or anti-inflammatory diet or pro-inflammatory diet or dietary inflammatory potential or DII) and (diabetes, gestational or diabetes, pregnancy-induced or pregnancy-induced diabetes or gestational diabetes or gestational diabetes mellitus or diabetes mellitus, gestational or GDM) Time span: All years. Index: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC. #2 Topic: (diabetes, gestational or diabetes, pregnancy-induced or pregnancy-induced diabetes or gestational diabetes or gestational diabetes mellitus or diabetes mellitus, gestational or GDM) Time span: All years. Index: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI, CCR-EXPANDED, IC. #3 #1 and #2
Cochrane Library	#1 (dietary inflammatory index or inflammatory potential of diet or inflammatory diet or anti-inflammatory diet or pro-inflammatory diet or dietary inflammatory potential or DII):ti,ab,kw #2 MeSH descriptor: [Diabetes, Gestational] explode all trees #3 (diabetes, pregnancy-induced or pregnancy-induced diabetes or gestational diabetes or gestational diabetes mellitus or diabetes mellitus, gestational or GDM):ti,ab,kw #4 #2 or #3 #5 #1 and #4



**Supplementary Table 1.** Main characteristics of the eligible studies (cont.)

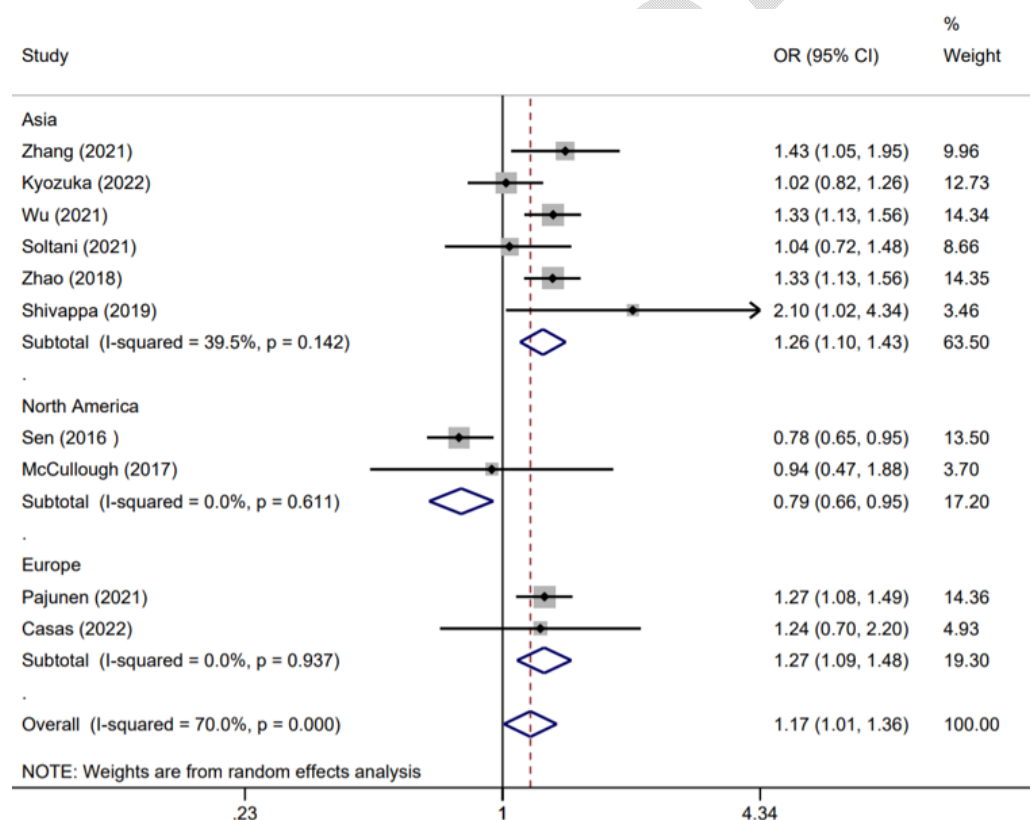
Database	Search strategy
Medline <i>via</i> EBSCO	#1 TX: dietary inflammatory index or inflammatory potential of diet or inflammatory diet or anti-inflammatory diet or pro-inflammatory diet or dietary inflammatory potential or DII #2 AB: dietary inflammatory index or inflammatory potential of diet or inflammatory diet or anti-inflammatory diet or pro-inflammatory diet or dietary inflammatory potential or DII #3 #1 or #2 #4 TX: Diabetes, Pregnancy-Induced OR Pregnancy-Induced Diabetes OR Gestational Diabetes OR Diabetes Mellitus, Gestational OR Gestational Diabetes Mellitus OR GDM #5 AB: Diabetes, Pregnancy-Induced OR Pregnancy-Induced Diabetes OR Gestational Diabetes OR Diabetes Mellitus, Gestational OR Gestational Diabetes Mellitus OR GDM #6 #4 or #5 #7 #3 and #6
CINAHL Complete	#1 TI: dietary inflammatory index or inflammatory potential of diet or inflammatory diet or anti-inflammatory diet or pro-inflammatory diet or dietary inflammatory potential or DII #2 AB: dietary inflammatory index or inflammatory potential of diet or inflammatory diet or anti-inflammatory diet or pro-inflammatory diet or dietary inflammatory potential or DII #3 #1 or #2 #4 MM: Diabetes, Gestational #5 TI: Diabetes, Pregnancy-Induced OR Pregnancy-Induced Diabetes OR Gestational Diabetes OR Diabetes Mellitus, Gestational OR Gestational Diabetes Mellitus OR GDM #6 AB: Diabetes, Pregnancy-Induced OR Pregnancy-Induced Diabetes OR Gestational Diabetes OR Diabetes Mellitus, Gestational OR Gestational Diabetes Mellitus OR GDM #7 #4 or #5 or #6 #8 #3 and #7

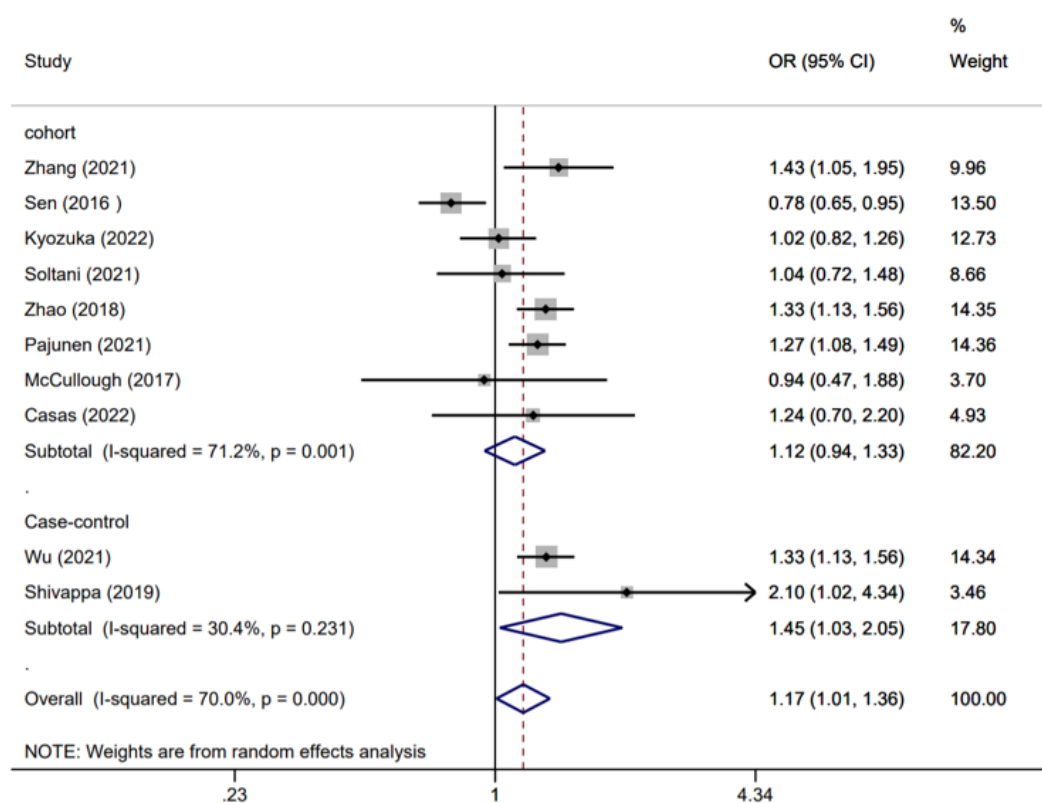
**Supplementary Table 2.** Quality assessments of the included studies

Study	Selection	Comparability	Outcome	Total score
Zhang et al. 2021	3	1	3	7
Sen et al. 2016	3	1	3	7
Kyozuka et al. 2022	4	0	3	7
Wu et al. 2021	4	0	3	7
Soltani et al. 2021	3	1	3	7
Zhao et al. 2018	4	1	3	8
Pajunen et al. 2021	4	1	3	8
McCullough et al. 2017	3	1	2	6
Shivappa et al. 2019	3	1	3	7
Casas et al. 2022	4	1	3	8

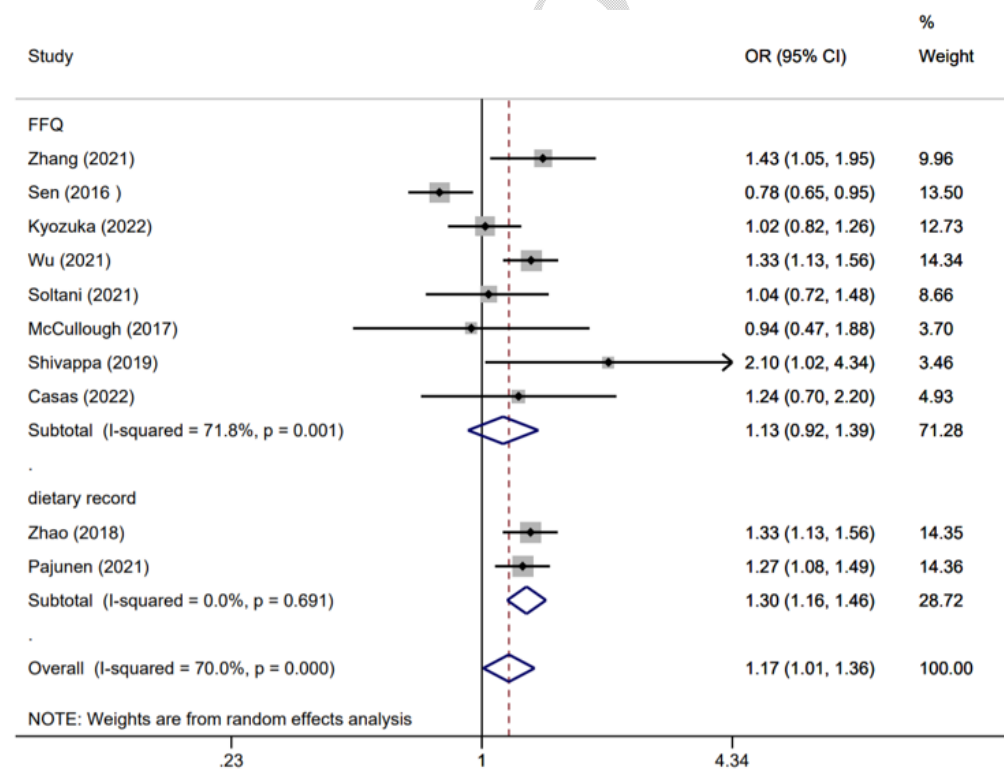
**Supplementary Table 3.** Meta-regression of the including studies

Factor	Coefficient	Standard error	T value	p value	95% CI of intercept
Region	0.446	0.132	3.39	0.010	0.142, 0.750
Study design	0.641	0.373	1.71	0.125	-0.220, 1.503
Dietary assessment tool	0.407	0.298	1.36	0.210	-0.282, 1.096
Adjustment for physical activity	-0.981	0.2341	-0.42	0.686	-0.448, 0.441
Adjustment for energy	-0.239	0.2064	-1.16	0.280	-0.715, 0.236

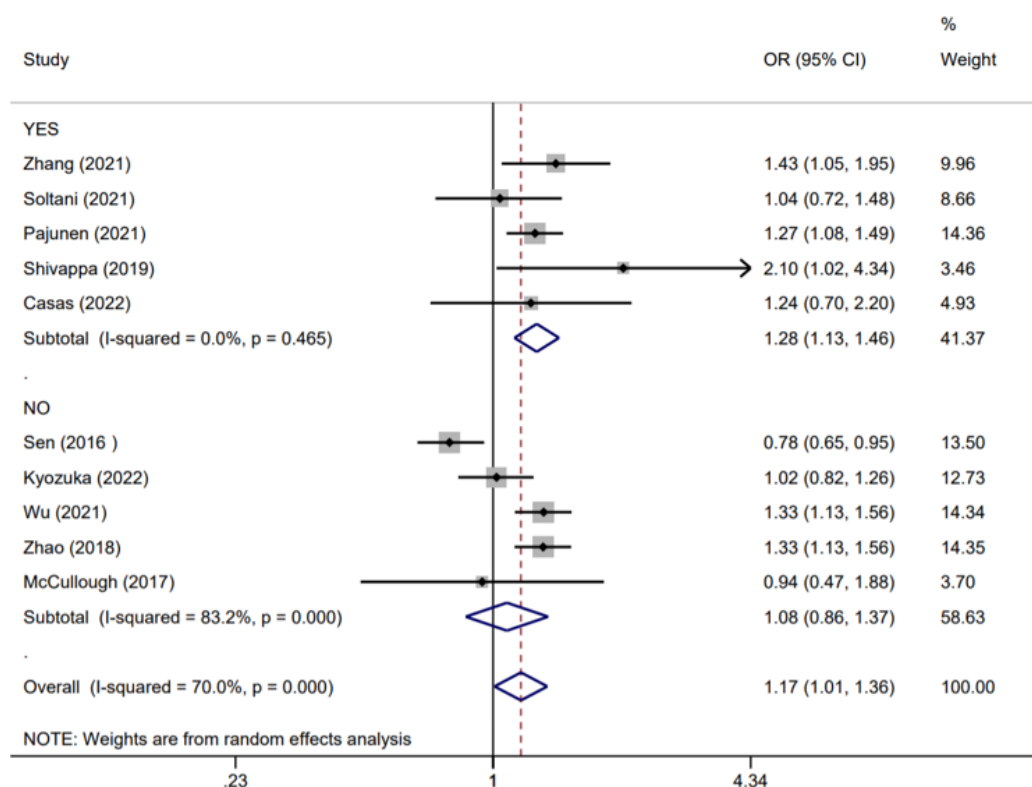
**Supplementary Figure 1.** Subgroup analyses stratified by region



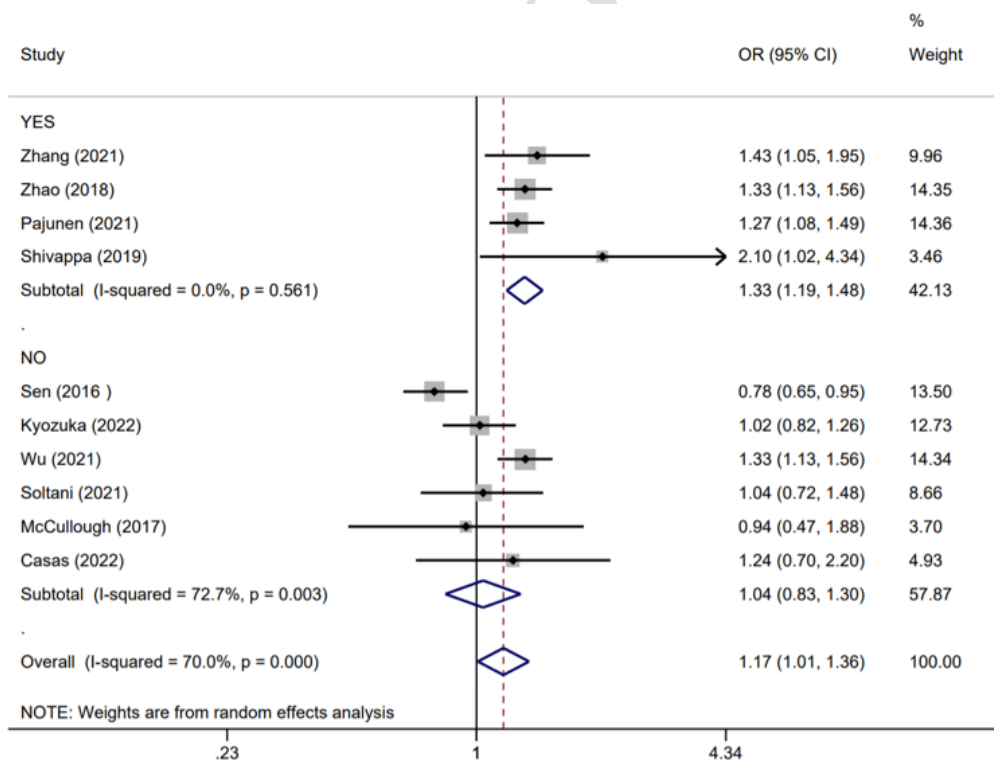
**Supplementary Figure 2.** Subgroup analyses stratified by study design



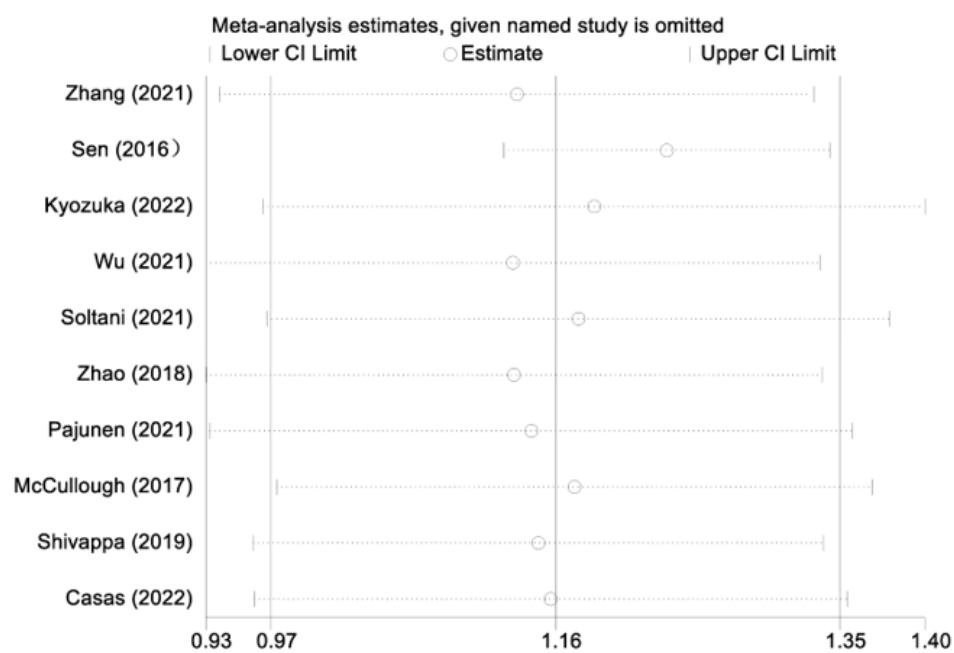
**Supplementary Figure 3.** Subgroup analyses stratified by dietary assessment tool



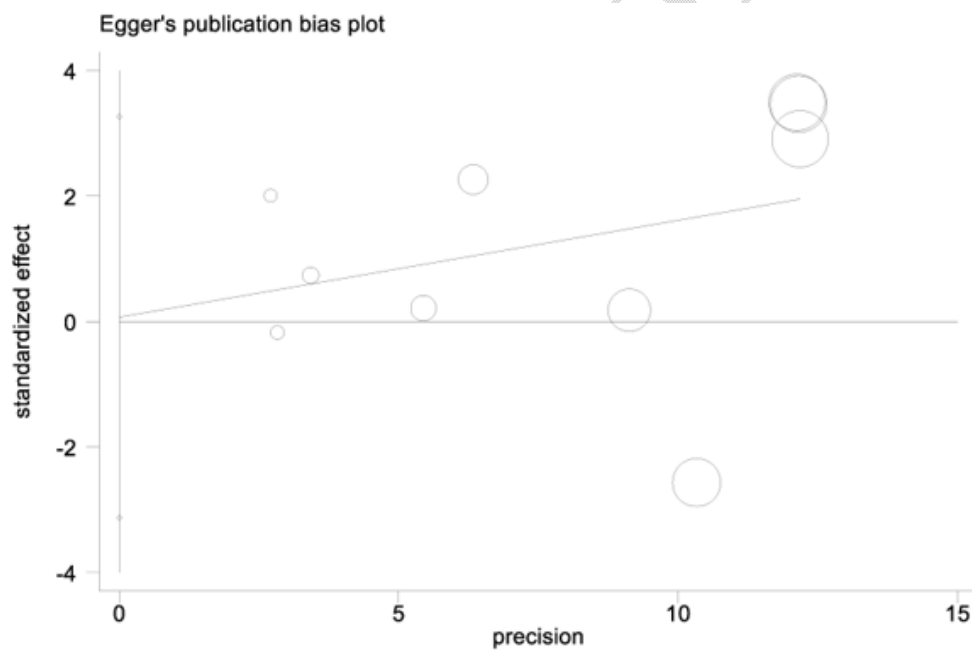
Supplementary Figure 4. Subgroup analyses stratified by adjustment for physical activity



Supplementary Figure 5. Subgroup analyses stratified by adjustment for adjustment for energy



Supplementary Figure 6. Sensitivity analysis of all included studies



Supplementary Figure 7. Egger's publication bias plot for the included study populations for the association between DII and GDM